# APPENDICES


Appendix 1 Common Fund Evaluation Working Group Roster

Appendix 2 Biosketches of Common Fund Evaluation Working Group Members

Appendix 3 List of Common Fund Evaluation Working Group Meetings

Appendix 4 List of Documents for Evaluation Questions

Appendix 5 2014 NIH Common Fund Evaluation Survey

Appendix 6 Success of Proposals from Different Strategic Planning Methods

Appendix 7 Examples of Ideas Submitted Through Various Strategic Planning Methods

Appendix 8 Summary of Common Fund Strategic Planning Activities

Appendix 9 Sample of Concepts Sent to Council of Councils

Appendix 10 Dealing with Rapidly Emerging Challenges and Opportunities

Appendix 11 Extracellular RNA Program Evolution

Appendix 12 Epigenomics Program Evolution

Appendix 13 Single Cell Analysis Program Evolution

Appendix 14 Detailed Strategic Planning Slides

Appendix 15 Intramural Research Program – Planning

Appendix 16 Funding Opportunity Announcements (FOAs) for Five Programs with Hyperlinks

Appendix 17 PROMIS Program Summary

Appendix 18 Molecular Libraries (ML) Program Summary

Appendix 19 National Centers for Biomedical Computing (NCBC) Program Summary

Appendix 20 Human Microbiome Project (HMP) Program Summary

Appendix 21 Epigenomics Program Summary

Appendix 22 Description of Common Fund Evaluative Processes

Appendix 23 Examples of Program Changes in Scientific Landscape

Appendix 24 Intramural Research Program – Management

## Appendix 1: Common Fund Evaluation Working Group Roster

**K.C. Kent Lloyd, D.V.M., Ph.D. (co-chair)**

Affiliation: University of California Davis
Professor of Surgery, School of Medicine
Director, Mouse Biology Program

**Janice Clements, Ph.D. (co-chair)**

Affiliation: Johns Hopkins University School of Medicine
Vice Dean for Faculty
Professor, Molecular and Comparative Pathobiology

**Steven DeKosky, M.D.**

Affiliation: University of Virginia School of Medicine
Vice President and Dean

**Marisa Bartolomei, Ph.D.**

Affiliation: University of Pennsylvania
Professor of Cell and Developmental Biology

**Martin Friedlander, M.D., Ph.D.**

Affiliation: The Scripps Research Institute
Professor, Department of Cell and Molecular Biology

**Sam Gerritz, Ph.D.**

Affiliation: Bristol-Myers Squibb
Senior Principal Scientist

**NIH Office of the Director Members**

**Elizabeth "Betsy" Wilder, Ph.D. (NIH Designated Federal Official)**

Affiliation: The National Institutes of Health
Director, Office of Strategic Coordination
Division of Program Coordination, Planning, and Strategic Coordination

**Scott Jackson, M.P.A**

Affiliation: The National Institutes of Health
Operations Team Leader, Office of Strategic Coordination

Division of Program Coordination, Planning, and Strategic Coordination

**James Anderson, M.D., Ph.D.**

Affiliation: The National Institutes of Health
Director, Division of Program Coordination, Planning, and Strategic Coordination

## Appendix 2: Biosketches of Common Fund Evaluation Working Group Members

**K.C. Kent Lloyd, D.V.M., Ph.D.**

Involvement in Common Fund Program: Knockout Mouse Phenotyping

University of California Davis
Professor, Department of Surgery, School of Medicine
Director, Mouse Biology Program

Biographical Summary:
Dr. Lloyd is a veterinarian and professor of surgery at the School of Medicine, UC Davis. His research emphasizes the application of mouse biology, genetics, stem cells, and reproductive physiology to resolve gene function, address biological questions, and decipher disease mechanisms. Dr. Lloyd serves as Director of the UC Davis Mouse Biology Program (MBP), in which he oversees the development, manipulation, and study of transgenic and genetically-altered (e.g., knockout) mutant mice.

Selected Affiliations:

- Director, UC Davis Mouse Biology Program
- Project Director, Knockout Mouse Project (KOMP2) DTCC Consortium
- Principle Investigator, Mutant Mouse Resource and Research Center (MMRRC)
- Director, UC Davis Mouse Metabolic Phenotyping Center
- Associate Director, Shared Resources, UC Davis Comprehensive Cancer Center
- Member, NIH Council of Councils
- Fellow, American Association for the Advancement of Science

Selected Publications:

Pettitt SJ, Liang Q, Rairdan XY, Moran JL, Prosser HM, Beier DR, Lloyd KC, Bradley A, Skarnes WC. Agouti C57BL/6N embryonic stem cells for mouse genetic resources. Nature Methods 2009;6:493-495.

Barros CS, Calabrese B, Chamero P, Roberts AJ, Korzus E, Lloyd KCK, Stowers L, Mayford M, Halpain S, Mueller U. Impaired maturation of dendritic spines without disorganization of cortical cell layers in mice lacking NRG1/ErbB signaling in the central nervous system. PNAS 2009;106(11):4507-4512.

Fazzari P, Paternain AV, Valiente M, Pla R, Luján R, Lloyd KCK, Lerma J, Marín O, Rico B. Control of cortical GABA circuitry development by Nrg1 and ErbB4 signalling. Nature 2010;464:1376-1380.

Yang R-Y, Yu L, Graham J, Hsu DK, Lloyd KCK, Havel PJ, Liu F-T. Ablation of a galectin preferentially expressed in adipocytes increases lipolysis, reduces adiposity, and improves insulin sensitivity in mice. Proc Natl Acad Sci U S A. 2011;108:18696-18701.

Lloyd KCK. A Knockout Mouse Resource for the Biomedical Research Community. Ann NY Acad Sci 2011;1245:24-26.

Mochida K, Hasegawa A, Li M-W, Fray M, Kito S, Vallelunga J, Lloyd KCK, Yoshiki A, Obata Y, Ogura A. High osmolarity vitrification: A new method for the simple and temperature-permissive cryopreservation of mouse embryos. PLoS One 2012;8:1-8 e49316.

Bradley A, Anastassiadis K, Ayadi A, Battey JF, Bell C, Birling M-C, Bottomley J, Brown SD, Bürger A, Bult CJ, Bushell W, Collins FS, Desaintes C, Doe B, Economides A, Eppig JT, Finnell RH, Fletcher C, Fray M, Frendewey D, Friedel R, Grosveld FG, Hansen J, Hérault Y, Hicks G, Hörlein A, Houghton R, Hrabé de Angelis M, Huylebroeck D, Iyer V, de Jong PJ, Kadin JA, Kaloff C, Kennedy K, Koutsourakis M, Lloyd KCK, Marschall S, Mason J, McKerlie C, McLeod MP, von Melchner H, Moore M, Mujica AO, Nagy A, Nefedov M, Nutter LM, Pavlovic G, Peterson JL, Pollock J, Ramirez-Solis R, Rancourt DE, Raspa M, Remacle JE, Ringwald M, Rosen B, Rosenthal N, Rossant J, Ruiz P, Ryder E, Schick JZ, Schnütgen F, Schofield P, Seisenberger C, Selloum M, Simpson EM, Skarnes WC, Smedley D, Stanford WL, Stewart AF, Stone K, Swan K, Tadepally H, Teboul L, Tocchini-Valentini GP, Valenzuela D, West AP, Yamamura K-I, Yoshinaga Y, Wurst W. The Mammalian Gene Function Resource - The International Knockout Mouse Consortium. Mammal Genome 2012;23:580-586.

Li M-W, Kinchen KL, Vallelunga JM, Young DL, Wright KDK, Gorano LN, Wasson K, Lloyd KCK. Safety, Efficacy and Efficiency of Laser Assisted IVF in Subfertile Mutant Mouse Strains. Reproduction 2013;145:245-254.

Heidler J, Fysikopoulos A, Wempe F, Seimetz M, Bangsow T, Tomasovic A, Veit F, Scheibe S, Pichl A, Weisel F, Lloyd KCK, Jaksch P, Klepetko W, Weissmann N, von Melchner H. Sestrin-2, a repressor of PDGFRβ signaling, promotes cigarette smoke-induced pulmonary emphysema in mice and is upregulated in patients with COPD. Dis Models Mechan 2013;6:1378-1387.

Takeo T, Fukumoto K, Kondo T, Haruguchi Y, Takeshita Y, Nakamuta Y, Tsuchiyama S, Yoshimoto H, Shimizu N, Li M-W, Kinchen K, Vallelunga J, Lloyd KCK, Nakagata N. Investigations of motility and fertilization potential in thawed cryopreserved mouse sperm from cold-stored epididymides. Cryobiology 2013;68:12-17.

Li M-W, Vallelunga JM, Kinchen KL, Rink KL, Zarrabi J, Shamamian A, Lloyd KCK. IVF Recovery of mutant mouse lines using sperm cryopreserved with MTG in cryovials. CryoLetters 2014;35:145-153.

**Janice E. Clements, Ph.D.**

Johns Hopkins University School of Medicine
Vice Dean for Faculty
Professor of Molecular and Comparative Pathobiology

Biographical Summary:
Dr. Clements has served as Vice Dean for Faculty of the Johns Hopkins University School of Medicine since 2000. She is the former Director of the Department of Molecular and Comparative Pathobiology, a department involved in animal model research, teaching medical students, graduate students, clinical and research post-doctoral fellows. Dr. Clements became the Director of the Retrovirus Laboratory in 1992, focusing on the molecular virology and pathogenesis of lentivirus infections. In particular, the simian immunodeficiency virus (SIV) is used to examine the molecular basis for the pathogenesis of HIV systemic and CNS disease. Her current studies are focused on identify and quantitating cellular reservoirs of SIV in vivo to identify therapeutic approaches to eliminating latent viral reservoirs to eradicate HIV.

Selected Affiliations:
- Johns Hopkins University Medical Scientist Training Program (MSTP) (2000- 2012)
- Johns Hopkins University Advisory Board of the Medical Faculty (1999- )
- Johns Hopkins University Women's Leadership Council (permanent member)

Selected Publications:
Witwer, K.W., et al., Relationships of PBMC microRNA expression, plasma viral load, and CD4+ T-cell count in HIV-1-infected elite suppressors and viremic patients. Retrovirology, 2012. 9: p. 5.

Zaritsky, L.A., L. Gama, and J.E. Clements, Canonical type I IFN signaling in simian immunodeficiency virus-infected macrophages is disrupted by astrocyte-secreted CCL2. J Immunol, 2012. 188(8): p. 3876-85.

Cary, D.C., J.E. Clements, and A.J. Henderson, RON Receptor Tyrosine Kinase, a Negative Regulator of Inflammation, Is Decreased during Simian Immunodeficiency Virus-Associated Central Nervous System Disease. J Immunol, 2013. 191(8): p. 4280-4287.

Sisk, J.M., et al., SIV replication is directly downregulated by four antiviral miRNAs. Retrovirology, 2013. 10(1): p. 95.

Abreu CM, Price SL, Shirk EN, Cunha RD, Pianowski LF, Clements JE, Tanuri A, Gama L. Dual Role of Novel Ingenol Derivatives from Euphorbia tirucalli in HIV Replication: Inhibition of De Novo Infection and Activation of Viral LTR. PLoS One. 2014 May 14;9(5):e97257. doi: 10.1371/journal.pone.0097257. eCollection 2014. PMID: 24827152 [PubMed - in process]

**Steven T. DeKosky, M.D.**

University of Virginia School of Medicine
Professor of Neurology and Psychiatry & Neurobehavioral Sciences

Biographical Summary:
Dr. DeKosky is a clinical and translational neurologist and immediate Past Vice President and Dean of the University of Virginia School of Medicine. His clinical and basic research have centered on understanding the genetics, neuropsychiatric symptoms and treatment and prevention of Alzheimer's disease, and he was a Principal Investigator in the clinical application of the amyloid-imaging agent Pittsburgh Compound B (PiB). He has served on and led numerous NIH review and advisory committees, and taught and mentored in clinical research training programs sponsored by the National Institute on Aging (NIA) and the National Institute of Neurological Disorders and Stroke (NINDS).

Selected Affiliations:
- American Board of Psychiatry and Neurology (Board Member 2003-2010; Vice President 2010)
- American College of Neuropsychopharmacology
- Fellow, American Academy of Neurology
- Behavioral Neurology Society
- Fellow, American Neurological Association; Member, Executive Council (2008-2011)
- New York Academy of Sciences

Selected Publication Editorial Services:
- Alzheimer Disease and Associated Disorders
- Annals of Neurology
- Archives of Neurology
- Neurodegenerative Diseases

Selected Publications:
DeKosky, S.T. and Scheff, S.W. Synapse loss in frontal cortex biopsies in Alzheimer's disease: Correlation with cognitive severity. Annals of Neurology 27:457-464, 1990.

Petersen, R.C., Stevens, J.C., Ganguli, M., Tangalos, E.G., Cummings, J.L., and DeKosky, S.T. Practice parameter: Early detection of dementia: Mild cognitive impairment (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 56:1133-1142,2001.

Lyketsos, C.G., Lopez, 0., Jones, B., Fitzpatrick, A.L., Breitner, J., and DeKosky, S. Prevalence of neuropsychiatric symptoms in dementia and mild cognitive impairment. JAMA 288:1475-1483, 2002.

Fagan, A.M., Mintun, M.A., Mach, R.H., Lee, S.-Y., Dence, C.S., Shah, A.R., LaRossa, G.N., Spinner, M.L., Klunk, W.E., Mathis, C.A., DeKosky, S.T., Morris, J.C., and Holtzman, D.M. Inverse relation between in vivo amyloid imaging load and cerebrospinal fluid A 42 in humans. Annals of Neurology 59:512-519, 2006.

Klunk, W.E., Price, J.C., Mathis, C.A., Tsopelas, N.D., Lopresti, B.J., Ziolko, S.K., Bi, W., Hoge, J.A., Ikonomovic, M.D., Saxton, J., Snitz, B., Pollen, D.A., Moonis, M., Lippa, C.F., Swearer, J., Johnson, K.A., Rentz, D.M., Fischman, A.J., Aizenstein, H., and DeKosky, S.T. Amyloid deposition begins in the striatum of presenilin-1 mutation carriers from two unrelated pedigrees. Journal of Neuroscience 27:6174-6184, 2007.

Ikonomovic, M.D., Klunk, W.E., Abrahamson, E.E., Mathis, C.A., Price, J.C., Tsopelas, N.D., Lopresti, B.J., Ziolko, S., Bi, W., Paljug, W.R., Debnath, M.L., Hope, C.E., Isanski, B.A., Hamilton, R.L. and DeKosky, S.T. Post-mortem correlates of in vivo PiB-PET amyloid imaging in a typical case of Alzheimer's disease. Brain 131:1630-1645, 2008. PMCID: 2408940

DeKosky, S.T., Williamson, J.D., Fitzpatrick, A., Kronrnal, R.A., Ives, D.G., Saxton, J.A., Lopez, O.L., Burke, G., Carlson, M.C., Fried, L.P., Kuller, L.H., Robbins, J., Tracy, R.P., Woolard, N.F., Dunn, L., Snitz, B.E., Nahin, R.L., Furberg, C.D. for the GEM Study Investigators. Ginkgo biloba for prevention of dementia: Results of the Ginkgo Evaluation of Memory (GEM) Study. JAMA 300(19):2253-2262, 2008. PMCID: 2823569

DeKosky, S.T., Ikonomovic, M.D. and Gandy, S. Traumatic brain injury: Football, warfare, and long-term effects. New England Journal of Medicine 363:1293-1296,2010. PMID: 21265421

Albert, M.S., DeKosky, S.T., Dickson, D., Dubois, B., Feldman, H.H., Fox, N.C., Gamst, A., Holtzman, D.M., Jagust, W.J., Petersen, R.C., Synder, P.J., Carrillo, M.C., Thies, B. and Phelps, C.H. The diagnosis of mild cognitive impairment due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers Dement 7:270-279, 2011. PMCID: 3312027

Gandy, S. and DeKosky, S.T. APOE E4 status and traumatic brain injury on the gridiron or the battlefield. Science Translational Medicine 4:134ed4, 2012. PMID: 22593171

Snitz, B.E., Weissfeld, L.A., Lopez, O.L., Kuller, L.H., Saxton, J., Singhabu, D.M., Klunk, W.E., Mathis, C.A., Price, J.C., Ives, D.G., Cohen, A.D., McDade, E. and DeKosky, S.T.
Cognitive trajectories associated with beta-amyloid deposition in the oldest old without dementia. Neurology, 80:1378-1384,2013. PMCID: 3662268

Mathis, C.A., Kuller, L.H., Klunk, W.E., Snitz, B.E., Price, J.C., Weissfeld, L.A., Rosario, B.L., Lopresti, B.J., Saxton, J.A., Aizenstein, H.J., McDade, E.M., Kamboh, M.I., DeKosky, S.T. and Lopez, O.L. In vivo assessment of amyloid-deposition in nondemented very elderly subjects. Annals of Neurology 73:751-761,2013.

Gandy, S. and DeKosky, S.T. Toward the treatment and prevention of Alzheimer's disease: Rational strategies and recent progress. Annual Review of Medicine 64:367-383, 2013. PMCID: 3625402

**Marisa Bartolomei, Ph.D.**

Involvement in Common Fund Program: Epigenomics

University of Pennsylvania
Professor of Cell and Developmental Biology

Biographical Summary:
Dr. Bartolomei participates extensively in graduate and medical education. Aside from her teaching activities, she is the Associate Director of an NIH-funded training grant program. She has served on numerous NIH-sponsored grant review panels and is a member the *Human Molecular Genetics* and *Molecular and Cellular Biology* editorial boards and is an Associate Editor at *PLOS Genetics*. In 2006, Dr. Bartolomei organized Gordon Research Conference on Mammalian Gametogenesis and Embryogenesis, and she was co-chair of the 2011 Gordon Research Conference on Epigenetics. Dr. Bartolomei's research addresses the epigenetic mechanisms of genomic imprinting and X inactivation, as well as the impact of adverse environmental insults on epigenetic gene regulation using the mouse as a model.

Selected Publications:
Susiarjo Martha, Sasson Isaac, Mesaros Clementina, Bartolomei Marisa S: *Bisphenol a exposure disrupts genomic imprinting in the mouse.* PLoS genetics 9(4): e1003401, Apr 2013.

Lee Jeannie T, Bartolomei Marisa S: *X-inactivation, imprinting, and long noncoding RNAs in health and disease.* Cell 152(6): 1308-23, Mar 2013.

Venkatraman, A., He, X.C., Thorvaldsen, J.L., Sugimura, R., Perry, J.M., Tao, F., Zhao, M., Christenson, M.K., Sanchez, R., Yu, J.Y., Peng, L., Haug, J.S., Paulson, A., Li, H., Zhong, X., Clemens, T.L. Bartolomei, M.S**.** and L. Li. (2013). Maternal-imprinting at H19-Igf2 locus maintains adults hematopoietic stem cell quiescence. Nature, 500:345-349.

Plasschaert, R.N., Vigneau, S., Tempera, I., Gupta, R., Maksimoska, J., Everett, L., Davuluri, R., Mamorstein, R., Lieberman, P.M., Schultz, D., Hannenhalli, S. and M.S. Bartolomei. (2013). CTCF binding site sequences differences are associated with unique regulatory and functional trends during embryonic stem cell differentiation, Nucleic Acids Research, In press.

**Martin Friedlander, M.D., Ph.D.**

Involvement in Common Fund Program: Nanomedicine

The Scripps Research Institute
Professor, Department of Cell and Molecular Biology
Scripps Clinic
Chief, Retina Service, Division of Ophthalmology, Department of Surgery

Biographical Summary:
Dr. Friedlander is an ophthalmologist specializing in retinal diseases and a research cell/developmental biologist who's laboratory is studying: (1) basic mechanisms of normal and pathological angiogenesis using models of ocular and tumor neovascularization; (2) the role of cytokines, adhesion receptors, microRNAs and stem cells in these processes; (3) trophic interactions between vascular endothelial, glial and neuronal cell types in the retina during normal and abnormal angiogenesis and (4) various anti-angiogenic and stem cell approaches to treating vasculo- and neurodegenerative diseases of the eye. In addition to his clinical and laboratory responsibilities, he is also the President of the Lowy Medical Research Institute, a biomedical research institute studying underlying pathophysiological mechanisms of, and developing treatments for, retinal neuro/vasculo diseases such as Macular Telangiectasia.

Selected Affiliations:

- Member, Visual Sciences C Study Section, National Eye Institute, 1999-2005
- Advisor, Diabetes Research Working Group Update, NIDDK, NIH, Bethesda, MD, 2002
- Member, National Eye Institute Retinal Diseases Program Planning Panel, 2003-2008
- Research Project Reviewer, Trans-NIH Angiogenesis Research Program, 2005
- Member, Nanomedicine Initiative Advisory and Review Panel, National Institutes of Health Roadmaps Program. 2004-present
- Advisory Board Member, Ohio Biomedical Research Technology Transfer/Wright Center Initiative (BRTT/WCI), Cleveland Clinic Cole Eye Institute. 2004-2009
- Faculty Liaison to the San Diego Consortium for Regenerative Medicine (SCRM), 2006-11
- Member, Scientific Steering Committee, SCRM, 2011-present
- Member, Clinical Safety and Data Monitoring Committee, CATT Trial, NEI, NIH, 2007-2012
- External Reviewer, Intramural Program, Surgery Branch, NCI, NIH, 2007, 2014
- Consultant, Cellular, Tissue and Gene Therapies Advisory Committee, Center for Biologics Evaluation and Research, Food and Drug Administration, Rockville, MD, April, 2008
- National Eye Institute Board of Scientific Advisors, Ad hoc member, 2008
- National Advisory Eye Council Planning Oversight Subcommittee Member, 2009
- Chairman, Special Emphasis Panel for R24 Reviews, NEI, NIH, 2009, 2010, 2011
- Member, Distinguished Editors Stem Cell Challenge Panel, CSR, NIH, 2009
- Editor, NIH Transformative R01 Review, 2012, 2014
- Participant, Beckman Institute/NIM Initiative on Macular Degeneration, Irvine, CA, 2009-13
- Participant, CIRM Alpha Clinics Workshop Planning, 2012
- Reviewer and Session Chair, NEI/NIH Audacious Goals Review and Meeting, 2013

Selected Publications:

Friedlander, M., Brooks, P., Shaffer, R., Kincaid, C., Varner, J., Cheresh, D. (1995). Two pathways of angiogenesis defined by homologous $\alpha_v$ integrins. Science, **270**:1500-1502.

Otani, A., Kinder, K., Schimmel, P. and Friedlander, M. (2002). Bone marrow derived stem cells target retinal astrocytes and have pro- or anti-angiogenic activity. Nat. Med. **8:** 1004-10.

Belting, M., Dorrell, M., Dorfleutner, D., Carmeliet, P., Mueller, B., Friedlander, M. and Ruf, W. (2004). Tissue factor signaling in angiogenesis. Nat. Med. 10:502-509.

Dorrell, M., Scheppke, L., Barnett, F., and Friedlander, M**.** (2007). Combination angiostatic therapy completely inhibits ocular and tumor angiogenesis. Proc. Natl. Acad. Sci. **104**:967-972.

Dorrell, M.I., Aguilar, E.A., Yanes, O., Gariano, R., Heckenlively, J., Eyal Banin, E., Ramirez, E.G., Gasmi, M., Bird, A., Suizdak, G., and Friedlander, M. (2009). Treatment with antioxidants or neurotrophic factors preserves function in neurons damaged by neovascularization-associated oxidative stress. J. Clin. Invest. 119(3):611-623. PMCID: PMC2648679

Marchetti, V., Krohne, T.U., Friedlander, D.F., and Friedlander, M. (2010). Stemming vision loss with stem cells. J Clin Invest. Sep 1;120(9):3012-21. PMCID: PMC2929728.

Marchetti, V., Aguilar, E., Friedlander, D.F., Moreno, S., Nemerow, G., Siuzdak, G., and M. Friedlander, (2011). Differential Macrophage Polarization is Required for Tissue Remodeling and Repair in a Model of Ischemic Retinopathy. Sci Rep. 2011;1:1-12. PMCID: PMC3216563.

Kurihara, T., Westenskow, P.D., Krohne,T.U., Aguilar, E., S. Johnson, R.S., and Martin Friedlander. (2011). Astrocyte pVHL and HIF-α isoforms are required for embryonic-to-adult vascular transition in the eye. J. Cell Biology, 195:689-701. PMCID: PMC3257537.

Kurihara, T., Westenskow, P.D., Aguilar, E., Friedlander, M. (2012). Targeted deletion of Vegfa in adult mice induces vision loss. J Clin Invest. 1;122(11):4213-7. PMCID: PMC3484459.

Krohne, T.U., Westenskow, P.D., Friedlander, D.F., S., Ding, S., and Friedlander, M. (2012). Generating functional RPE cells from human iPSC reprogrammed using exogenous transcription factors and small molecules. Stem Cells Transl. Med. 2012(1):96-109. PMCID: PMC3328503.

Westenskow, P.D., Kurihara, T., Aguilar, E.,. Scheppke, E.L., Marchetti, V., Michael, I.P., Anand, S., Nagy, A., Cheresh, D.A. and Friedlander, M**.** (2013). Ras pathway inhibition prevents neovascularization by repressing endothelial cell sprouting. J. Clin. Invest., 123:4900-4908.

Michael, I.P., Westenskow, P.D., Kurihara, T., Aguilar, E., Marchetti, V., Iruela-Arispe, M.L., van der Kooy, D., Friedlander, M. & Andras Nagy (2014). Local acting Sticky-trap inhibits vascular endothelial growth factor dependent pathological angiogenesis in the eye. EMBO Mol Med. 2014 May 1;6(5):604-23.

**Sam Gerritz, Ph.D.**

Involvement in Common Fund Program: Molecular Libraries

Bristol-Myers Squibb
Senior Principal Scientist

Biographical Summary:
Sam Gerritz received his bachelor's degree in chemistry in 1988 from the College of Wooster (OH) where he conducted senior research with Professor Paul Gaus. He then proceeded to the Massachusetts Institute of Technology as an NSF Predoctoral Fellow in the group of Professor Satoru Masamune, where he made significant contributions to the successful total synthesis of Calyculin A. In 1993, Sam received his Ph.D. from M.I.T. and joined Glaxo in Research Triangle Park, North Carolina. During his 8 years at Glaxo-GlaxoWellcome-GlaxoSmithKline, Sam's research focused on the application of combinatorial chemistry/parallel synthesis techniques to ongoing drug discovery projects. In 2001, Sam joined Bristol-Myers Squibb in Wallingford, Connecticut, as a Group Leader in Early Discovery Chemistry, and his research has focused on the identification and optimization of promising hits for nascent drug discovery targets. Most recently, Sam led the chemistry effort in the discovery of molecules that inhibit influenza virus replication via oligomerization of an essential flu protein. This work recently appeared in the *Proceedings of the National Academy of Sciences*. Sam's research has been published in over 30 journal articles and 22 patent applications. He is currently a Senior Principal Scientist in the Discovery Chemistry Platforms department, where he leads a fragment-based drug discovery team.

In 2005, Sam chaired the Gordon Research Conference on Combinatorial Chemistry, and has served on External Scientific Panels for the NIH Molecular Libraries Probe Production Centers Network (MLPCN) and BioAssay Research Database (BARD), the Scientific Advisory Board for the Boston University Center for Chemical Methodology and Library Development (BU-CMLD), and as a consultant for the University of Kansas Specialized Chemistry Center (KU-SCC). He has been a member of the editorial advisory board for *ACS Combinatorial Sciences* since 2010.

## Appendix 3: List of Common Fund Evaluation Working Group Meetings

| Meeting Dates | Documents Reviewed and Discussed in Meetings |
|---|---|
| November 19th, 2013 | - Charter for CF Evaluation Working Group<br>- CF Evaluation Work plan and Timeline<br>- List of Questions for CF Evaluation |
| December 3rd, 2013 | - Meeting Minutes from Nov.19th, 2013 conference call<br>- Phase I Planning Questions excerpt<br>- Common Fund Strategic Planning Report, 2013<br>- Examples of Ideas Submitted Through Various Strategic Planning Methods<br>- Summary of Common Fund Strategic Planning Activities<br>- Common Fund Strategic Planning Report, 2011<br>- Success of Proposals from Different Strategic Planning Methods<br>- Sample of Concepts Sent to Council of Councils<br>- Detailed Strategic Planning Slides<br>- Report – Design and Implementation of a Process Survey of the NIH Roadmap for Medical Research<br>- Dealing with Rapidly Emerging Challenges and Opportunities |
| December 17th, 2013 | - Meeting Minutes from Dec. 3rd, 2013 conference call<br>- Phase II Planning Questions excerpt<br>- Extracellular RNA Program Evolution<br>- Epigenomics Program Evolution<br>- Single Cell Analysis Program Evolution<br>- Detailed Strategic Planning Slides |
| January 7th, 2014 | - Meeting Minutes from Dec. 17th, 2013 conference call<br>- Intramural Research Program – Planning |
| January 21st, 2014 | - Meeting Minutes from Jan.7th, 2014 conference call<br>- Funding Opportunity Announcements (FOAs) for Five Programs with Hyperlinks<br>- Kick-off Program Materials for Selected Programs<br>- PROMIS Program Summary<br>- Molecular Libraries (ML) Program Summary<br>- National Centers for Biomedical Computing (NCBC) Program Summary |

| | |
|---|---|
| | - Human Microbiome Project (HMP) Program Summary<br>- Epigenomics Program Summary<br>- Description of Common Fund Evaluative Processes |
| January 30th, 2014 (Face-to-face meeting) | - Meeting Minutes from Jan.21st, 2014 conference call<br>- Examples of Program Changes in Scientific Landscape<br>- Intramural Research Program – Management |
| February 11th, 2014 | - Meeting Minutes from Jan.30th, 2014 face-to-face meeting<br>- Sample Outline of for Final Report<br>- Recommendations and Questions from Meeting Minutes |
| February 25th, 2014 (Only CFEWG members) | - Discuss results of the interviews |
| March 11th, 2014 | - Meeting Minutes from Feb. 11th, 2014 conference call<br>- Update on the 2014 NIH Common Fund Evaluation Survey<br>- Update on CFEWG Subcommittees |
| March 25th, 2014 | - Meeting Minutes from Mar. 11th, 2014 conference call<br>- Update on CFEWG Subcommittees |
| April 8th, 2014 | - Meeting Minutes from Mar. 25th, 2014 conference call<br>- Update on CFEWG Subcommittees<br>- Discuss results of the survey |
| May 15th, 2014 (Face-to-face meeting) | - Meeting Minutes from Apr. 8th, 2014 conference call<br>- Update on CFEWG Subcommittees |
| May 20th, 2014 (Only CFEWG members) | - Discuss the report |
| June 3rd , 2014 (Only CFEWG members) | - Discuss the report |

## Appendix 4: List of Documents for Evaluation Questions

**Part 1: Document List to Assist with Addressing Questions**

| Document Number | Document Title |
|---|---|
| #1 | Dr. Wilder's Presentation to the Council of Councils September 24th, 2013 – Provides background and overview of the NIH Common Fund. |
| #2 | Common Fund Strategic Planning Report, 2011 (Lessons Learned, pg. 10) – Describes the lessons learned from the various strategic planning methods used prior to 2011. |
| #3 | Common Fund Strategic Planning Report, 2013 (Strategic Planning Description, pg. 4-9) – Provides the goals of strategic planning and a description of the strategic planning process used in 2011 and 2012. |
| #4 | Congressional Justification FY14 – brief summary of Common Fund programs and budget information – Provides a brief summary of Common Fund programs and budget information. |
| #5 | Report – Design and Implementation of a Process Survey of the NIH Roadmap for Medical Research, May 2005 (Appendix A, Survey Instrument, pg. 1-12; Appendix C, Frequencies of Survey Responses, pg. 1-9 ) – This survey was conducted in 2005 to gather input from those involved in the planning and implementation phases of the NIH Roadmap initiative. |
| #6 | Examples of Ideas Submitted Through Various Strategic Planning Methods with Attachments – Provides examples of ideas generated through the various strategic planning methods. |
| #7 | Success of Proposals from Different Strategic Planning Methods – Lists the strategic planning method(s) that generated the ideas for each of the Common Fund programs. |
| #8 | Questions (OSC Staff, IC Staff, IC Directors, GuLF Leaders, and IC Staff NOT Involved in CF Programs) |
| #9 | Sample of Concepts Sent to Council of Councils – Provides samples of concepts sent to the Council of Councils for clearance. |
| #10 | Detailed Strategic Planning Slides – Provides detailed information about the Common Fund strategic planning process. |
| #11 | Dealing with Rapidly Emerging Challenges and Opportunities – Describes how the NIH addresses rapidly emerging challenges through the example of the intramural GuLF program. |
| #12 | ExRNA Program Evolution and Attachments – Describes the evolution of the ExRNA Program from initial idea to the final decision to create the program. |
| #13 | Epigenomics Program Evolution and Attachments – Describes the evolution of the Epigenomics Program from initial idea to the final decision to create the program. |
| #14 | Single Cell Analysis Program Evolution and Attachments – Describes the evolution of the Single Cell Analysis Program from initial idea to the final decision to create the program. |
| #15 | Intramural Research Program – Planning – This document provides an examination of occasions when the IRP has been determined to be uniquely positioned to address key roadblocks in biomedical research as part of the CF. |
| #16 | Patient Reported Outcomes Information Measurement System (PROMIS) Program Summary – Provides an overview of the program and contains the following sections: |

| | |
|---|---|
| | allocation of funds per year, CF criteria, program description, goals, management process, challenges, selected outputs, and plans for transitioning out of the Common Fund. |
| #17 | Molecular Libraries (ML) Program Summary – Provides an overview of the program and contains the following sections: allocation of funds per year, CF criteria, program description, goals, management process, challenges, selected outputs, and plans for transitioning out of the Common Fund. |
| #18 | National Centers for Biomedical Computing (NCBC) Program Summary – Provides an overview of the program and contains the following sections: allocation of funds per year, CF criteria, program description, goals, management process, challenges, selected outputs, and plans for transitioning out of the Common Fund. |
| #19 | Human Microbiome Project (HMP) Program Summary – Provides an overview of the program and contains the following sections: allocation of funds per year, CF criteria, program description, goals, management process, challenges, selected outputs, and plans for transitioning out of the Common Fund. |
| #20 | Epigenomics Program Summary – Provides an overview of the program and contains the following sections: allocation of funds per year, CF criteria, program description, goals, management process, challenges, selected outputs, and plans for transitioning out of the Common Fund. |
| #21 | Funding Opportunity Announcements (FOAs) for Five Programs with Hyperlinks – Provides the links of the FOAs for the five programs: Epigenomics, HMP, ML, NCBC, and PROMIS |
| #22 | Description of Common Fund Evaluative Processes – Provides an overview of the processes to monitor and evaluate CF programs. |
| #23 | Common Fund Standard Operating Procedures – Budget |
| #24 | Examples of Program Changes in Scientific Landscape – This document will provide examples of the changes in Scientific Landscape. |
| #25 | Intramural Research Program – Management – This document provides description about the Management & Oversight phase of the Intramural Common Fund Program. |
| #26 | Kick-off Program Materials for Selected Programs |
| #27 | Summary of Common Fund Strategic Planning Activities By Year – Provides strategic planning methods used by year and phase. |

## Part 2: Questions for evaluation, data collection methods, and supporting reference documents

**STRATEGIC PLANNING: Are planning processes optimal for identifying program areas that meet the Common Fund (CF) criteria?**

- **For Phase 1 Planning:**

I. <u>What are the best methods to engage the broader scientific community?</u>

A. Comparison of various methods tried (Documents: #6, #1, #2 (Lessons Learned, pg. 10), #3 (Strategic Planning Description, pg. 4-9), #27)

- Meetings with invited thought leaders
  - Ideas articulated by individual participants
  - Ideas articulated after "group think"
- Meetings that are open to anyone interested

- Ideas articulated after "group think"
- Input via Request For Information (RFI)
- Input from Institutes and Centers (ICs)

B. Analysis of success of proposals from different methods: Do more CF programs originate from the ideas of ICs than from outside experts? (Document: #7)

C. Interview/survey Office of Strategic Coordination (OSC) staff (Documents: #8, #5)

D. Interview/survey IC staff involved with CF programs (Documents: #8, #5)

II. Do the concepts, as currently written at the end of Phase 1, allow effective review by the Council of Councils (CoC)? Should the format and content of the concepts be adjusted? Should DPCPSI more stringently filter concepts that are not clearly articulated and ask the CoC to review only those concepts for which there is enthusiasm?

E. Review of example concepts that were submitted for Concept Clearance (Document: #9)

F. Interview of OSC staff (Documents: #8, #5)

III. Is 6 months for Phase 1 planning an appropriate time frame?

G. Analysis of the typical Phase 1 process (Documents: #10, #5, #3)

H. Interview/survey OSC staff (Documents: #8, #5)

IV. Should an alternate process be developed for rapid planning for "emergency concepts"?

I. Analysis of the process that led to GuLF (Document: #11)

J. Interview/survey GuLF leaders (Documents: #8, #5)

K. Interview/survey OSC staff (Documents: #8, #5)

- **For Phase 2 Planning:**

V. Do Phase 2 processes result in clearly articulated goals and expected milestones?

L. Review of the evolution of concepts: Phase 1 Concepts, Phase 2 Proposals (including portfolio analyses), and Detailed Plans

- ExRNA Program (Document: #12)
- Epigenomics Program (Document: #13)
- Single Cell Analysis (Document: #14)

M. Interview/survey OSC staff (Documents: #8, #5)

N. Interview/survey IC staff involved in CF programs (Documents: #8, #5)

VI. Is 12 months an appropriate timeframe for Phase 2 planning?

O. Analysis of a typical timeline (Document: #10)

P. Interview/survey OSC staff (Documents: #8, #5)

Q. Interview/survey IC staff involved in CF programs (Documents: #8, #5)

VII. Do IC Directors and the Council of Councils have appropriate levels of input to guide the development of Phase 2 proposals?

R. Review of process (Document: #10)

S. Interview/survey IC Directors (Documents: #8, #5)

- **For both Phase 1 and Phase 2:**

VIII. What should the process be for planning intramural-only programs?

T. Review document describing intramural CF programs (Document: #15)

U. Interview/survey OSC staff (Documents: #8, #5)

V. Interview/survey IC staff involved in CF programs (Documents: #8, #5)

IX. What are the attitudes and level of understanding of NIH staff toward the current planning processes, including how decisions are made? What difficulties in the process can staff identify in order to facilitate greater satisfaction and engagement?

W. Survey OSC staff (Documents: #8, #5)

X. Interview/survey IC staff involved in CF programs (Documents: #8, #5)

Y. Interview/survey IC staff NOT involved in CF programs (Documents: #8, #5)

**MANAGEMENT/OVERSIGHT: Are management/oversight processes optimal for achieving program goals?**

- **Questions pertaining to interactions with awardees:**

I. Are expectations for programs clearly articulated in funding announcements, program kick-off documents, websites, program materials? Are the goals and responsibilities clear?

A. Review FOAs and Kick-off materials for five programs (Documents: #21, #26)

B. Review program summaries: Patient Reported Outcomes Information Measurement System [PROMIS], Molecular Libraries [ML], National Centers for Biomedical Computing [NCBC], Human Microbiome Project [HMP], Epigenomics) (Selected pages in documents: #16, #17, #18, #19, #20, #21)

C. Interview/survey OSC staff (Documents: #8, #5)

D. Interview/survey IC staff involved in CF programs (Documents: #8, #5)

II. Are evaluative processes sufficient to provide critical assessment throughout the program's lifespan?

E. Review description of evaluative processes (Document: #22)

F. Review program summaries (Documents: #16, #17, #18, #19, #20)

III. Are goals and milestones met?

G. Review program summaries (Documents: #16, #17, #18, #19, #20)

IV. Are management processes flexible and adaptive to changing scientific landscapes?

H. Analysis of annual operating budget request process and end of year budget request processes; compare with goals for prior years (Documents: #23, #24)

I. Interview/survey OSC staff (Documents: #8, #5)

J. Interview/survey IC staff involved in CF programs (Documents: #8, #5)

V. What should the process be for management of intramural-only programs?

K. Review summary of intramural programs (Document: #25)

L. Interview/survey OSC staff (Documents: #8, #5)

M. Interview/survey IC staff involved in CF programs (Documents: #8, #5)

- **Questions pertaining to intra-NIH interactions**: [NOTE: Survey extended list of IC staff who are involved in CF programs, including Grants Management, Budget, Executive Officers]

VI. Are OSC/IC interactions working well?

N. Interview/survey OSC staff (Documents: #8, #5)

O. Interview/survey IC staff involved in CF programs (Documents: #8, #5)

VII. Is the Working Group structure meeting the management and oversight needs of the programs?

P. Review of survey of the NIH Roadmap, May 2005 (Document: #5)

Q. Interview/survey OSC staff (Documents: #8, #5)

R. Interview/survey IC staff involved in CF programs (Documents: #8, #5)

VIII. Are the roles and responsibilities of Working Group members clear?

S. Interview/survey IC staff involved in CF programs (Documents: #8, #5)

IX. Is the value of the program worth the effort?

T. Interview/survey IC Directors and senior staff (Documents: #8, #5)

U. Interview/survey IC staff involved in CF programs (Documents: #8, #5)

X. Do IC Directors get appropriate amounts of information about CF programs and at an appropriate frequency?

V. Interview/survey IC Directors (Documents: #8, #5)

XI. Does participation by IC staff on CF Working Groups enable efficient information exchange with IC Directors, IC Councils, other IC staff, and IC research communities?

W. Interview/survey OSC staff (Documents: #8, #5)

X. Interview/survey IC Directors (Documents: #8, #5)

Y. Interview/survey IC staff involved in CF programs (Documents: #8, #5)

**Appendix 5: 2014 NIH Common Fund Evaluation Survey**

# 2014 NIH Common Fund Evaluation Survey

---

Prepared by:


windrose@windrosevision.com

## Acronyms, alphabetized

| | |
|---|---|
| BO | Budget Officer |
| BPOCs | Budget Points of Contact |
| CF | Common Fund |
| CFEWG | Common Fund Evaluation Working Group |
| CGMO | Chief Grants Management Officer |
| CoC | Council of Councils |
| DPCPSI | Division of Program Coordination, Planning, and Strategic Initiatives |
| EMPC | Extramural Program Management Committee |
| EOs | Executive Officer |
| FOA | Funding Opportunity Announcement |
| FTE(s) | Full-time employee(s) |
| GMO | Grants Management Officer |
| FY | Fiscal Year |
| ICs | Institutes and Centers |
| NIH | National Institutes of Health |
| NEDS | NIH Enterprise Directory System |
| OD | Office of the Director |
| OSC | Office of Strategic Coordination |
| P&E | Planning and Evaluation |
| WG | Working Group |

# 2014 NIH COMMON FUND EVALUATION SURVEY

## PURPOSE OF THE SURVEY

On September 24, 2013, the Director of the Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI) established the Common Fund Evaluation Working Group (CFEWG) to evaluate the strategic planning and management processes of the National Institutes of Health (NIH) Common Fund (CF). The NIH asked the CFEWG to provide recommendations for consideration by the NIH Council of Councils (CoC) meeting on June 20th, 2014.

As part of this effort, an online survey was develop to assess the strategic planning and management processes of the NIH CF. The results of the online survey assisted the CFEWG in developing recommendations for improving the processes.

## SURVEY POPULATION

The survey targeted NIH staff involved in CF programs. The survey was developed to gather input from the following groups: Institute and Center (IC) Directors, members of the Extramural Program Management Committee (EPMC) of lead ICs for CF programs, Planning and Evaluation (P&E) Officers, Working Group (WG) Members of CF programs, Executive Officers (EOs), Budget Points of Contact (BPOCs), and Grants Management Officers (GMOs). Names were retrieved from the CF website and NIH lists. The email addresses were obtained from the NIH Enterprise Directory System (NEDS). There were duplicate names due to individuals listed in multiple programs and/or having multiple roles in programs. Duplicate names were removed from the list, as well as staff with no NIH email address or who were no longer at NIH. Windrose Vision worked with NIH to develop the final survey population of 743 individuals.

## SURVEY DESCRIPTION

The survey consisted of different branching patterns based on the role and level of involvement of respondents. Respondents were directed to different sections, therefore not all questions were answered by everyone. The survey responses have been summarized and are presented in the aggregate in this report so that opinions cannot be traced to specific respondents.

The survey encompassed several sections, and is attached in Appendix 1.

- Strategic Planning Process: This section focused on the overall and specific aspects of the CF strategic planning process and the scientific initiatives that resulted from the process. It included questions about the process that ICs use to submit ideas for CF programs, referred to as Phase I. It also focused on the process of refining concepts that are cleared by the Council into program proposals, conducting portfolio analyses, and making the decision to implement new CF programs, referred to as Phase 2.

- Collaboration: This section focused on work experiences or personal opinions about collaboration within NIH and the effect the CF has on the changing culture.
- External Community: This section focused on perceptions of the external community about the CF.
- Office of Strategic Coordination (OSC) Organizational Structure and Staff Roles: This section focused on the understanding among respondents of the structure and functions of the OSC.
- Working Group Structure: This section focused on respondents' role in WGs, and their overall experience as a member of one or more WGs. This section also had questions focusing on communications between OSC and the WGs.
- Satisfaction: This section focused on respondents' satisfaction with the information they receive and the time spent on CF program activities.
- Grants Management Processes: This section focused on processes for developing and approving FOAs, administrative supplements, and paylists.
- Budget Management Processes: This section focused on operating budgets, FTE loans, Inter-Agency Agreements, and the Strategic Initiative Database.
- Common Fund Resource Use: This section focused on the use of CF Resources - such as SharePoint, Handbook, website, and the Common Fund portion of QVR.
- IC Staff Working on Common Fund Programs: This section, for Executive Officers, focused on experiences when staff are approached to work on CF programs.
- Closing Questions: This section had questions related to length of time respondents worked at NIH, CF Programs they were involved with, and information about the home ICs of the respondents.

## DATA COLLECTION

The survey was open from February 27th to March 18th, 2014. Participants were sent an email including a unique web link to access the survey. The survey schedule is summarized below.

- November 2013: The Director of DPCPSI sent an email to IC Directors and WG members informing them of the CF evaluation and telling them to expect a survey within a few months.
- February 27th, 2014: The NIH Director sent an email encouraging participants to complete the survey. Shortly thereafter, the initial email invitations were sent to participants. Email addresses with errors were reconciled where possible.
- March 5, 10, 13, and 18th, 2014: Participants who had not completed the survey on that date received a reminder email.
- March 11th, 2014: The Director of OSC sent reminder emails to EPMC and P&E Officers.
- March 18th, 2014: The survey website was closed at midnight.

## RESPONSE TO THE SURVEY

Of the 743 NIH staff that were contacted, 348 participated in the survey. Of the 348, twenty-two individuals did not provide an answer to any of the questions in the survey and were treated as non-respondents. The 326 respondents represent 44% of the total target population.

Response rates varied based on target audience as seen in Table 1. The highest response rates were from OSC Staff with a 95% percent response rate, and the EMPC of lead ICs with a 56% response rate. The numbers below refer to how respondents were categorized in the survey population. In some cases, respondents self-reported a role different than the role on the NIH and CF list. Numbers in the survey analysis for categories may differ for EPMC and P&E Officers due to the role which participants self-reported. In the analyses of questions, participants were categorized based on their self-reported position, title and/or role.

Table 1: Response Rates by Target Audiences

| Target Audience | NIH Staff | Number of Respondents | Response Rate |
|---|---|---|---|
| OSC Staff | 20 | 19 | 95% |
| EPMC of lead ICs of CF programs | 18[1] | 10 | 56% |
| Executive Officers | 20 | 9 | 45% |
| Grants Management Officers | 22 | 10 | 45% |
| WG Members | 584 | 257 | 44% |
| IC Directors (WG members) | 20 | 8 | 40% |
| IC Directors (Non-WG members) | 7 | 2 | 29% |
| P&E Officers (WG members and non-members) | 35[2] | 8 | 23% |
| Budget Points of Contact | 17 | 3 | 18% |
| Total | 743 | 326 | 44% |

[1] Six are also WG members
[2] Nine are also WG members

## INVOLVEMENT IN COMMON FUND PROGRAMS

The survey population was designed to include individuals who have experience with CF Programs. The WG members invited to participate in the survey were from 28 Common Fund programs.

Table 2: Programs Included in the Survey

| | CF Programs |
|---|---|
| 1 | Bioinformatics and Computational Biology |
| 2 | Bridging Interventional Development Gaps (BrIDGs) (Formerly known as NIH-RAID) |
| 3 | Building Blocks, Biological Pathways and Networks |
| 4 | Enhancing the Diversity of the NIH-Funded Workforce |

| | |
|---|---|
| 5 | Epigenomics |
| 6 | Extracellular RNA Communication |
| 7 | Genotype-Tissue Expression (GTEx) |
| 8 | Global Health |
| 9 | Gulf Oil Spill |
| 10 | HCS Research Collaboratory |
| 11 | Health Economics |
| 12 | High-Risk Research: NIH Director's Early Independence Award (EIA) |
| | High-Risk Research: NIH Director's New Innovator Award |
| | High-Risk Research: NIH Director's Pioneer Award |
| | High-Risk Research: NIH Director's Transformative Research Awards |
| 13 | Human Microbiome Project |
| 14 | Illuminating the Druggable Genome |
| 15 | Interdisciplinary Research |
| 16 | Knockout Mouse Phenotyping |
| 17 | Library of Integrated Network-Based Cellular Signatures (LINCS) |
| 18 | Metabolomics |
| 19 | Molecular Libraries and Imaging |
| 20 | Nanomedicine |
| 21 | Patient-Reported Outcomes Measurement Information System (PROMIS) |
| 22 | Protein Capture Reagents |
| 23 | Regulatory Science |
| 24 | Science of Behavior Change |
| 25 | Single Cell Analysis |
| 26 | Strengthening the Biomedical Research Workforce |
| 27 | Structural Biology |
| 28 | Undiagnosed Diseases |

### Membership Status By Role

Of respondents who identified as members of a WG, 103 were currently members of only one WG, 79 were members of multiple WGs, and 41 were previous members of at least one WG but not current members. Fifty-seven respondents reported that they had never been a member of a WG. This number includes NIH staff who are involved with the CF in some capacity, such as EPMC members and P&E Officers, just not as WG members.

Table 3: Membership Status by Role

| Membership Status | IC Director | P&E Officer | WG Member | Other | Total |
|---|---|---|---|---|---|
| Never been a member of a CF WG | 2 | 7 | 0 | 48 | 57 |
| Currently a member of one CF WG | 1 | 5 | 97 | 0 | 103 |
| Currently a member of more than one CF WG | 5 | 3 | 71 | 0 | 79 |
| Not a currently member of a CF WG, but I was previously a member | 2 | 2 | 37 | 0 | 41 |
| Don’t know | 0 | 0 | 0 | 5 | 5 |
| Total | 10 | 17 | 205 | 53 | 285 |

### Number of Years Participating in Common Fund Working Groups

Approximately a third of the respondents who were current WG members (35%) were involved in the CF WG for more than a year but less than three years, another 27% were involved at least three years but less than five, and 28% were involved five years or more. Among the past WG members, 34% of the respondents were involved with the CF for three years or more but less than five, and 32% were involved between one and three years. For both past and current members, about 10% reported being involved less than one year.

Table 4: Number of Years Participating in Common Fund Working Groups

| Number of Years | Current WG Member | Past WG Member |
|---|---|---|
| Less than 1 year | 17 (9%) | 4 (10%) |
| Greater than or equal to 1, but less than 3 years | 63 (35%) | 13 (32%) |
| Greater than or equal to 3 years, but less than 5 years | 48 (27%) | 14 (34%) |
| Five or more years | 51 (28%) | 6 (15%) |
| Don't remember | 1 (1%) | 4 (10%) |
| Total | 180 | 41 |

### Numbers of Years Involved in Common Fund – GMOs, BPOC, and EO

The survey respondents included Executive Officers and staff involved in Grants Management and Budget. Of this population, more than half the respondents (54%) were involved with the CF five years or more. Thirty-six percent of the respondents were involved in the CF for three or more years but less than five years, and 9% were involved for less than three years.

Table 5: Numbers of Years Involved in Common Fund – GMOs, BPOC, and EO

| Number of Years | Frequency |
|---|---|
| Greater than or equal to 1, but less than 3 years | 2 (9%) |
| Greater than or equal to 3 years, but less than 5 years | 8 (36%) |
| Five or more years | 12 (54%) |
| Total | 22 |

### 2005 Roadmap Survey Compared with the 2014 Common Fund Survey

Twenty-three questions from the 2005 Roadmap Survey were included in the 2014 Common Fund survey to allow for comparison. Results and descriptions of these comparisons are included in the section entitled Findings from the Survey.

# FINDINGS FROM THE SURVEY

The survey probed various questions related to the strategic planning and management processes associated with the NIH CF. Where the results relate to the specific question being probed by the CFEWG, those results are matched to the question and reported along with the analysis of the responses. Where the question corresponds to a question in the 2005 survey, a comparison is shown.

A number of respondents reported that they did not know the answer to certain questions, or they felt the question was not applicable to them. The CFEWG was interested in maintaining those responses as indications of the knowledge of respondents, and therefore those responses are considered in the analysis of the question. For illustrative purposes, the percentage that is "Do not know" or "Not applicable" are shown beside the bar chart and are not shown in the actual chart. However, when resposes in the 2014 survey are compared to responses in the 2005 survey, the "Do not know" or "Not applicable" responses are factored out to be consistent with the way the data were presented there.

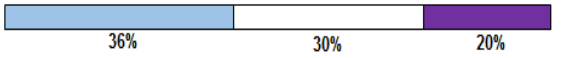
Appendix 2 shows all survey responses with the "Do not know" or "Not applicable" factored out. For analysis purposes, very satisfied and satisfied responses were combined, as were dissatisfied and very dissatisfied. Not all respondents answered every question, therefore, the valid responses varied for each question. Throughout this report, numbers in tables may not add to exactly 100% due to rounding.

## QUESTION 1: STRATEGIC PLANNING: ARE PLANNING PROCESSES OPTIMAL FOR IDENTIFYING PROGRAM AREAS THAT MEET THE COMMON FUND (CF) CRITERIA?

### Q1.1 For Phase 1 Planning:

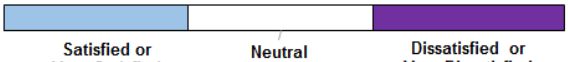
#### I. What are the best methods to engage the broader scientific community?

During Phase 1 planning, the broader scientific community is engaged through the process of soliciting ideas. Institutes and Centers (ICs) have different ways of engaging the broader community in soliciting these ideas. Thirty-six percent of survey participants generally felt very satisfied or satisfied with the process for soliciting ideas from ICs, 30% were neutral on the question, and 20% were very dissatisfied or dissatisfied.

| | Responses | | |
|---|---|---|---|
| | Satisfied or Very Satisfied / Neutral / Dissatisfied or Very Dissatisfied | VS-VD[1] | DNK /NA |
| The process for soliciting ideas from the ICs |   | 256 | 14% |

[1] Please note throughout the report where VS-VD and SA-SD appear, this column includes all responses in the five categories, and does not include those that selected Do not know or Not applicable.

As part of the process of soliciting ideas, OSC sends a one page template to the ICs to submit ideas for new programs. When asked about this process, 45% of respondents indicated they were very satisfied or satisfied, 28% responded neutrally, and 9% reported being very dissatisfied or dissatisfied.

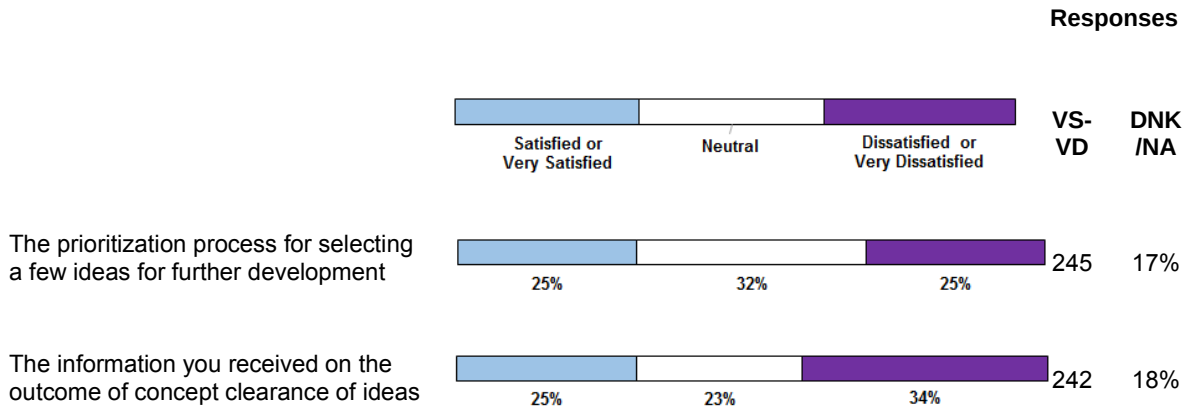
| | Responses | | |
|---|---|---|---|
| | Satisfied or Very Satisfied / Neutral / Dissatisfied or Very Dissatisfied | VS-VD | DNK /NA |
| The initial one-page template to submit ideas for new programs |   | 243 | 18% |

## II. Do the concepts, as currently written at the end of Phase 1, allow effective review by the Council of Councils? Should the format and content of the concepts be adjusted? Should DPCPSI more stringently filter concepts that are not clearly articulated and ask the CoC to review only those concepts for which there is enthusiasm?

The survey questions related to Question II probed respondents' opinions about the process of selecting new ideas to be further developed into programs and how the results of the clearance process are communicated. Survey participants were almost evenly divided in their satisfaction of the prioritization process for selecting ideas for further development. Twenty-five percent felt very satisfied or satisfied with the process, 32% were neutral, while another 25% of respondents felt very dissatisfied or dissatisfied.

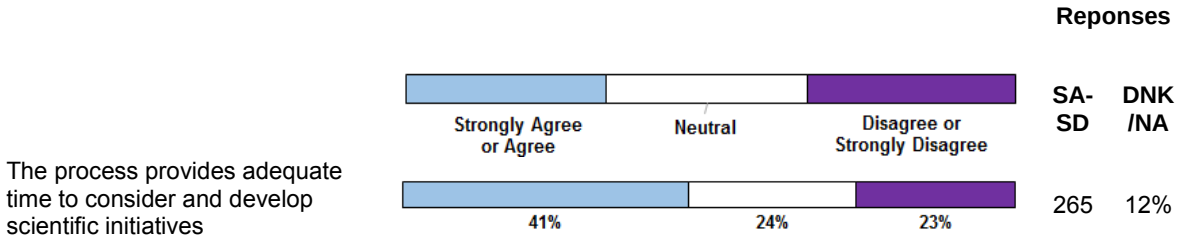
Respondents were generally dissatisfied with the information they received on the outcome of concept clearance of ideas. Twenty-five percent of respondents felt very satisfied or satisfied with the information they are received on the outcome of concept clearance of ideas, 23% of

participants respondend neutrally, and 34% indicated they were very dissatisfied or dissatisfied. A relatively high percentage, 18%, responded that they did not know or felt the question was not applicable to them.



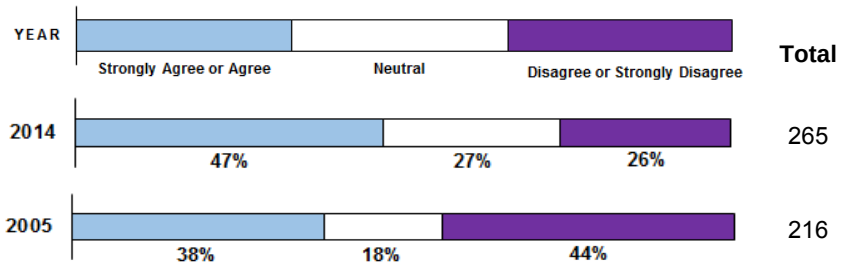

## III. Is 9 months for Phase 1 planning an appropriate time frame?

Respondents generally felt that the strategic planning process provides time to develop initiatives and were generally satisfied with the time provided. Forty-one percent of respondents strongly agreed or agreed that the process provided time to develop initiatives, while 24% were neutral, and 23% strongly disagreed or disagreed with this statement.



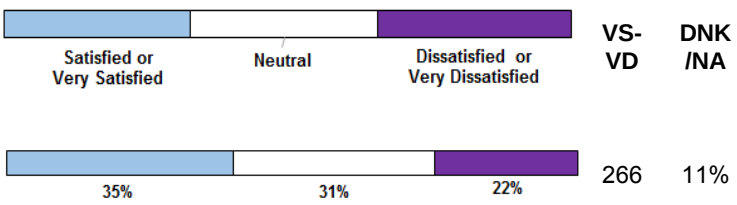

When "Do not know" or "Not applicable" responses are factored out of the analysis, 47% strongly agreed or agreed there was adequate time for developing initiatives, 27% were neutral, and 26% strongly disagreed or disagreed on the question. These responses represent a positive shift in attitudes from 2005, where a higher percentage of respondents disagreed that the process provides adequate time. In 2005 respondents were asked their opinions about the overall strategic planning process, which was not in separate phases at that time. Only 38% strongly agreed or agreed that there was adequate time to develop initiatives, 18% were neutral, and 44% strongly disagreed or disagreed. Appendix 3 shows all comparisons which were made to 2005 survey responses.

The process provides adequate time to consider and develop scientific initiatives



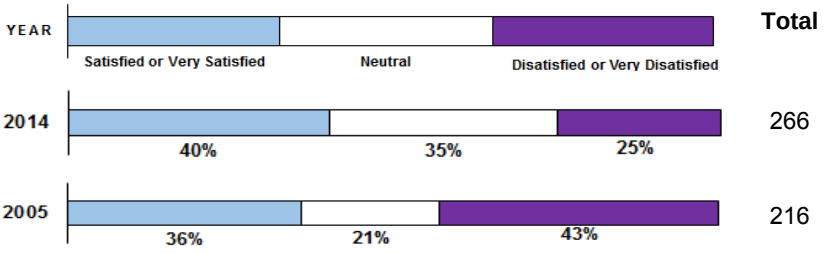

Respondents were generally satisfied with the pace and time provided during the strategic planning process. Thirty-five percent respondents were very satisfied or satisfied with this aspect of strategic planning, 31% were neutral, and 22% were very dissatisfied or dissatisfied.

The pace and length of time provided for the overall planning process




When "Do not know" or "Not applicable" responses are factored out of the analysis, 40% were very satisfied or satisfied with the pace and time provided, 35% were neutral, and 25% were very dissatisfied or dissatisfied. These responses represent a positive shift in attitudes from 2005, where a higher percentage of respondents were dissatisfied with the pace and time provided with the overall process. In 2005, only 36% were very satisfied or satisfied with the pace and time provided, 21% were neutral, and 43% were very dissatisfied or dissatisfied.

The pace and length of time provided for the overall planning process



## IV. Should an alternate process be developed for rapid planning for "emergency concepts?"

The survey did not specifically cover this topic.

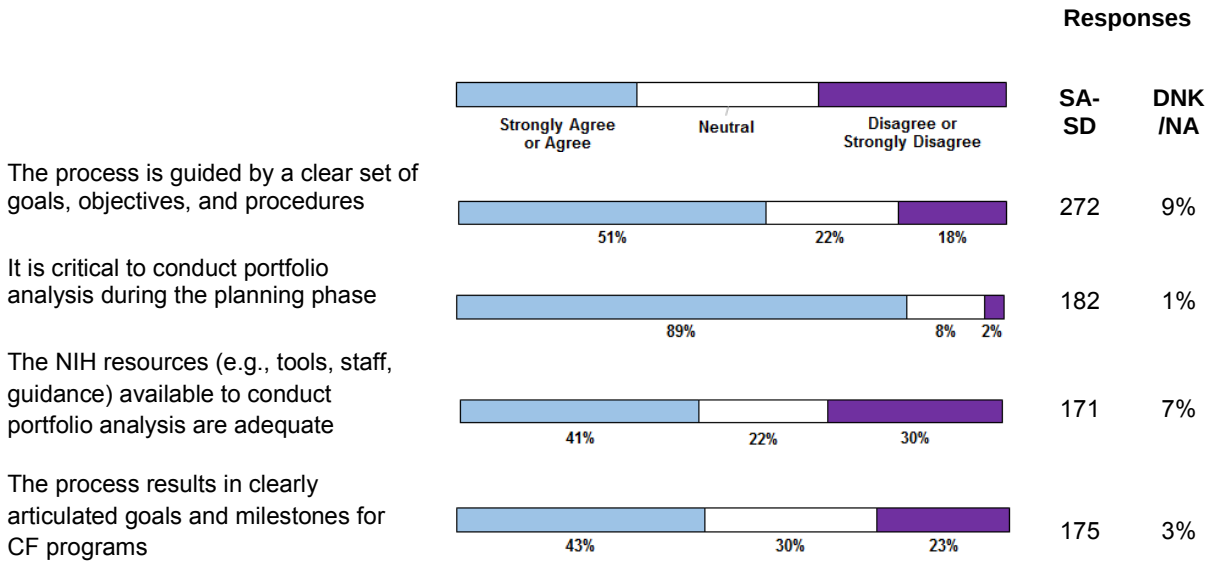
## Q1.2 For Phase 2 Planning:

## V. Do Phase 2 processes result in clearly articulated goals and expected milestones?

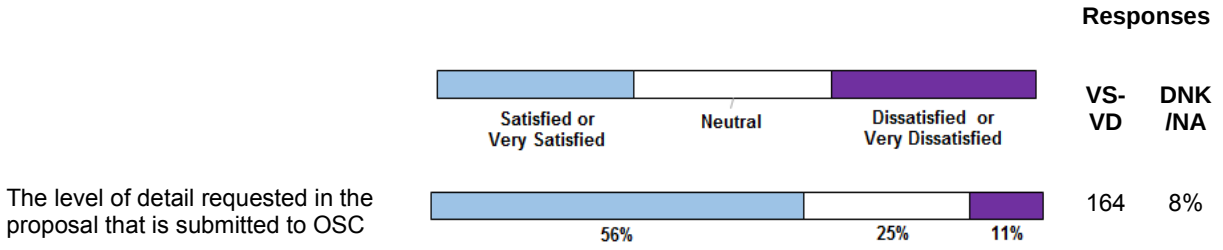
A majority of respondents (51%) strongly agreed or agreed that the strategic planning process is guided by a clear set of goals, objects, and procedures. Twenty-two percent of respondents responded neutrally, while 18% strongly disagreed or disagreed with this statement.

Participants strongly agreed or agreed that it is critical to conduct portfolio analysis during the planning phase. An overwhelming majority (89%) strongly agreed or agreed that it is critical to conduct portfolio analysis during the program planning phase, while a small proportion chose neutral (8%), or strongly disagree or disagree (2%).

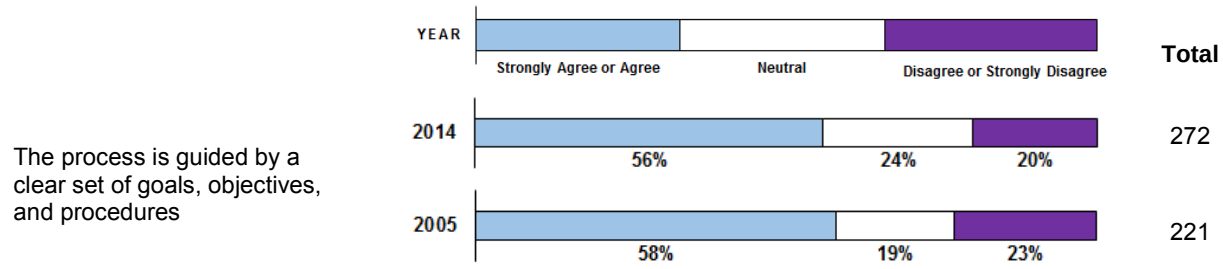
When asked if NIH resources are adequate to conduct portfolio analysis, 41% strongly agreed or agreed, 22% were neutral, and 30% strongly disagreed or disagreed. Additionally, 43% of respondents agreed that the strategic planning process results in clearly articulated goals and milestones. Thirty percent felt neutral about clear goals and milestones, while 23% strongly disagreed or disagreed.



Finally, a majority of participants (56%) were very satisfied or satisfied with the level of detail requested in the proposal submitted to OSC. Twenty-five percent of respondents felt neutral, and 11% were very dissatisfied or dissatisfied with the level of detail requested. Differences in the target audiences completing different survey sections resulted in different sample sizes for these questions.




Respondents' opinion of whether or not the strategic planning process is guided by a clear set of goals, objectives, and procedures did not change much from 2005. When participants who responded "Do not know" or "Not applicable" are factored out, responses to the 2014 survey show that the majority (56%) strongly agreed or agreed, while 24% felt neutral, and 20% strongly disagreed or disagreed. Similarly, in 2005, 58% strongly agreed or agreed with this statement, 19% felt neutral, and 23% strongly disagreed or disagreed.

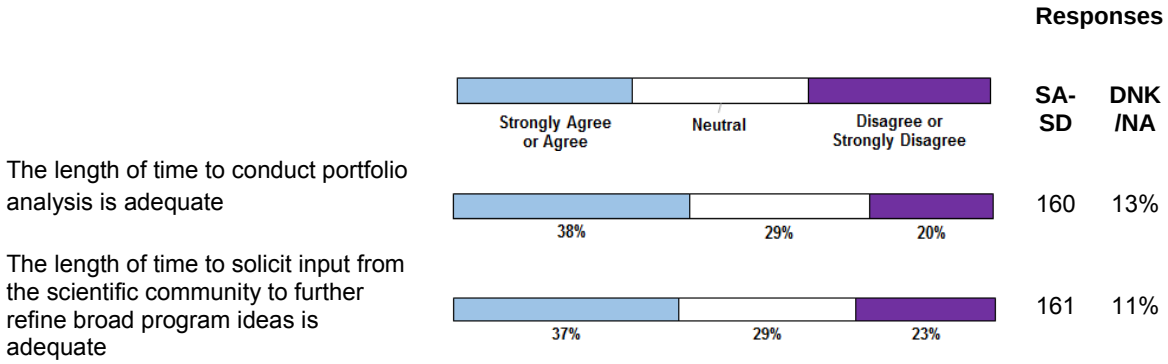



## VI. Is 9 months an appropriate timeframe for Phase 2 planning?

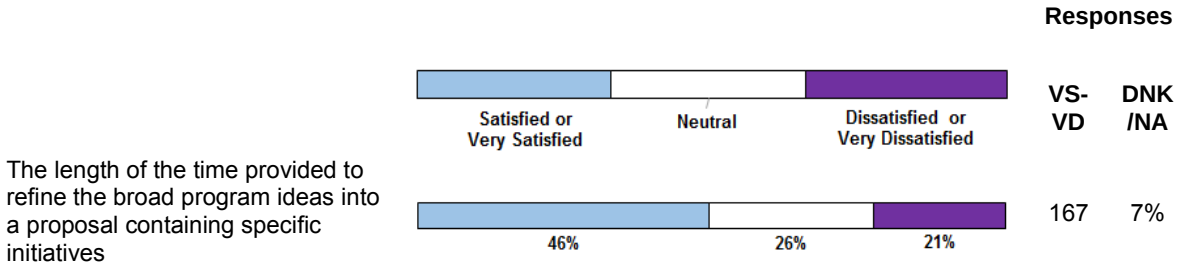
As noted above in question 1.1.III, respondents generally felt that the strategic planning process provides time to develop initiatives and were generally satisfied with the time provided. Respondents were asked specifically about the time provided related to two aspects of Phase 2 planning: conducting the portfolio analysis and gathering input from the scientific community for program ideas. When asked specifically about the time provided to conduct portfolio analysis, respondents generally felt the time was adequate. Thirty-eight percent strongly agreed or agreed that the process provided adequate time for portfolio analysis, while 29% felt neutral, and 20% strongly disagreed or disagreed with this statement.

When asked specifically about the time provided to solicit input to help refine broad program ideas, respondents generally felt the time was adequate and were satisfied with the time

provided. Thirty-seven percent strongly agreed or agreed that the process provided adequate time to solicit input from the scientific community, while 29% felt neutral, and 23% strongly disagreed or disagreed with this statement.




When asked about their level of satisfaction with the time provided to refine broad program ideas into specific initiatives, 46% were very satisfied or satisfied with the time provided, while 26% felt neutral, and 21% were very dissatisfied or dissatisfied.




## VII. Do IC Directors and the Council of Councils have appropriate levels of input to guide the development of Phase 2 proposals?

Respondents were asked about their level of satisfaction with the CoCs' role in the process of approving ideas to become programs. Thirty percent of respondents were very satisfied or satisfied with the CoCs' role in concept clearance, 41% were neutral on the question, and just 11% indicated they were very dissatisfied or dissatisfied. A relatively high percentage, 18%, indicated that they did not know or felt the question was not applicable to them.

| | | Responses | |
|---|---|---|---|
| | Satisfied or Very Satisfied / Neutral / Dissatisfied or Very Dissatisfied | VS-VD | DNK /NA |
| The Council of Councils' role in concept clearance | 30% / 41% / 11% | 242 | 18% |

IC Directors were specifically asked about their level of input in the process for selecting new CF programs. Three of nine (33%) strongly agreed or agreed the process allowed adequate input by IC Directors, two were neutral, and four of nine (44%) strongly disagreed or disagreed.

| | | Responses | |
|---|---|---|---|
| | Strongly Agree or Agree / Neutral / Disagree or Strongly Disagree | SA-SD | DNK/ NA |
| The process for selecting new CF programs allows adequate input by IC Directors | 33% / 22% / 44% | 9[1] | 0 |

[1] This question was only answered by IC Directors. One IC Director who responded to the survey did not answer this question.

## Q1.3 For both Phase 1 and Phase 2:

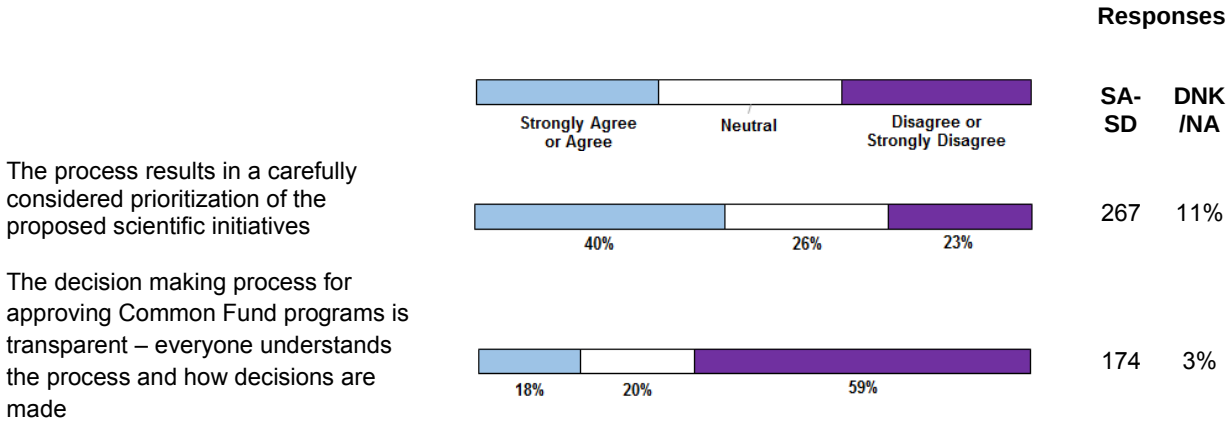
### VIII. What should the process be for planning intramural-only programs?

The survey did not specifically cover this topic.

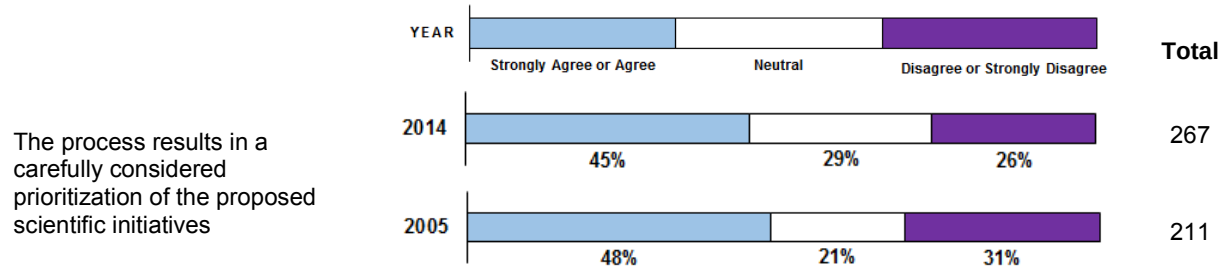
### IX. What are the attitudes and level of understanding of NIH staff toward the current planning processes, including how decisions are made? What difficulties in the process can staff identify in order to facilitate greater satisfaction and engagement?

Several questions were asked in the survey that related to the respondents' opinions and level of understanding of the current process. Forty percent of respondents strongly agreed or agreed that the process resulted in carefully considered prioritization of proposed scientific initiatives, while 26% responded neutrally, and 23% strongly disagreed or disagreed with this statement. However, when asked about the decision making process for approving CF programs, 18% of participants strongly agreed or agreed that the process was transparent, 20% were neutral, and 59% strongly disagreed or disagreed. The two questions were asked to different target audiences. The first question was asked to all respondents except EOs, GMOS, and BPOCs. The second question was asked to respondents who have been involved in program planning after WG are

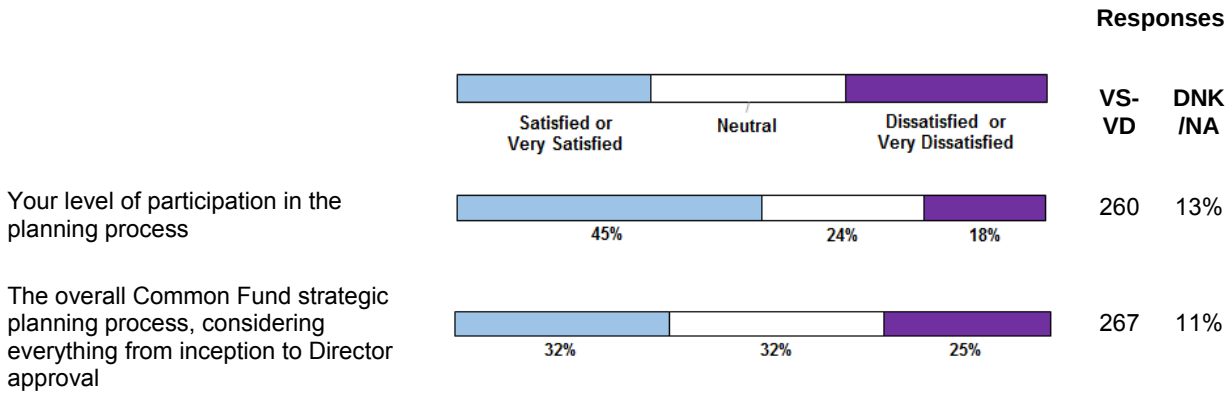
formed to refine cleared concepts into program proposals. This second group has more experience with the entire strategic planning process.




When "Do not know" or "Not applicable" responses are factored out, 45% of respondents strongly agreed or agreed that the process resulted in a carefully considered prioritization of the proposed scientific initiatives. This response is similar to 2005, when 48% strongly agreed or agreed with the same statement. In 2014 29% of respondents felt neutral compared with 21% of respondents in 2005. The percentage of respondents who strongly disagreed or disagreed with the statement decreased from 31% in 2005 to 26% in 2014.

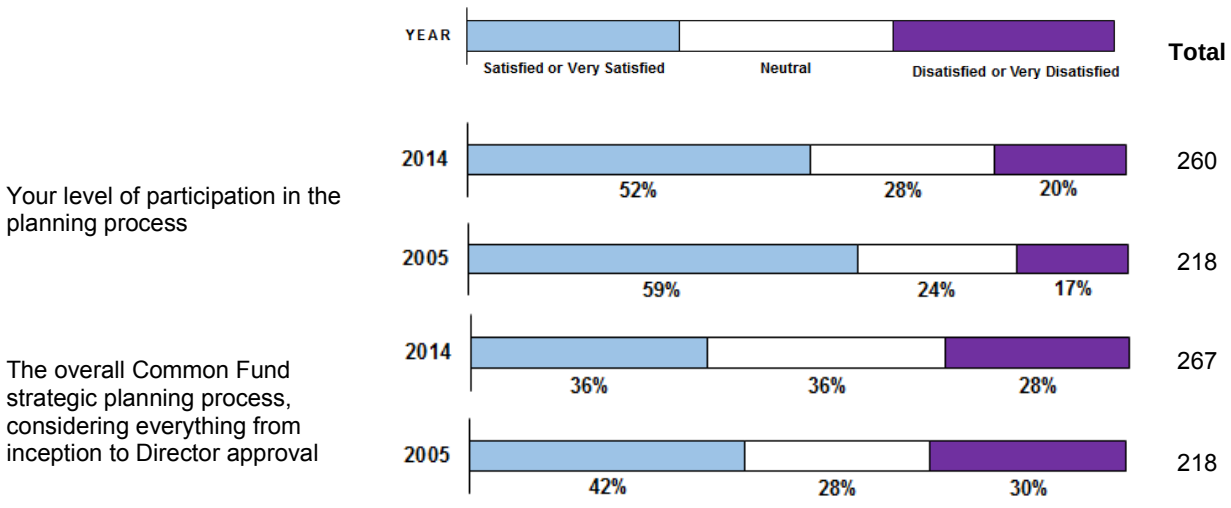



Respondents were two and a half times more favorable than unfavorable about their personal level of participation in the process. Forty-five percent were very satisfied or satisfied, while 24% felt neutral and 18% were very dissatisfied or dissatisfied. When asked about their level of satisfaction with the overall Strategic Planning process, 32% were very satisfied or satisfied while 32% were neutral, and 25% were very dissatisfied or dissatisfied.

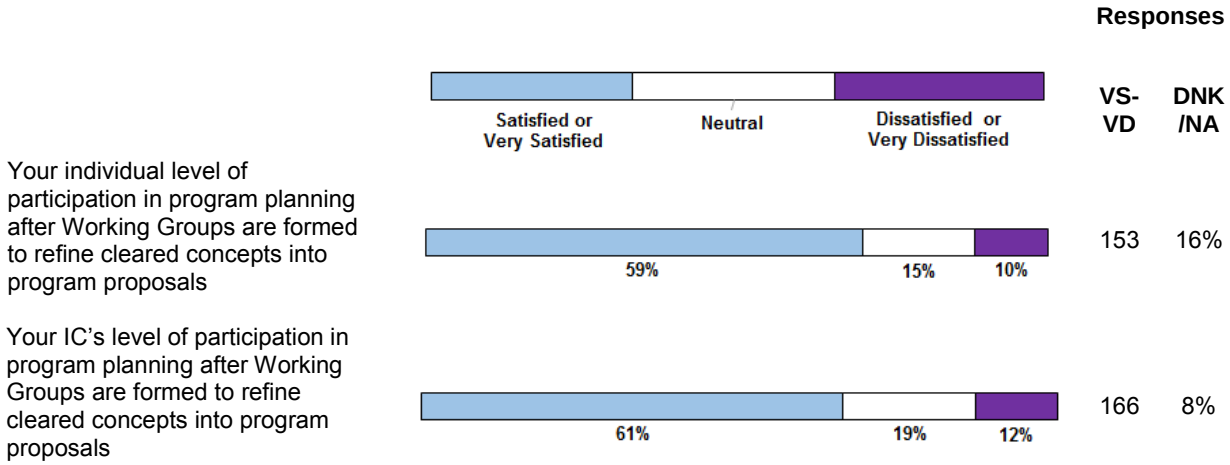



Survey participants expressed somewhat less satisfaction with strategic planning and decision making processes in the 2014 survey than in 2005. Factoring out "Do not know" and "Not applicable" responses, 52% of participants were very satisfied or satisfied with their level of participation in the planning process in 2014, compared to 59% who indicated satisfaction in the 2005 survey. The number of respondents reporting that they were very dissatisfied or dissatisfied was 20% in 2014, compared to 17% in 2005, and those who responded neutrally rose from 24% to 28% in 2014.

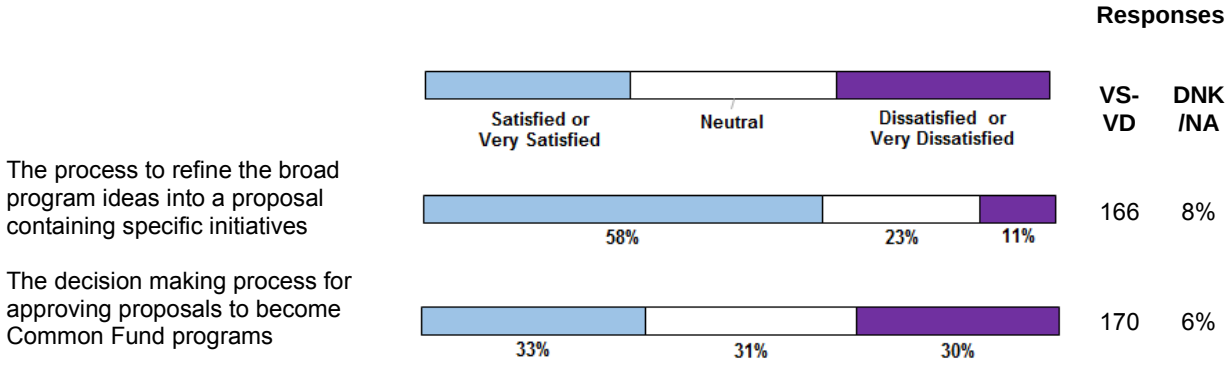
Similarly, fewer respondents indicated satisfaction with the overall strategic planning process, though slightly fewer also reported dissatisfaction. In the 2005 survey, 42% of participants were very satisfied or satisfied, 28% were neutrally, and 30% were very dissatisfied or dissatisfied. In 2014, the number of satisfied responses decreased to 36%, while the number of neutral responses grew to 36%. The percentage of respondents indicating very dissatisfied or dissatisfied decreased slightly from 30% in 2005 to 28% in 2014.



A majority of participants responded that they were very satisfied or satisfied when asked about both their individual and ICs level of participation in program planning. Regarding their individual participation, 59% were very satisfied or satisfied, while 15% felt neutral, and 18% were very dissatisfied or dissatisfied. A majority of participants were very satisfied or satisfied with their IC's level of participation in program planning after WGs are formed (61%), while 19% felt neutral, and 12% were very dissatisfied or dissatisfied.




Fifty-eight percent of participants were very satisfied or satisfied when asked about the process of refining broad program ideas into specific initiatives, while 23% were neutral, and just 11% were very dissatisfied or dissatisfied. However, the level of satisfaction decreased when participants were asked about the decision-making process for the approval of proposals to become CF programs. Thirty-three percent were very satisfied or satisfied, 31% were neutral, and 30% indicated they were very dissatisfied or dissatisfied.

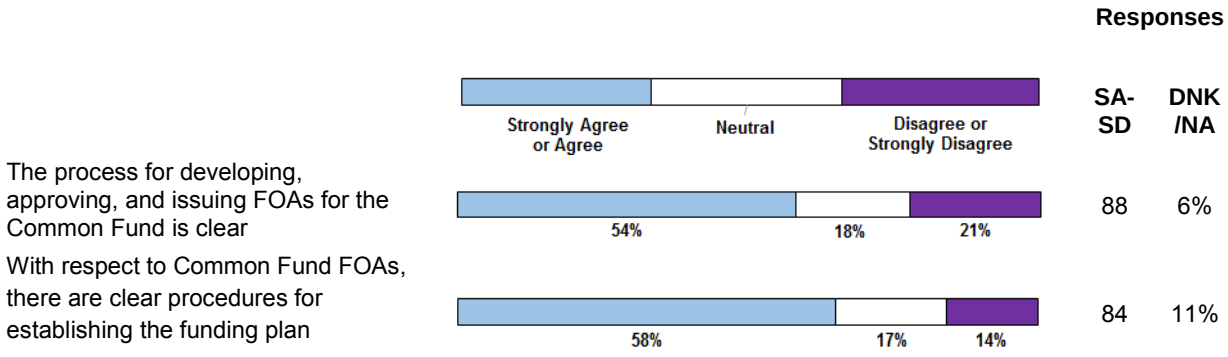


## QUESTION 2: MANAGEMENT/OVERSIGHT: ARE MANAGEMENT/OVERSIGHT PROCESSES OPTIMAL FOR ACHIEVING PROGRAM GOALS?

### Q2.1 Questions pertaining to interactions with awardees:

### I. Are expectations for programs clearly articulated in funding announcements, program kick-off documents, websites, program materials? Are the goals and responsibilities clear?

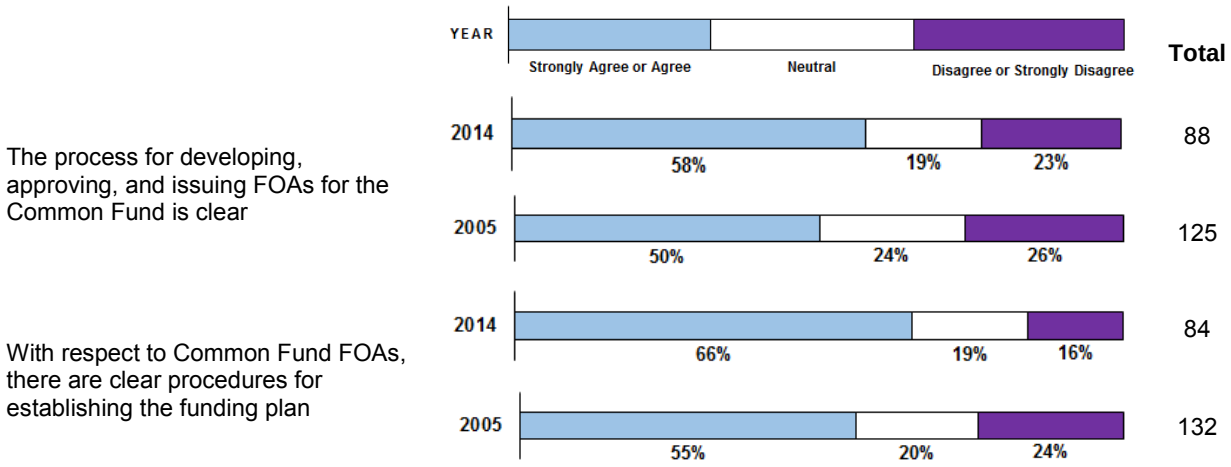
A majority of respondents feel that processes associated with Funding Opportunity Announcements (FOAs) are clear. Fifty-four percent of respondents strongly agreed or agreed that the CF FOA process is clear, while 18% were neutral, and 21% strongly disagreed or disagreed. A majority of respondents also felt that CF processes specifically associated with establishing funding plans are clear. Fifty-eight percent of respondents strongly agreed or agreed that the process is clear, while 17% were neutral, and 14% strongly disagreed or disagreed with this statement.



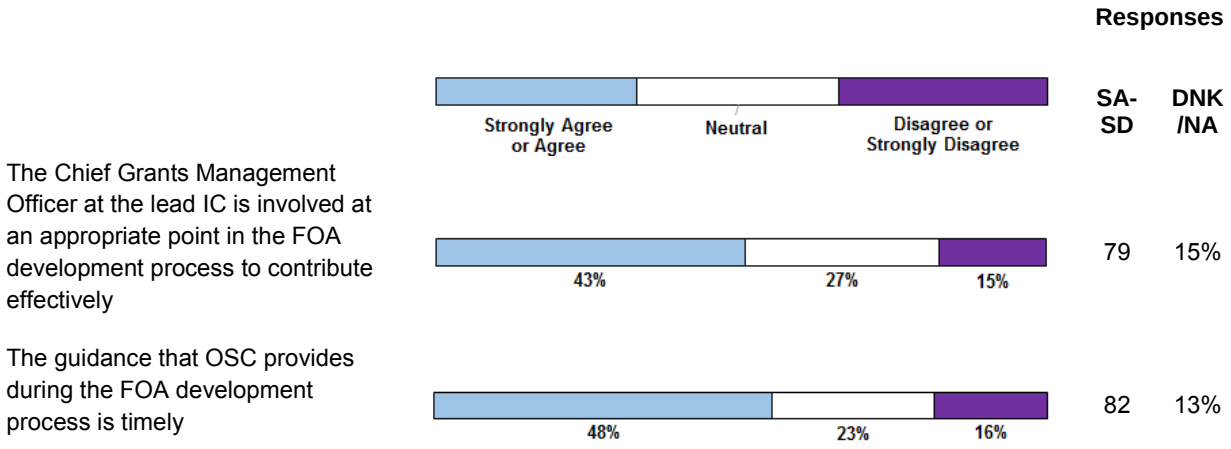

When "Do not know" or "Not applicable" responses are factored out of the analysis, 58% strongly agreed or agreed the processes are clear, 19% were neutral, and 23% strongly disagreed or disagreed. These responses are similar, though slightly more positive, than attitudes from 2005 related to similar issues. In 2005, respondents were asked their feelings about the processes and mechanisms for obtaining clearance associated with the Roadmap RFAs, RFPs, and contracts. In 2005, 50% strongly agreed or agreed there were clear procedures and mechanisms related to RFAs, RFPs, and contracts, 24% were neutral, and 26% strongly disagreed or disagreed.

Regarding procedures for establishing CF FOA funding plans, 66% strongly agreed or agreed the processes are clear, 19% were neutral, and 16% strongly disagreed or disagreed. These responses are more positive than attitudes from 2005 related to similar issues. In 2005, respondents were also asked their feelings about establishing a funding plan, and 55% strongly agreed or agreed

the procedures and mechanisms were clear, 20% were neutral on this issue, and 24% strongly disagreed or disagreed.

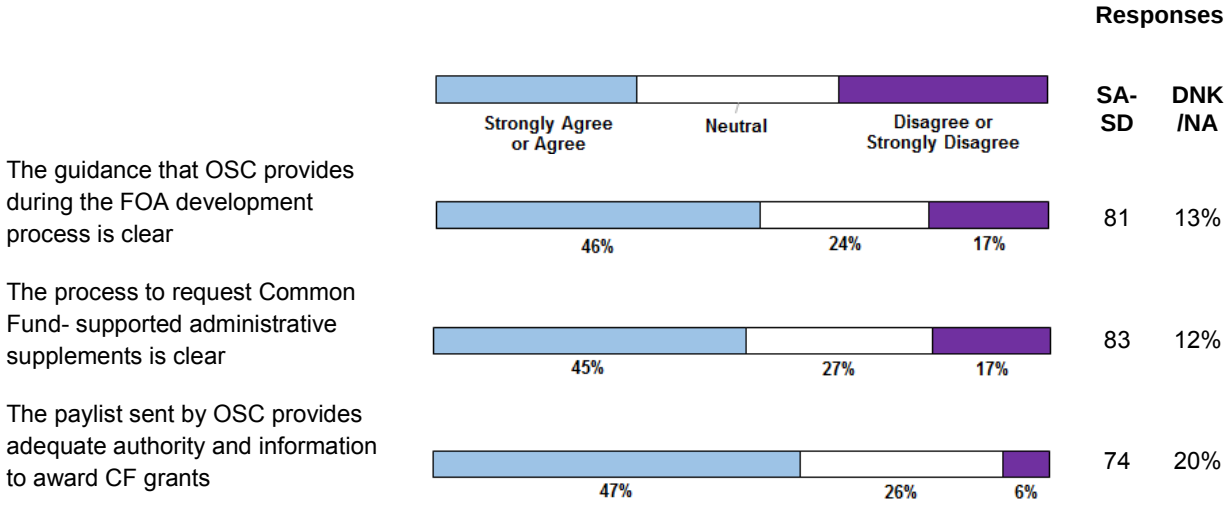



When asked about their agreement with the time at which Grant's Manager Officers are involved in the FOA process, 43% strongly agreed or agreed that the GMO is involved at the appropriate time, while 27% were neutral, and 15% strongly disagreed or disagreed. When asked about their agreement with the statement that OSC provides timely guidance during the FOA development process, 48% strongly agreed and agreed, while 23% were neutral, and 16% strongly disagreed or disagreed.




Respondents had similar responses when asked about the clarity of OSC guidance during the FOAs and the process to request administrative supplements. Forty-six percent of respondents strongly agreed or agreed that the OSC guidance is clear, 24% were neutral, and 17% strongly disagreed or disagreed with this statement. Similarly, 45% strongly agreed or agreed that the process to request supplements is clear, 27% were neutral, and 17% strongly disagreed or

disagreed. When specifically asked about the paylist that OSC sends, 47% strongly agreed or agreed that it provides adequate authority and information to award grants, 26% were neutral, and 6% strongly disagreed or disagreed.




## II. Are evaluative processes sufficient to provide critical assessment throughout the program's lifespan?

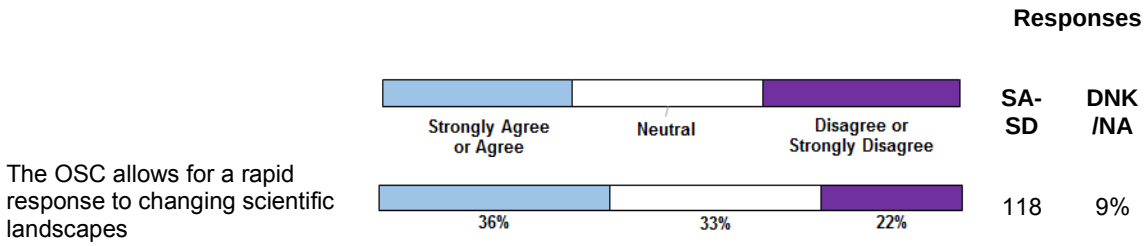
The survey did not specifically cover this topic.

## III. Are goals and milestones met?

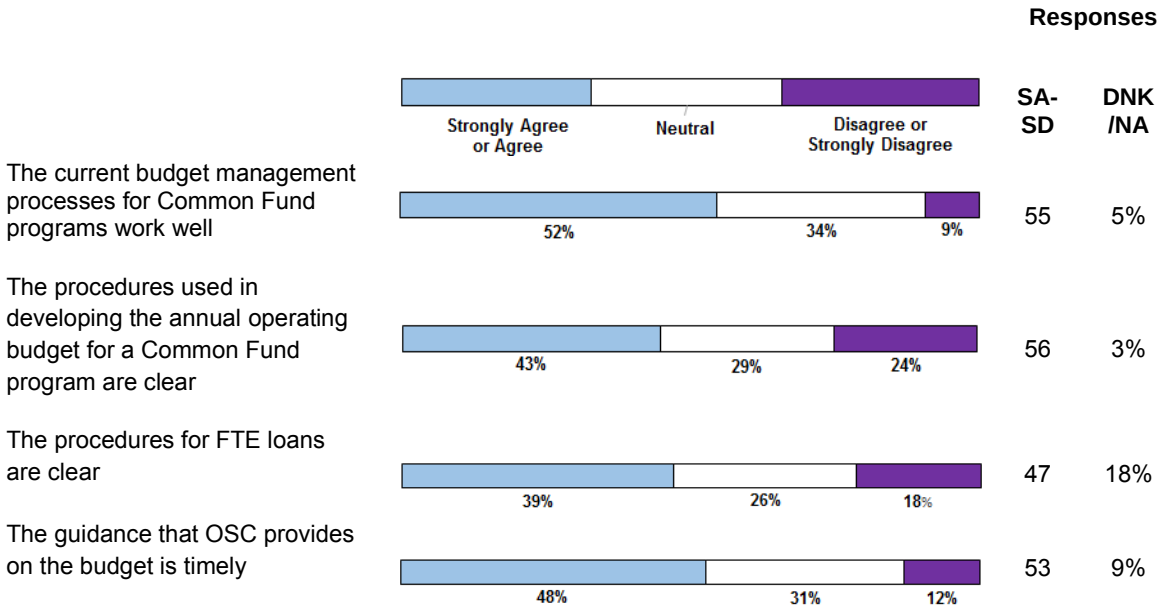
The survey did not specifically cover this topic.

## IV. Are management processes flexible and adaptive to changing scientific landscapes?

The survey specifically asked respondents about the response to changing landscapes. Respondents were also asked their opinions on various aspects of the budgetary guidance. Thirty-six percent of respondents strongly agreed or agreed that the OSC allows for a rapid response of changing scientific landscapes, 33% were neutral, and 22% strongly disagreed or disagreed.

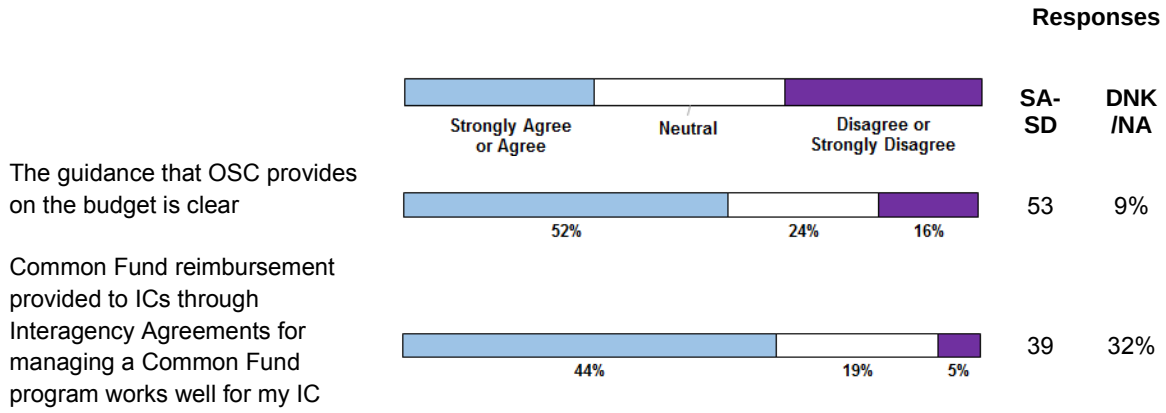



The majority of participants (52%) strongly agreed or agreed that current budget management processes for CF programs work well, 34% were neutral, and 9% strongly disagreed or disagreed. Survey participants were somewhat less positive in their views of other budget management processes, though still more favorable than unfavorable. Forty-three percent of respondents agreed that the procedures used to develop the annual operating budgets are clear, 29% were neutral, and 24% strongly disagreed or disagreed. Thirty-nine percent of participants strongly agreed or agreed that the procedures for FTE loans are clear, 26% were neutral, and 18% strongly disagreed or disagreed. Eighteen percent either did not know or felt the question was not applicable. Forty-eight percent of respondents felt that guidance provided by OSC is timely, 31% were neutral, and 12% strongly disagreed or disagreed.

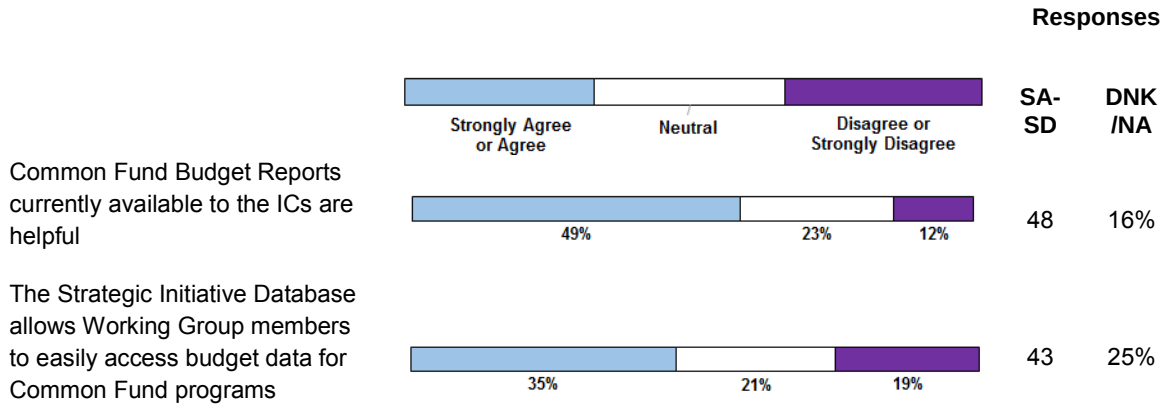



Fifty-two percent of participants strongly agreed or agreed that the guidance provided by OSC on the budget is clear, 24% were neutral, and 16% strongly disagreed or disagreed. Forty-four percent of respondents strongly agreed or agreed that CF reimbursements provided to their ICs through Interagency Agreements work well, 19% were neutral, and 5% strongly disagreed or

disagreed. Thirty-two percent indicated they did not know or felt the question was not applicable to them.




Forty-nine percent of participants agreed that CF Budget Reports that are currently available to ICs are helpful, 23% were neutral, and 12% strongly disagreed or disagreed. Thirty-five percent of participants strongly agreed or agreed that the Strategic Initiative Database allows WG members to easily access budget data, 21% were neutral, and 19% strongly disagreed or disagreed. Twenty-five percent indicated they did not know or felt the question was not applicable to them.



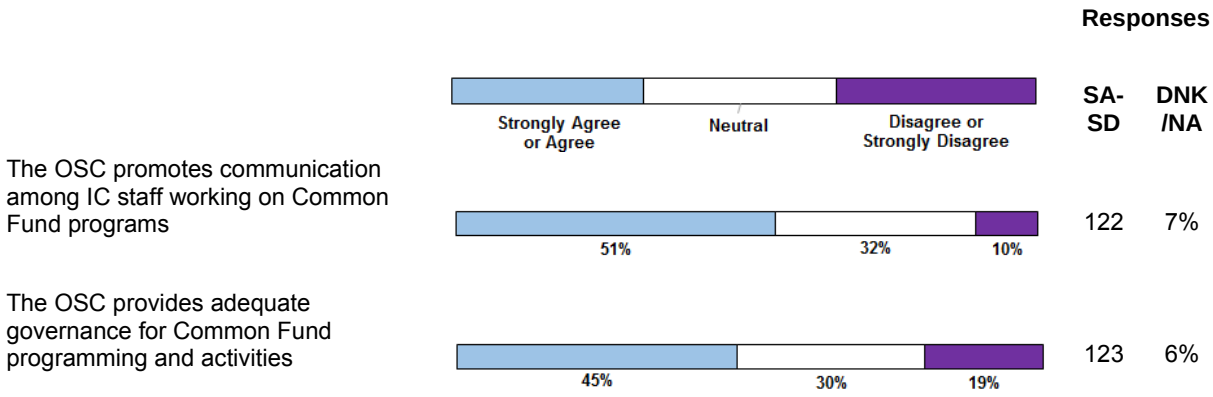

## V. What should the process be for management of intramural-only programs?

The survey did not specifically cover this topic.

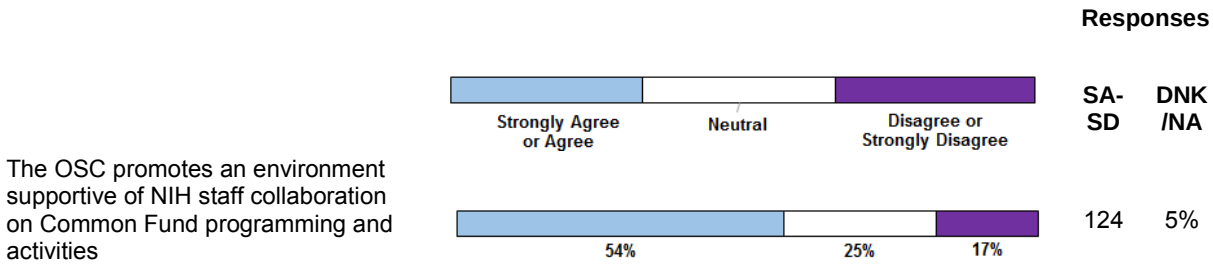
## Q2.2: Questions pertaining to intra-NIH interactions:

## VI. Are OSC/IC interactions working well?

Participants were generally positive regarding OSC communication and guidance. Fifty-one percent of respondents felt that OSC promotes communication among IC staff, 32% were neutral, and 10% strongly disagreed or disagreed. Similarly, 45% of survey respondents strongly agreed or agreed that the OSC provides adequate governance for CF programs and activities, 30% were neutral, and 19% strongly disagreed or disagreed with this statement.

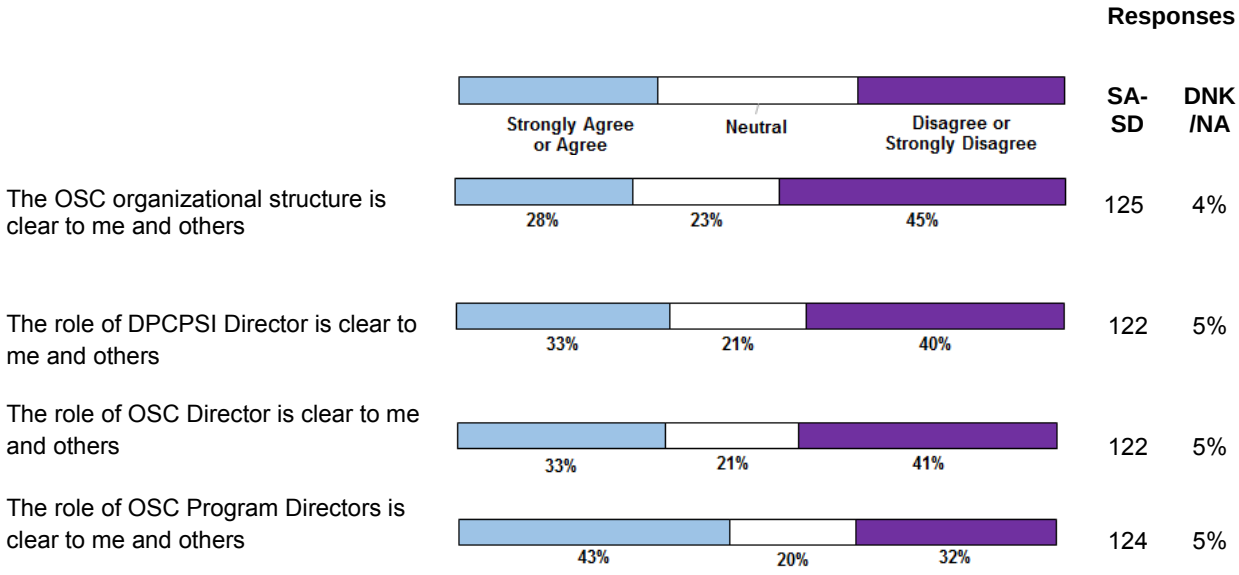



A majority of participants (54%) strongly agreed or agreed that the OSC promotes a collaborative environment, 25% were neutral, and only 17% strongly disagreed or disagreed with this statement.

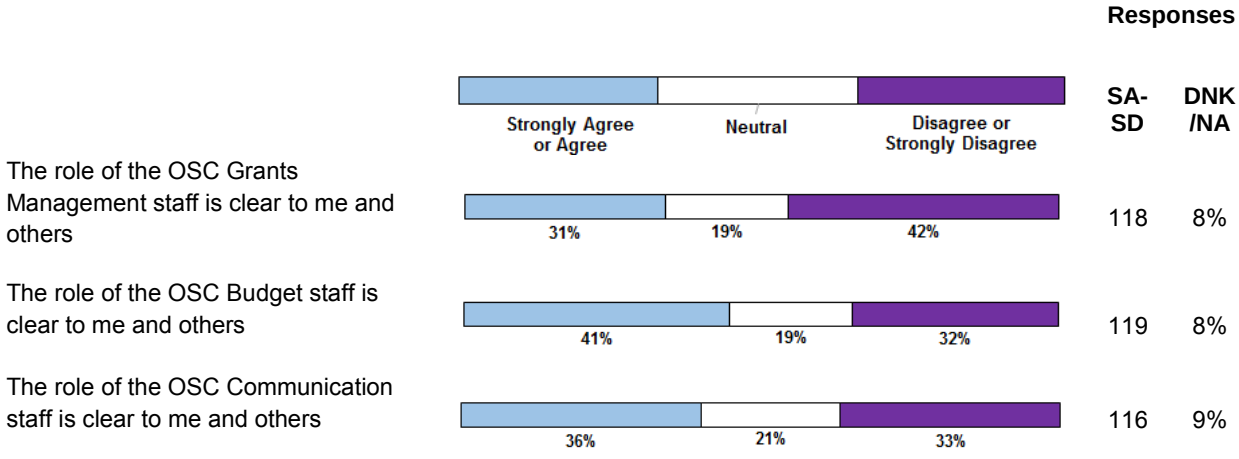



Participants were somewhat unclear about the structures and roles within OSC. Only 28% of respondents strongly agreed or agreed that the structure was clear, 23% responded neutrally, and 45% strongly disagreed or disagreed. The numbers were similar when asked about the roles of directors within OSC. When asked if the role of the DPCPSI Director was clear to them, 33% of respondents felt this role was clear to them, 21% were neutral, and 40% strongly disagreed or disagreed. Similarly, 33% felt the role of the OSC Director was clear, 21% were neutral, and

41% strongly disagreed or disagreed. However, forty-three percent of respondents were clear on the roles of OSC Program Directors, 20% were neutral, and 32% strongly disagree or disagreed.

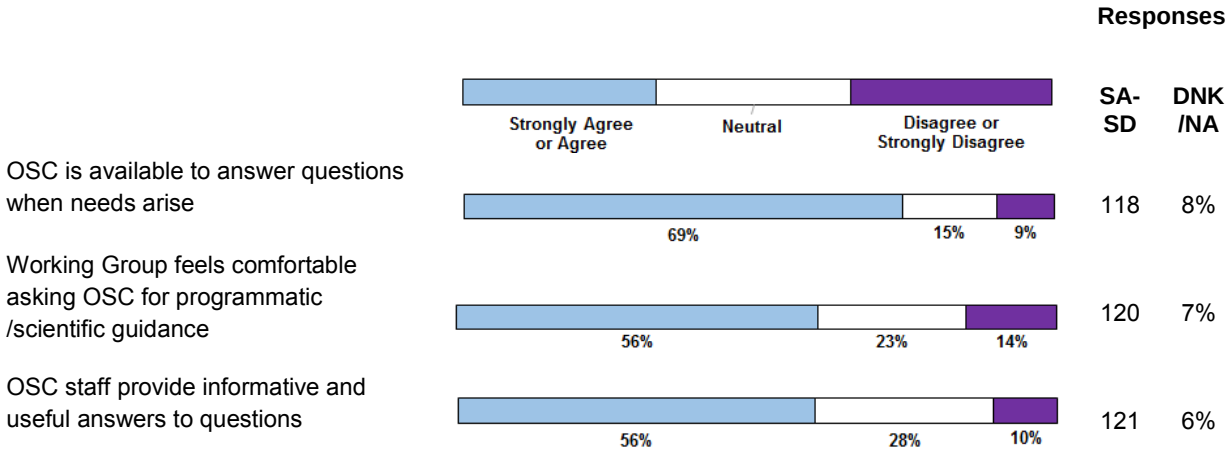



Thirty-one percent felt the role of the OSC Grants Management staff was clear, 19% were neutral, and 42% strongly disagreed or disagreed. However, 41% of survey participants felt the role of the OSC budget staff was clear to them, 19% were neutral, and 32% strongly disagreed or disagreed. The views on the OSC Communication staff were mixed: 36% strongly agreed or agreed that they understood the role, 21% responded neutrally, while 33% strongly disagreed or disagreed.

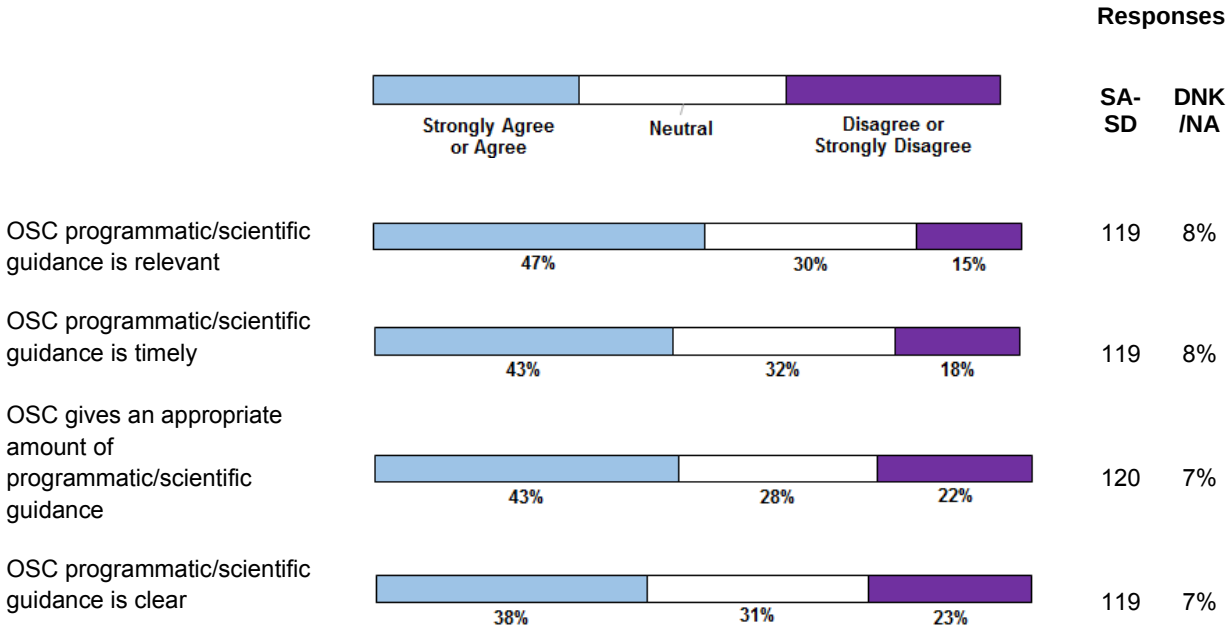



Most survey respondents (69%) strongly agreed or agreed that OSC staff are available to answer questions when a need arises, 15% were neutral, and a small number (9%) strongly disagreed or disagreed. A majority of survey participants (56%) indicated that WGs feel comfortable asking OSC for programmatic/scientific guidance, 23% were neutral, and 14% strongly disagreed or

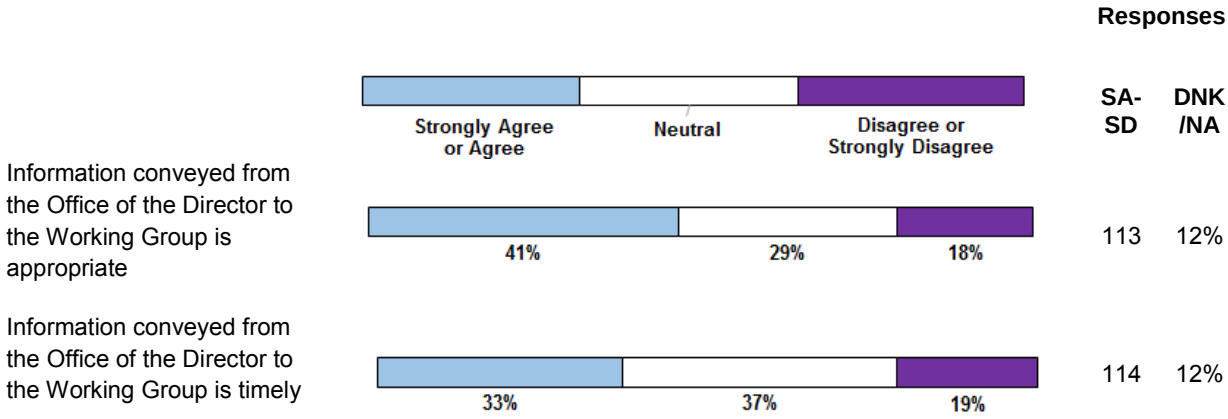
disagreed. Similarly, 56% strongly agreed or agreed that OSC staff provided informative and useful answers to questions, 28% were neutral, and only 10% strongly disagreed or disagreed.




However, while the survey participants were positive in their view of OSC's availability and ability to answer questions, they were somewhat less positive in their view of regular communications, though the responses were still more positive than negative. Forty-seven percent strongly agreed or agreed that OSC programmatic/scientific guidance was relevant, 30% were neutral, and 15% strongly disagreed or disagreed. Forty-three percent strongly agreed or agreed that OSC guidance was timely, 32% were neutral, and 18% strongly disagreed or disagreed. Forty-three percent strongly agreed or agreed that OSC gives an appropriate amount of guidance, 28% were neutral, and 22% strongly disagreed or disagreed. A small plurality of participants (38%) agreed that this guidance was clear, whereas 31% were neutral, and 23% strongly disagreed or disagreed.



Regarding information conveyed from the Office of the Director to WGs, 41% of survey participants strongly agreed or agreed that it was appropriate, 29% were neutral, and 18% strongly disagreed or disagreed. Thirty-three percent felt that information from the Office of the Director to WGs was timely, 37% were neutral, and 19% strongly disagreed or disagreed.

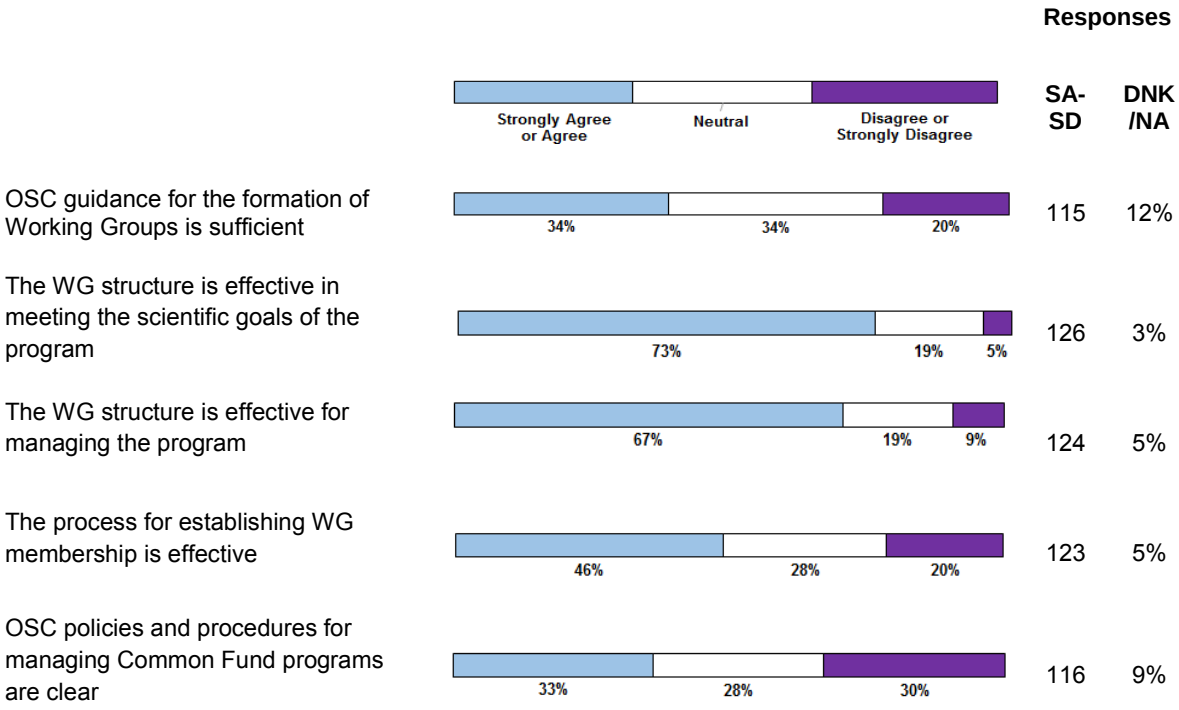



## VII. Is the Working Group structure meeting the management and oversight needs of the programs?

As noted previously, respondents generally agreed that OSC guidance is relevant, clear, of the appropriate amount, and allows for a rapid response to changing scientific landscapes. Survey respondents were asked about their opinions related to the WG structure. Thirty-four percent of respondents strongly agreed or agreed that OSC guidance on forming WGs was sufficient, 34% felt neutral, and 20% strongly disagreed or disagreed.

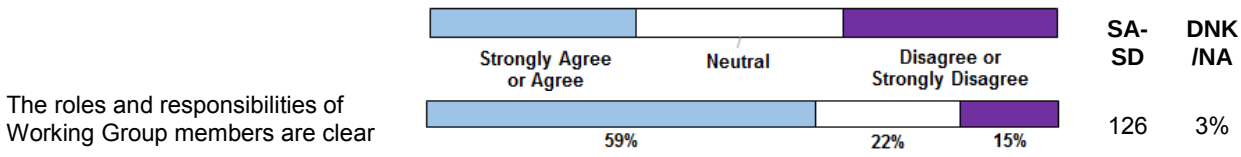
A large majority of respondents (73%) strongly agreed or agreed that the current structure is effective in meeting the scientific goals of the program, 19% responded neutrally, and just 5% strongly disagreed or disagreed with this statement. Similarly, 67% of participants strongly agreed or agreed that the current WG structure is effective for managing CF programs, 19% were neutral, and 9% strongly disagreed or disagreed.

A smaller percentage of respondents (46%) strongly agreed or agreed that the process for establishing membership on WGs is effective, 28% were neutral, and 20% of respondents stongly disagreed or disagreed. Finally, 33% of respondents felt the OSC policies and procedures for managing WGs are clear, compared with 28% who were neutral, and 30% who strongly disagreed or disagreed.

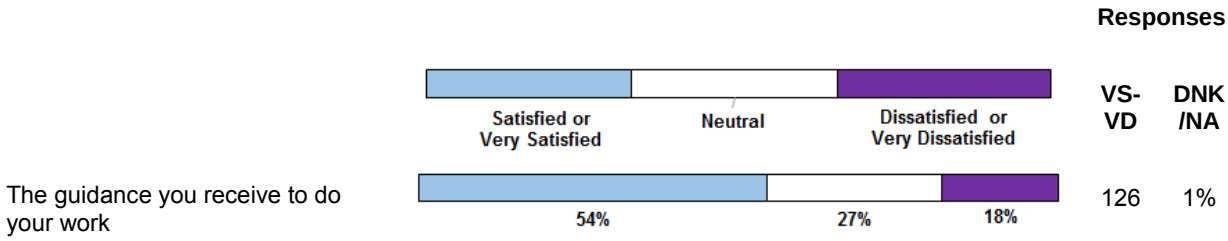



## VIII. Are the roles and responsibilities of Working Group members clear?

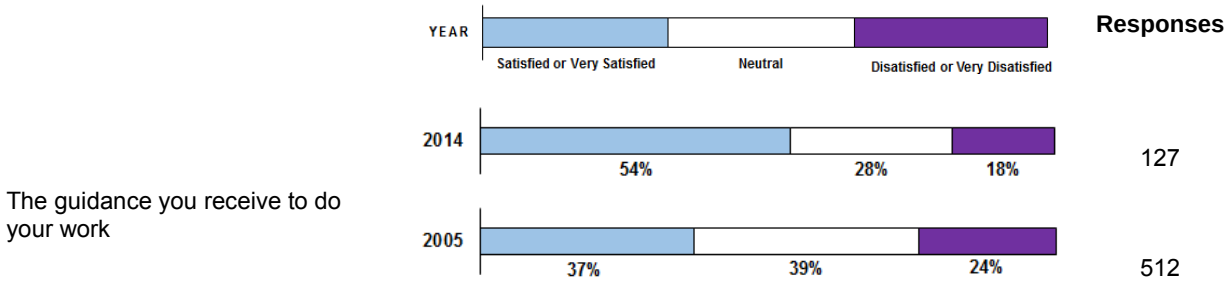
Survey respondents generally understood the roles and responsibilities of WG members. Fifty-nine percent of participants strongly agreed or agreed that the roles and responsibilities of WG members are clear, 22% were neutral, and 15% strongly disagreed or disagreed.




A majority of survey participants (54%) were very satisfied or satisfied with the guidance they receive to do their work, 27% were neutral, and 18% were very dissatisfied or dissatisfied.



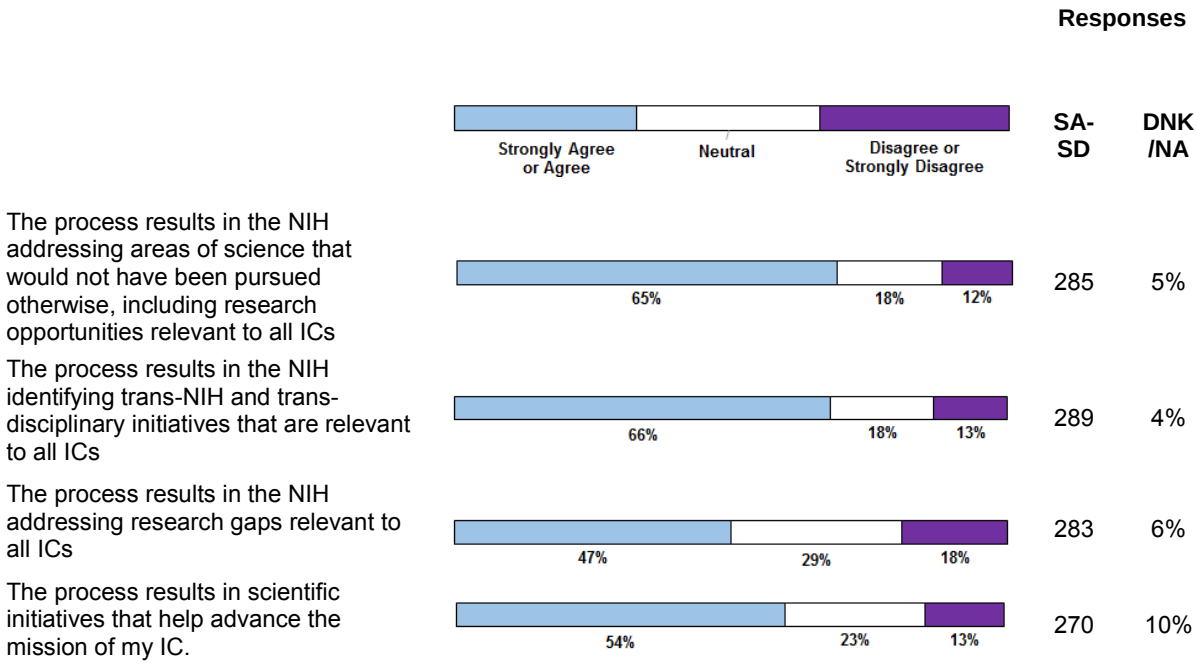

Respondents were more satisfied with the guidance they receive to do their work now than was reflected in the 2005 survey. When "Do not know" or "Not applicable" responses are factored out in the 2014 survey responses, 54% of respondents were very satisfied or satisfied with the guidance they receive, compared to just 37% who were very satisfied or satisfied in 2005. Eighteen percent were very dissatisfied or dissatisfied with the guidance they received to do their work, compared to 24% who were very dissatisfied or dissatisfied in 2005.



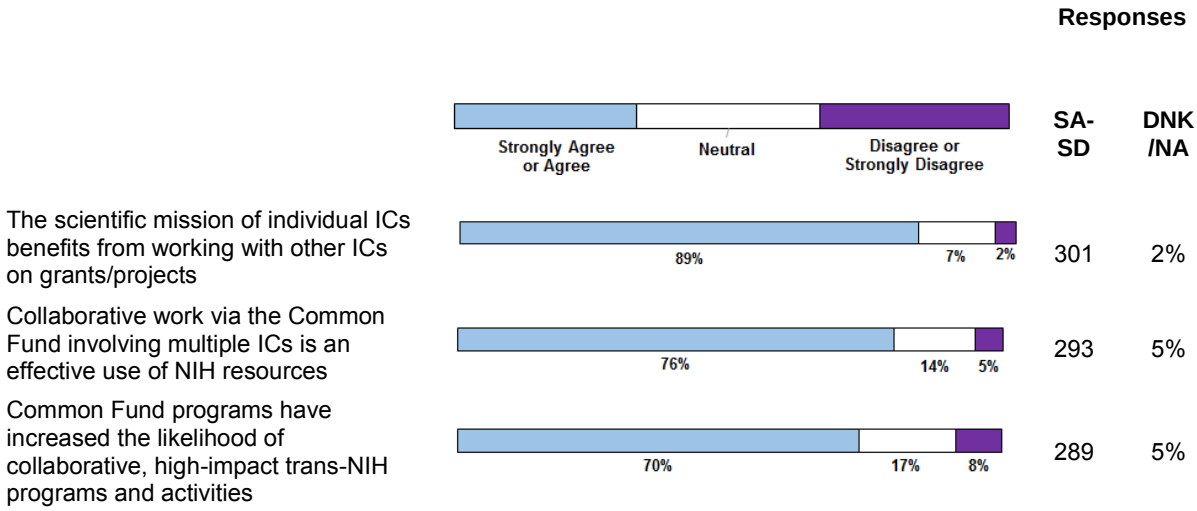

## IX. Is the value of the program worth the effort?

***Benefits and Impact of the Common Fund***

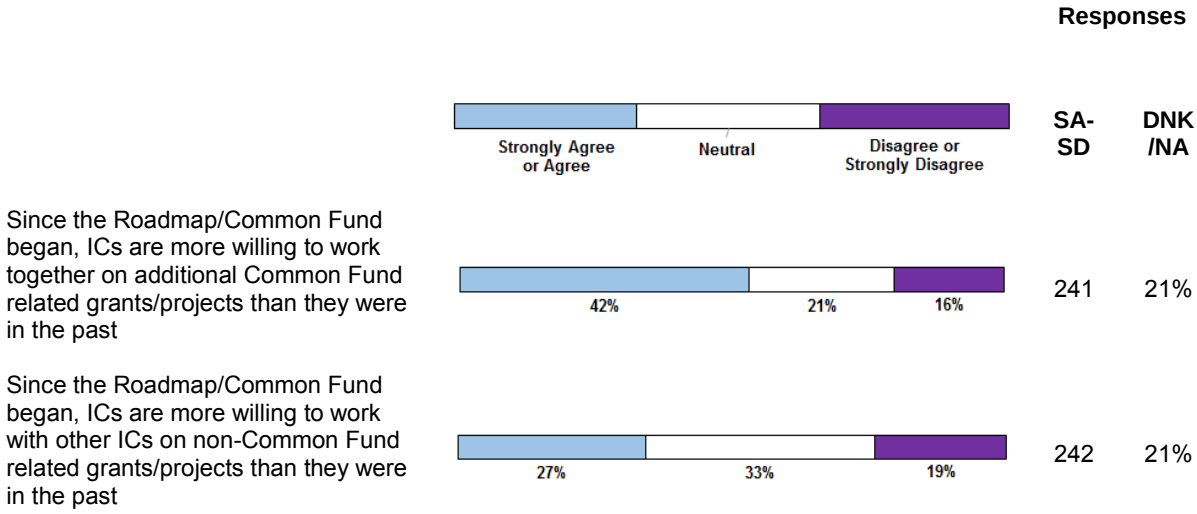
A majority of respondents strongly agree or agree that the strategic planning process results in NIH addressing areas of science that would not have been pursued otherwise (65%), while 18% felt neutral, and 12% strongly disagreed or disagreed with this statement. Similarly, the majority of respondents strongly agreed or agreed that the strategic planning process results in NIH identifying trans-NIH and trans-disciplinary initiatives that are relevant to all ICs (66%), while 18% felt neutral and 13% strongly disagreed or disagreed. Forty-seven percent of respondents strongly agreed or agreed that the process results in the NIH addressing research gaps relevant to all ICs, 29% were neutral, and 18% strongly disagreed or disagreed. Participants also strongly agreed or agreed that the process results in scientific initiatives that help advance their particular IC's mission (54%), while 23% responded neutral, and 13% strongly disagreed or disagreed.




Participants responded positively about the effect of the CF on collaboration across ICs. The overwhelming majority of respondents strongly agreed or agreed that their IC's mission benefits from working with other ICs on grants/projects (89%), 7% were neutral, and 2% strongly disagreed or disagreed. A large majority of respondents strongly agreed or agreed that collaborative work via the CF involving multiple ICs is an effective use of NIH resources (76%), 14% were neutral, and 5% strongly disagreed or disagreed. Similarly, a large majority felt that CF programs have increased the likelihood of collaborative, high-impact trans-NIH programs and activities (70%), 17% were neutral, and 8% were strongly disagree or disagreed.

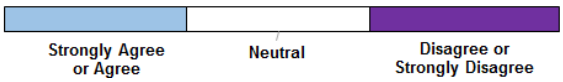


Forty-two percent of respondents strongly agreed or agreed that since the Roadmap/CF began, ICs are more willing to work together on additional CF related projects than they were in the past, 21% felt neutral, and 16% strongly disagreed or disagreed. Additionally, 27% strongly agreed or agreed that ICs are more willing to work with other ICs on non-CF related projects than they were in the past, 33% were neutral, and 19% strongly disagreed or disagreed. For both questions, 21% of participants reported that they either did not know or did not think the question was applicable to them.

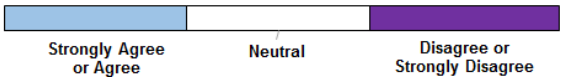



## ***Involvement in Common Fund Programs***

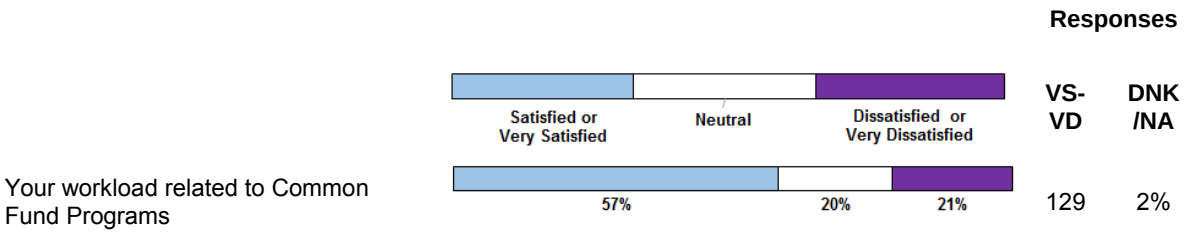
Respondents felt positively about their specific efforts in CF programs. Eighty-nine percent of participants strongly agreed or agreed that they are enthusiastic about the science of the CF programs they are or were involved in, only 6% were neutral, and 3% strongly disagreed or disagreed. Ninety-one percent of respondents strongly agreed or agreed that it is worth their effort to participate in a CF program, only 4% were neutral, and 5% strongly disagreed or disagreed. Seventy-five percent agreed that they felt encouraged to come up with better ways of doing things in their CF program, 10% were neutral, and 13% strongly disagreed or disagreed. Eighty-two percent strongly agreed or agreed that their CF responsibilities make good use of their skills and abilities, 10% were neutral, and 6% strongly disagreed or disagreed.

| | | Responses | |
|---|---|---|---|
| |  | SA-SD | DNK /NA |
| I am enthusiastic about the science of the Common Fund program in which I am or have been involved |  | 128 | 2% |
| It is worth my effort to participate in a Common Fund program |  | 128 | 1% |
| I feel encouraged to come up with better ways of doing things in my Common Fund program |  | 128 | 2% |
| My Common Fund program responsibilities makes good use of my skills and abilities |  | 128 | 2% |

Finally, 78% strongly agreed or agreed that their CF responsibilities give them the feeling of personal accomplishment, 12% were neutral, and 8% strongly disagreed or disagreed. Half of respondents strongly agreed or agreed that participation in a CF program had help them advance their career at NIH, while 30% felt neutral and 17% strongly disagreed or disagreed. However, respondents were more evenly split on whether NIH recognizes and rewards CF work that is well-done. Forty-four percent of respondents strongly agreed or agreed with that statement, 28% were neutral, and 22% strongly disagreed or disagreed.

| | | Responses | |
|---|---|---|---|
| |  | SA-SD | DNK /NA |
| My Common Fund program responsibilities give me the feeling of personal accomplishment |  | 128 | 2% |
| The NIH recognizes and rewards Common Fund work that is well-done |  | 123 | 5% |
| Participation in a Common Fund program has helped me to advance in my career at the NIH |  | 124 | 4% |

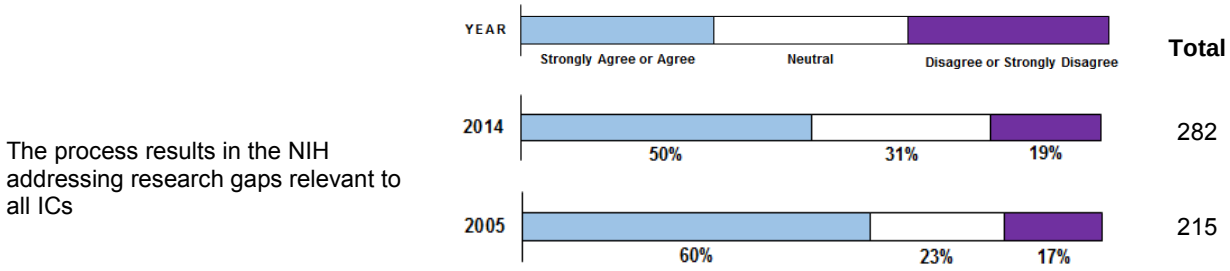
Fifty-seven percent of participants felt very satisfied or satisfied with their workload related to CF programs, 20% felt neutral, and 21% felt very dissatisfied or dissatisfied.



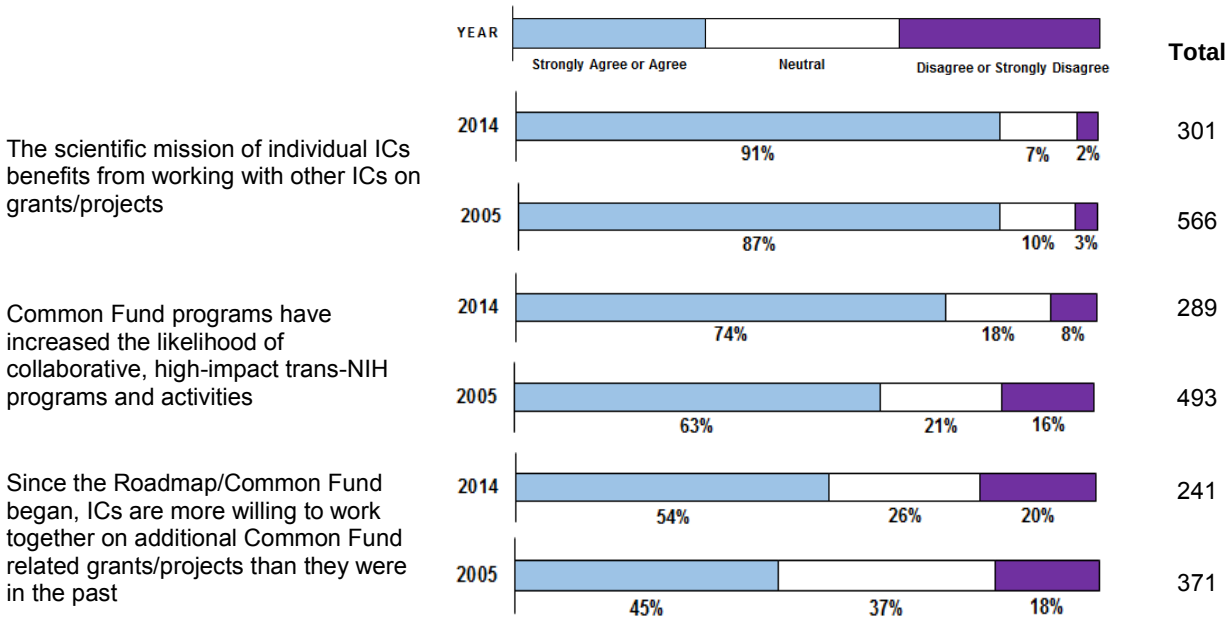

***Data Comparisons***

Several of the survey items related to this evaluation question were also part of the 2005 survey. In order to compare responses to the 2005 previous survey, "Do not know" and "Not applicable" responses were factored out of the responses in the 2014 survey. Highlights from comparison follow.

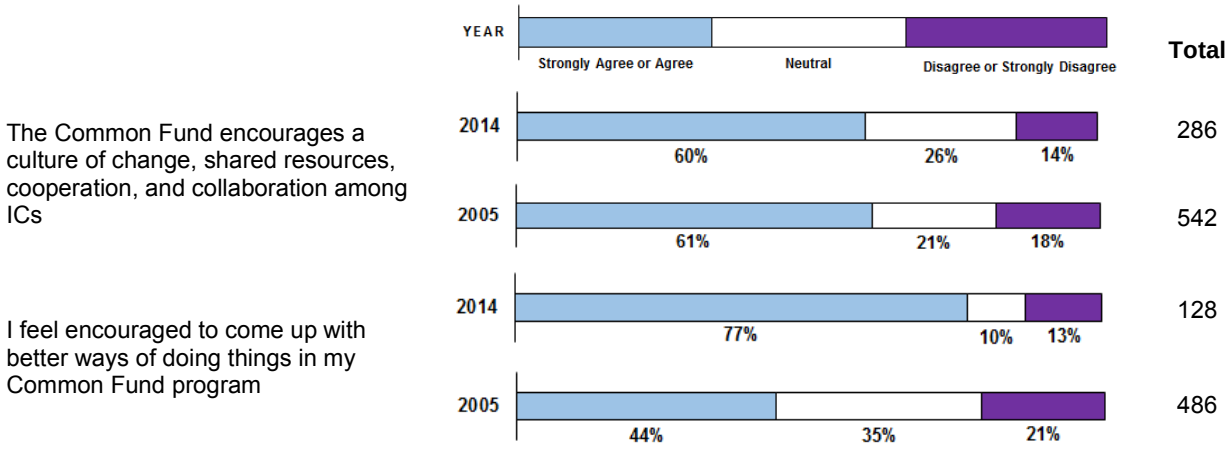
When comparing the data, there was a decrease in the percentage of people who agreed that the strategic planning process results in the NIH addressing research gaps relevant to all ICs, from 60% in 2005 to 50% in 2014. In 2005 only 23% of respondents felt neutral and 17% strongly disagreed or disagreed.




In both surveys, respondents overwhelmingly felt that their IC's mission benefited from work with other ICs on Roadmap and CF programs, and the percentage that strongly agreed or agreed with this statement increased slightly from 87% in 2005 to 91% in 2014. Seventy-four percent of respondents felt CF programs increased the likelihood of collaborative, high-impact trans-NIH programs and activities, as compared to 63% strongly agreeing or agreeing with this statement in 2005. Participants reported 54% agreement that since the Roadmap/Common Fund began, ICs are more willing to work together on additional CF related projects. This represents a small increase from 2005, where 45% of respondents strongly agreed or agreed, 37% were neutral, and 18% strongly disagreed or disagreed.

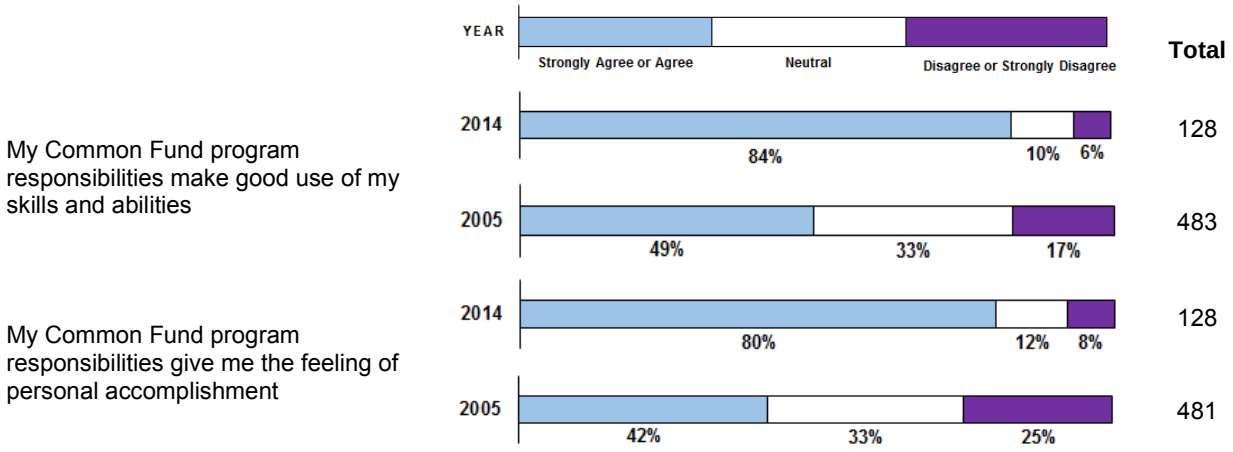



There was little change in participants' opinions of the effect that either the Roadmap or CF had on the culture of change, shared resources, cooperation, and collaboration among ICs. The majority of respondents were positive on the effect on both surveys. However, significantly higher percentages of respondents reported that they are encouraged to improve their CF program, feel their skills are well utilized, and feel personal accomplishment than in 2005. In 2014, 77% of respondents felt they are encouraged to come up with better ways of doing things in their CF program, compared to 44% in 2005.

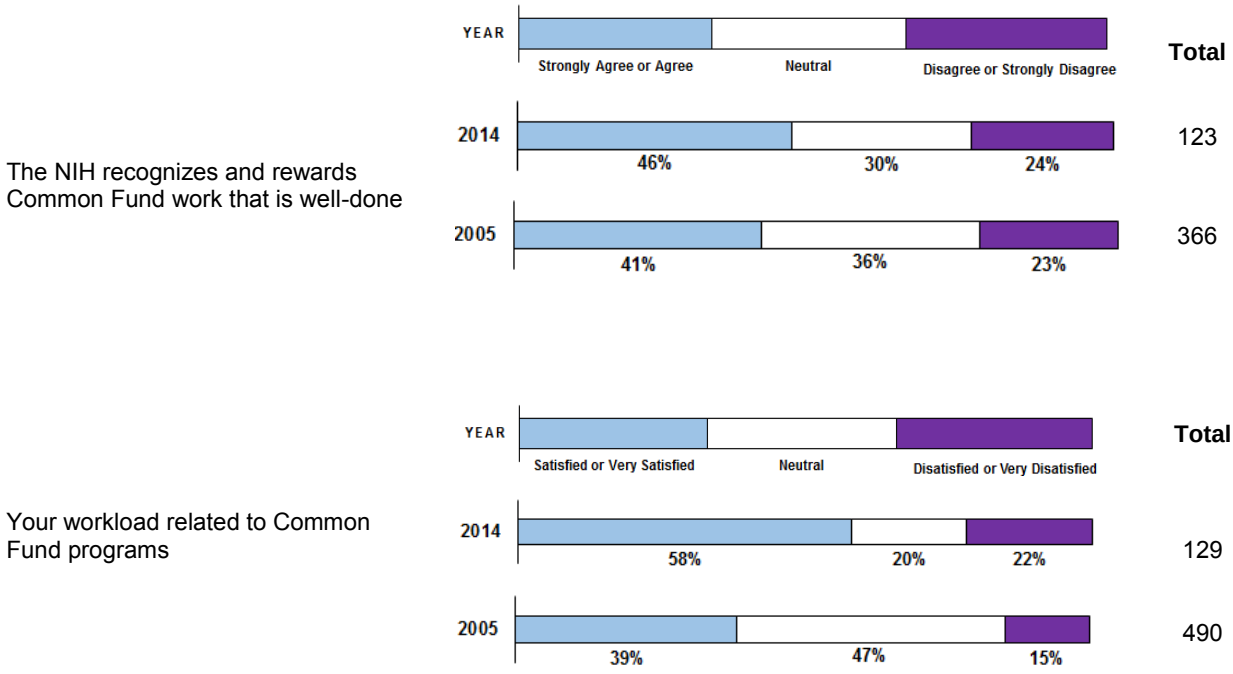



A much higher percentage of 2014 participants felt that their CF responsibilities made a good use of their skills and abilities (84%), than in 2005 (49%). Also, a smaller percentage (10%) chose neutral in 2014 than in 2005 (33%). Similarly, 80% of participants in 2014 felt their CF

responsibilities gave them a feeling of personal accomplishment, compared with only 42% of participants in 2005.




In 2014, 46% of respondents agreed that NIH recognizes and rewards CF work that is well done, compared to 41% who agreed with this statement in 2005. There was an increase in participants who were satisfied with their workload related to CF programs from 39% in 2005 to 58% in 2014. However, there was also a slight increase in participants who were dissatisfied with this aspect, from 15% in 2005 to 22% in 2014.

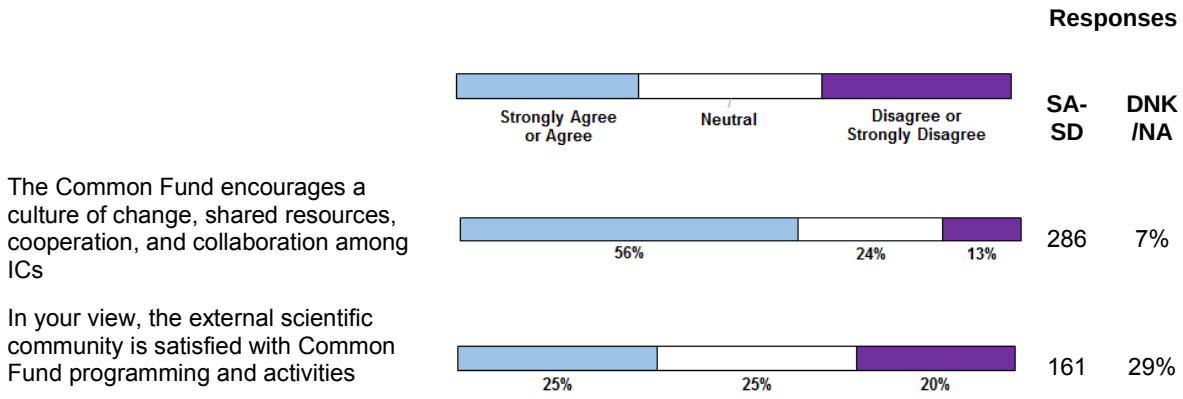


## X. Do IC Directors get appropriate amounts of information about CF programs and at an appropriate frequency?

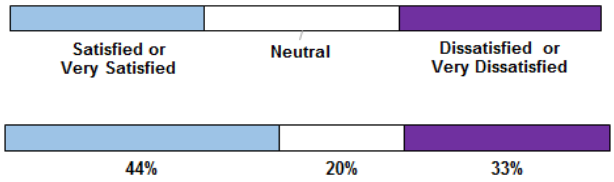
The survey did not specifically cover this topic.

## XI. Does participation by IC staff on CF Working Groups enable efficient information exchange with IC Directors, IC Councils, other IC staff, and IC research communities?

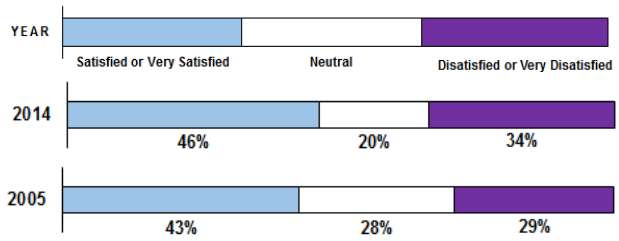
As noted in question IX, in 2014 higher percentages of respondents reported that they are encouraged to improve their CF program, feel their skills are well utilized, and feel personal accomplishment than in 2005. The majority of respondents (56%) felt that the CF encourages a culture of change and collaboration among ICs, 24% were neutral, and 13% strongly disagreed or disagreed. However, regarding the research community, respondents were not sure about the opinions of the external scientific community related to the CF. Twenty-five percent strongly agreed or agreed that the external scientific community was satisfied with CF program activities, another 25% were neutral, and 20% strongly disagreed or disagreed. Almost 30% of respondents reported that they did not know about the opinions of the external community or felt the question was not applicable.




When asked how satisfied they are with the information they receive from senior management about the CF, respondents were generally more satisfied than dissatisfied. Forty-four percent were very satisfied or satisfied with the information they receive, 33% were very dissatisfied or dissatisfied, and 20% were neutral.

| | | Responses | |
|---|---|---|---|
| | | VS-VD | DNK /NA |
| The information you receive from senior management about what is going on with the Common Fund |  | 127 | 3% |

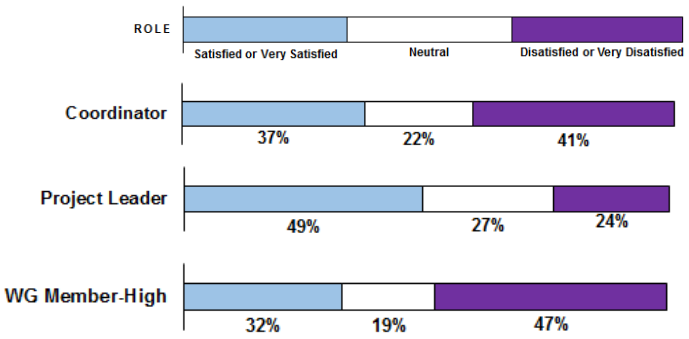
When the "Do not know" and "Not applicable" responses are factored out, the results are comparable to the 2005 survey. The number of participants who indicated they were very satisfied or satisfied increased slightly from 43% in 2005 to 46% in 2014. However, the number of dissatisfied responses also increased – from 29% in 2005 to 34% in 2014. The number of respondents who were neutral on the question decreased from 28% in 2005 to 20% in 2014.

| | | Total |
|---|---|---|
| The information you receive from senior management about what is going on with the Common Fund |  | 127<br>531 |

***<u>Comparison of Current Working Group members by roles.</u>***

As compared to Cooridnators and highly involved WG members, the Project Leaders were the most satisfied (49%) with the information they receive from the senior management about the Common Fund. Highly-involved WG members were least satisfied, with 47% being very dissatisfied or dissatisfied with information received, followed by the Coordinators (41%), and the Project Team Leaders (24%). Twenty-seven percent of the Project Team Leaders were neutral about this statement. Highly involved WG members chose very dissatisfied or dissatisfied (47%) more than the Coordinators (41%) and Project Team Leaders (24%). Finally, a higher percentage of Project Team Leaders chose neutral (27%) than Coordinators (22%) or highly involved WG members (19%).

The information you receive from senior management about what is going on with the Common Fund.

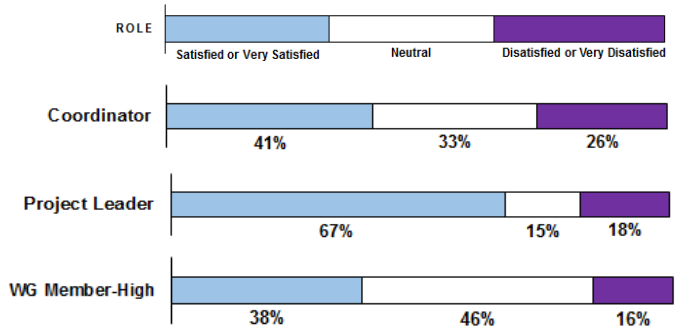



Total

97

The Project Leaders were the most satisfied (67%) with the guidance they receive to do their work, followed by the Coordinators (41%), and highly-involved WG members (38%). Coordinators were the least satisfied with guidance received (26%), followed by the Project Team Leaders (18%), and highly involved WG members (16%). A plurality of the highly-involved WG members responded neutrally (46%) about this statement.

The guidance you receive to do your work.

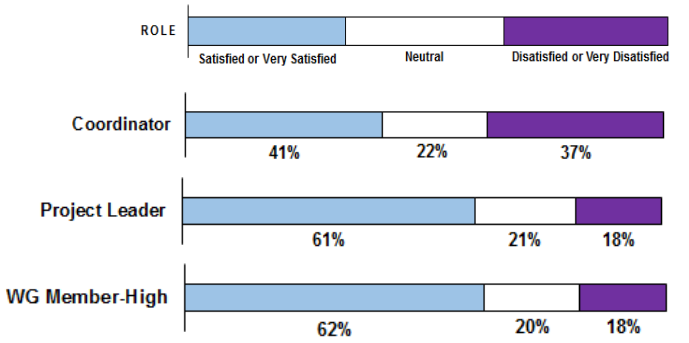



Total

97

Highly involved WG members were mostly satisfied with the work-load related to the CF Programs (62%), followed closely by the Project Leaders (61%), and then Cooridnators (41%). Thirty-seven percent of the Coordinators expressed dissatisfaction with the workload related to the CF programs, followed by Project Team Leaders and highly-involved WG members (18%).

Your workload related to Common Fund programs.




Total

99

# Appendix 1: 2014 NIH Common Fund Online Survey

**SECTION - INVOLMENT IN COMMON FUND PROGRAMS**

The following questions ask about your involvement and roles in Common Fund programs. Your answers to these questions will help us examine survey results by subgroups. Responses will **NOT** be used to identify individual respondents.

1, 1A, 2. Which best describes your current position at NIH?

| Responses | Frequency |
|---|---|
| IC Director | 10 (3%) |
| OSC Staff | 19 (6%) |
| Working Group (WG) members | 258 (79%) |
| Planning and Evaluation (P&E) Officer | 17 (5%) |
| Chief Grants Management Officer (CGMO) | 10 (3%) |
| Budget Point of Contact (BPOC) | 3 (1%) |
| Executive Officer (EO) | 9 (3%) |
| Total | 326 |

Note: ICD Directors, P&E Officers, OSC staff may also be Working Group members, but are only listed under their position in these counts.

3A. How long have you been involved with the Common Fund? *(answered by CGMOs, BPOCs, and EOs)*

| Number of Years | Frequency |
|---|---|
| Greater than or equal to 1, but less than 3 years | 2 (9%) |
| Greater than or equal to 3 years, but less than 5 years | 8 (36%) |
| Five or more years | 12 (54%) |
| Total | 22 |

4. Are you a currently a member of the Extramural Program Management Committee (EPMC)?
   a. Yes = 19
   b. No = 254

5. Which of the following best describes your involvement with the Common Fund (CF) Working Groups? *(answered by IC Directors, WG members, and P&E Officers who are WG members)*

| Membership Status | Frequency |
|---|---|
| I have never been a member of a CFWG | 57 (20%) |
| I am currently a member of one CFWG | 103 (36%) |
| I am currently a member of more than one CFWG | 79 (28%) |
| I am not a currently member of a CFWG, but I was previously a member | 41 (14%) |
| Don't know | 5 (2%) |
| Total | 285 |

5A. How long have you been a WG member of a Common Fund program? If you have been a member of more than one CF WG, please select the longest number of years you have been involved with any WG. *(answered by current WG members, n=182)*

| Number of Years | Frequency |
|---|---|
| Less than 1 year | 17 (9%) |
| Greater than or equal to 1, but less than 3 years | 63 (35%) |
| Greater than or equal to 3 years, but less than 5 years | 48 (27%) |
| Five or more years | 51 (28%) |
| Don't remember | 1 (1%) |
| Total | 180 |

5B. How long were you a WG member of the Roadmap/Common Fund program? If you were a member of more than one CF WG, please select the longest number of years you were involved with any WG. *(answered by past WG members, n=41)*

| Number of Years | Frequency |
|---|---|
| Less than 1 year | 4 (10%) |
| Greater than or equal to 1, but less than 3 years | 13 (32%) |
| Greater than or equal to 3 years, but less than 5 years | 14 (34%) |
| Five or more years | 6 (15%) |
| Don't remember | 4 (10%) |
| Total | 41 |

6. Which of the following best describes your current role in a CF WG? If you are a member of more than one WG, please list all the roles you hold. *(answered by current WG members)*

| Role in CF WG | Frequency |
|---|---|
| Co-Chair | 13 |
| Coordinator | 29 |
| Project Leader or Project Team Leader | 54 |
| Member/Other | 135 |

Note: Respondents could choose more than one role.

6A. Which of the following best describes your role in a CF WG? If you were a member of more than one WG, please list all the roles you held. *(answered by past WG members)*

| Role in CF WG | Frequency |
|---|---|
| Co-Chair | 1 |
| Coordinator | 2 |
| Project Leader or Project Team Leader | 6 |
| Member/Other | 36 |

Note: Respondents could choose more than one role.

| Working Group Role | Current member of one CF WG | Current member of more than one CF WG | Not a current member of a CF WG, but was previously a member | Total |
|---|---|---|---|---|
| Current Co-Chair | 4 | 9 | 0 | 13 |
| Current Coordinator | 13 | 16 | 0 | 29 |
| Current Project Leader | 16 | 19 | 0 | 35 |
| Current Member – High | 28 | 14 | 0 | 42 |
| Current Member – Low | 41 | 21 | 0 | 62 |
| Past Co-Chair | 0 | 0 | 1 | 1 |
| Past Coordinator | 0 | 0 | 2 | 2 |
| Past Project Leader | 0 | 0 | 6 | 6 |
| Past Member | 0 | 0 | 32 | 32 |
| Total | 102 | 79 | 41 | 222 |

6B. How would you rate your level of involvement in the Working Group(s) – Scale from 1-10? *(answered by current WG members who are not in leadership positions)*

| Level of Involvement | Frequency |
|---|---|
| Low Involvement | 62 (60%) |
| High Involvement | 42 (41%) |
| Total | 104 |

Note: Low involvement = self-rated from 1-6; High involvement = self-rated from 7-10

Please comment on the factors that encourage or discourage your participation in Common Fund programs.

## SECTION - MAIN SURVEY CONTENT

**SECTION - OVERALL IMPRESSION OF STRATEGIC PLANNING PROCESS** *(Answered by IC Directors, P&E Officers, OSC Staff, and WG Members; Target Audience = 304)*

**7. This section focuses on your overall impression of the Common Fund strategic planning process and the scientific initiatives that resulted from the process. Please keep the process illustrated in the figure below in mind when responding to the questions.**


| **Please rate your <u>agreement</u> with the following statements:** | | | | | |
|---|---|---|---|---|---|
| a. The process is guided by a clear set of goals, objectives, and procedures | 153 (51%) | 65 (22%) | 54 (18%) | 30 (10%) | 302 |
| b. The process provides adequate time to consider and develop scientific initiatives | 124 (41%) | 72 (24%) | 69 (23%) | 38 (12%) | 303 |
| c. The process results in a carefully considered prioritization of the proposed scientific initiatives | 120 (40%) | 77 (26%) | 70 (23%) | 34 (11%) | 301 |

| | | | | | |
|---|---|---|---|---|---|
| d. The process results in the NIH addressing areas of science that would not have been pursued otherwise, including research opportunities relevant to all ICs | 196 (65%) | 54 (18%) | 35 (12%) | 16 (5%) | 301 |
| e. The process results in the NIH identifying trans-NIH and trans-disciplinary initiatives that are relevant to all ICs | 198 (66%) | 53 (18%) | 38 (13%) | 13 (4%) | 302 |
| f. The process results in the NIH addressing research gaps relevant to all ICs | 141 (47%) | 87 (29%) | 55 (18%) | 18 (6%) | 301 |
| g. The process results in scientific initiatives that help advance the mission of my IC. | 164 (54%) | 68 (23%) | 38 (13%) | 31 (10%) | 301 |
| **How satisfied are you with:** | **Very Satisfied/ Satisfied** | **Neutral** | **Dissatisfied/ Very Dissatisfied** | **Not Applicable** | **Total** |
| a. Your level of participation in the planning process | 135 (45%) | 72 (24%) | 53 (18%) | 38 (13%) | 298 |
| b. The pace and length of time provided for the overall planning process | 106 (35%) | 94 (31%) | 66 (22%) | 34 (11%) | 300 |
| c. The overall Common Fund strategic planning process, considering everything from inception to Director approval | 96 (32%) | 95 (32%) | 76 (25%) | 33 (11%) | 300 |

**7A. Has your IC ever submitted ideas for Common Fund Programs?** *(Answered by IC Directors, P&E Officers, and WG Members; Target Audience = 285)*

| Responses | Frequency |
|---|---|
| Yes | 192 (69%) |
| No | 19 (7%) |
| I Don't Know | 67 (24%) |
| Total | 278 |

**7b. Please describe the process your IC uses to submit ideas for Common Fund Programs.**

**7c. Please comment on the reasons your IC has not submitted ideas for Common Fund Programs.**

**8. This section focuses on different aspects of the strategic planning process.** *(Answered by IC Directors, P&E Officers, OSC Staff, and WG Members; Target Audience = 304)*

| **Please rate your level of satisfaction with the following:** | **Very Satisfied/ Satisfied** | **Neutral** | **Dissatisfied/ Very Dissatisfied** | **Not Applicable** | **Total** |
|---|---|---|---|---|---|
| a. The process for soliciting ideas from the ICs | 106 (36%) | 90 (30%) | 60 (20%) | 40 (14%) | 296 |
| b. The initial one-page template to submit ideas for new programs | 134 (45%) | 83 (28%) | 26 (9%) | 53 (18%) | 296 |
| c. The prioritization process for selecting a few ideas for further development | 74 (25%) | 96 (32%) | 75 (25%) | 50 (17%) | 295 |
| d. The Council of Councils' role in concept clearance | 89 (30%) | 121 (41%) | 32 (11%) | 53 (18%) | 295 |
| e. The information you received on the outcome of concept clearance of ideas | 73 (25%) | 68 (23%) | 101 (34%) | 53 (18%) | 295 |

**8a. Has your IC ever been involved in program planning after Working Groups are formed to refine cleared concepts into program proposals?** *(Answered by IC Directors, P&E Officers, and WG Members; Target Audience = 285)*

| Response | Frequency |
|---|---|
| Yes | 166 (61%) |
| No | 19 (7%) |
| I Don't Know | 87 (32%) |
| Total | 272 |

**8b. This section focuses on the process of refining cleared concepts into program proposal.***(Answered by OSC Staff and WG members; Target Audience = 186)*

| Please rate your level of satisfaction with the following: | Very Satisfied/ Satisfied | Neutral | Dissatisfied/ Very Dissatisfied | Not Applicable | Total |
|---|---|---|---|---|---|
| f. Your individual level of participation in program planning after Working Groups are formed to refine cleared concepts into program proposals | 108 (59%) | 27 (15%) | 18 (10%) | 29 (16%) | 182 |
| g. Your IC's level of participation in program planning after Working Groups are formed to refine cleared concepts into program proposals | 110 (61%) | 34 (19%) | 22 (12%) | 15 (8%) | 181 |
| h. The process to refine the broad program ideas into a proposal containing specific initiatives | 105 (58%) | 42 (23%) | 20 (11%) | 14 (8%) | 180 |
| i. The length of the time provided to refine the broad program ideas into a proposal containing specific initiatives | 83 (46%) | 47 (26%) | 37 (21%) | 13 (7%) | 180 |
| j. The level of detail requested in the proposal that is submitted to OSC | 100 (56%) | 45 (25%) | 19 (11%) | 14 (8%) | 178 |
| k. The decision making process for approving proposals to become Common Fund programs | 60 (33%) | 56 (31%) | 54 (30%) | 10 (6%) | 180 |

**9. This section focuses on portfolio analysis and the decision making process for new Common Fund programs. .***(Answered by OSC Staff and WG members; Target Audience = 186)*

| Please rate your agreement with the following statements: | Strongly Agree/ Agree | Neutral | Disagree/ Strongly Disagree | Do Not Know or N/A | Total |
|---|---|---|---|---|---|
| a. It is critical to conduct portfolio analysis during the planning phase | 164 (89%) | 14 (8%) | 4 (2%) | 2 (1%) | 184 |
| b. The NIH resources (e.g., tools, staff, guidance) available to conduct portfolio analysis are adequate | 75 (41%) | 40 (22%) | 56 (30%) | 13 (7%) | 184 |
| c. The length of time to conduct portfolio analysis is adequate | 69 (38%) | 54 (29%) | 37 (20%) | 24 (13%) | 184 |
| d. The length of time to solicit input from the scientific community to further refine broad program ideas is adequate | 67 (37%) | 52 (29%) | 42 (23%) | 21 (12%) | 182 |

| | | | | | |
|---|---|---|---|---|---|
| e. The decision making process for approving Common Fund programs is transparent – everyone understands the process and how decisions are made | 32 (18%) | 36 (20%) | 106 (59%) | 6 (3%) | 180 |
| f. The process for selecting new CF programs allows adequate input by IC Directors | 3 (33%) | 2 (22%) | 4 (44%) | 0 | 9 (Answered by IC Directors) |
| g. The process results in clearly articulated goals and milestones for CF programs | 78 (43%) | 55 (30%) | 42 (23%) | 6 (3%) | 181 |
| h. What is your overall impression of the Common Fund planning process?<br><br>i. What suggestions do you have for improving the Common Fund **strategic** planning process? | | | | | |

**SECTION - COLLABORATION** *(Answered by all groups; Target Audience = 326)*

**10. This section focuses on your own work experiences or personal opinion about collaboration within NIH and the changing culture.**

| **Please rate your <u>agreement</u> with the following statements:** | **Strongly Agree/ Agree** | **Neutral** | **Disagree/ Strongly Disagree** | **Not Applicable** | **Total** |
|---|---|---|---|---|---|
| a. The scientific mission of individual ICs benefits from working with other ICs on grants/projects | 274 (89%) | 22 (7%) | 5 (2%) | 7 (2%) | 308 |
| b. Collaborative work via the Common Fund involving multiple ICs is an effective use of NIH resources | 233 (76%) | 43 (14%) | 17 (5%) | 14 (5%) | 307 |
| c. Common Fund programs have increased the likelihood of collaborative, high-impact trans-NIH programs and activities | 214 (70%) | 51 (17%) | 24 (8%) | 17 (6%) | 306 |
| d. Since the Roadmap/Common Fund began, ICs are more willing to work together on additional Common Fund related grants/projects than they were in the past | 130 (42%) | 63 (21%) | 48 (16%) | 65 (21%) | 306 |
| e. Since the Roadmap/Common Fund began, ICs are more willing to work with other ICs on non-Common Fund related grants/projects than they were in the past | 82 (27%) | 101 (33%) | 59 (19%) | 64 (21%) | 306 |
| f. The Common Fund encourages a culture of change, shared resources, cooperation, and collaboration among ICs | 171 (56%) | 74 (24%) | 41 (13%) | 21 (7%) | 307 |
| g. Please provide any comments you have about your own experiences or personal opinion about working with other ICs on CF programs. | | | | | |

**SECTION - PERCEPTION OF THE EXTERNAL COMMUNITY ABOUT THE COMMON FUND** *(Answered by IC Directors, P&E Officers, OSC Staff, WG members – high involvement; Target Audience = 240)*

**11. This section focuses on the perception of the external community about the Common Fund.**

| **Please rate your <u>agreement</u> with the following statements:** | **Strongly Agree/ Agree** | **Neutral** | **Disagree/ Strongly Disagree** | **Not Applicable** | **Total** |
|---|---|---|---|---|---|

| | | | | | |
|---|---|---|---|---|---|
| a. In your view, the external scientific community is satisfied with Common Fund programming and activities | 57 (25%) | 58 (25%) | 46 (20%) | 67 (29%) | 228 |

**SECTION - OSC Organizational Structure and roles of OSC staff** *(Answered by OSC Staff, IC Directors, WG Co-chairs, WG Coordinators, WG Project Team Leaders, WG Members (Highly Involved); Target Audience =138)*

**12. This section focuses on communications and support you receive from OSC staff, not the Common Fund Working Groups.**

**The NIH Common Fund is overseen by the Office of Strategic Coordination (OSC). OSC is housed within the Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI), Office of the Director (OD), National Institutes of Health (NIH). DPCPSI was created as a result of the 2006 NIH Reform Act.**

| **Please rate your agreement with the following statements:** | **Strongly Agree/ Agree** | **Neutral** | **Disagree/ Strongly Disagree** | **Not Applicable** | **Total** |
|---|---|---|---|---|---|
| a. The OSC organizational structure is clear to me and others | 36 (28%) | 30 (23%) | 59 (45%) | 6 (5%) | 131 |
| b. The OSC promotes communication among IC staff working on Common Fund programs | 67 (51%) | 42 (32%) | 13 (10%) | 9 (7%) | 131 |
| c. The OSC provides adequate governance for Common Fund programming and activities | 59 (45%) | 39 (30%) | 25 (19%) | 8 (6%) | 131 |
| d. The OSC promotes an environment supportive of NIH staff collaboration on Common Fund programming and activities | 70 (54%) | 32 (25%) | 22 (17%) | 6 (5%) | 130 |
| e. The role of DPCPSI Director is clear to me and others | 43 (33%) | 27 (21%) | 52 (40%) | 7 (5%) | 129 |
| f. The role of OSC Director is clear to me and others | 42 (33%) | 27 (21%) | 53 (41%) | 7 (5%) | 129 |
| g. The role of OSC Program Directors is clear to me and others | 56 (43%) | 26 (20%) | 42 (32%) | 6 (5%) | 130 |
| h. The role of the OSC Grants Management staff is clear to me and others | 40 (31%) | 24 (19%) | 54 (42%) | 10 (8%) | 128 |
| i. The role of the OSC Budget staff is clear to me and others | 53 (41%) | 25 (19%) | 41 (32%) | 10 (8%) | 129 |
| j. The role of the OSC Communication staff is clear to me and others | 47 (36%) | 27 (21%) | 42 (33%) | 12 (9%) | 128 |
| k. What aspects of OSC organizational structure are working well? | | | | | |
| l. What suggestions do you have for improving the OSC organizational structure? | | | | | |

**SECTION - WORKING GROUP STRUCTURE** *(Answered by OSC Staff, IC Directors, WG Co-chairs, WG Coordinators, WG Project Team Leaders, WG Members (Highly Involved); Target Audience =138)*

**14. This section focuses on the Common Fund Working Groups structure. When responding to this question, think about your overall experience as a member of one or more Working Groups.**

| **Please rate your agreement with the following statements:** | **Strongly Agree/ Agree** | **Neutral** | **Disagree/ Strongly Disagree** | **Do Not Know or N/A** | **Total** |
|---|---|---|---|---|---|
| a. The Working Group structure (e.g., Co-Chairs, Coordinator, Budget Point of Contact, Communication Point of Contact, and Project Leader) is effective in meeting the scientific goals of the program | 95 (73%) | 24 (19%) | 7 (5%) | 4 (3%) | 130 |

| | | | | | |
|---|---|---|---|---|---|
| b. The Working Group structure (e.g., Co-Chairs, Coordinator, Budget Point of Contact, Communication Point of Contact, and Project Lead) is effective for managing the program | 87 (67%) | 25 (19%) | 12 (9%) | 6 (5%) | 130 |
| c. The roles and responsibilities of Working Group members are clear | 77 (59%) | 29 (22%) | 20 (15%) | 4 (3%) | 130 |
| d. The process for establishing Working Group membership is effective | 60 (46%) | 37 (28%) | 26 (20%) | 7 (5%) | 130 |
| e. What is your overall impression of the Common Fund Working Group structure? | | | | | |
| f. What suggestions do you have for improving the Common Fund Working Group structure? | | | | | |

**15. This section focuses on communications between OSC and the Working Groups. Think about your role in one or more Working Groups, and your overall experience working with OSC.**

| **Please rate your <u>agreement</u> with the following statements.** | **Strongly Agree/ Agree** | **Neutral** | **Disagree/ Strongly Disagree** | **Not Applicable** | **Total** |
|---|---|---|---|---|---|
| a. OSC guidance for the formation of Working Groups is sufficient | 44 (34%) | 45 (34%) | 26 (20%) | 15 (12%) | 130 |
| b. OSC programmatic/scientific guidance is relevant | 61 (47%) | 39 (30%) | 19 (15%) | 10 (8%) | 129 |
| c. OSC programmatic/scientific guidance is timely | 55 (43%) | 41 (32%) | 23 (18%) | 10 (8%) | 129 |
| d. OSC gives an appropriate amount of programmatic/scientific guidance | 55 (43%) | 36 (28%) | 29 (22%) | 9 (7%) | 129 |
| e. OSC programmatic/scientific guidance is clear | 49 (38%) | 40 (31%) | 30 (23%) | 9 (7%) | 128 |
| f. The OSC allows for a rapid response to changing scientific landscapes | 47 (36%) | 42 (33%) | 29 (22%) | 11 (8%) | 129 |
| g. Information conveyed from the Office of the Director to the Working Group is appropriate | 53 (41%) | 37 (29%) | 23 (18%) | 16 (12%) | 129 |
| h. Information conveyed from the Office of the Director to the Working Group is timely | 42 (33%) | 48 (37%) | 24 (19%) | 15 (12%) | 129 |
| i. OSC is available to answer questions when needs arise | 88 (69%) | 19 (15%) | 11 (9%) | 10 (8%) | 128 |
| j. Working Group feels comfortable asking OSC for programmatic/scientific guidance | 72 (56%) | 30 (23%) | 18 (14%) | 9 (7%) | 129 |
| k. OSC staff provide informative and useful answers to questions | 72 (56%) | 36 (28%) | 13 (10%) | 8 (6%) | 129 |
| l. OSC policies and procedures for managing Common Fund programs are clear | 42 (33%) | 36 (28%) | 38 (30%) | 11 (9%) | 127 |
| m. What is your overall impression of communication between OSC and the CF Working Groups? | | | | | |

**16. This section focuses on your <u>personal experience with Common Fund programs.</u> Think about your role in one or more Working Groups, and your <u>overall experience</u> working with the Common Fund.**

| **Please rate your <u>agreement</u> with the following statements:** | **Strongly Agree/ Agree** | **Neutral** | **Disagree/ Strongly Disagree** | **Not Applicable** | **Total** |
|---|---|---|---|---|---|
| a. I am enthusiastic about the science of the Common Fund program in which I am or have been involved | 116 (89%) | 8 (6%) | 4 (3%) | 2 (2%) | 130 |
| b. It is worth my effort to participate in a Common Fund program | 117 (91%) | 5 (4%) | 6 (5%) | 1 (1%) | 129 |
| c. I feel encouraged to come up with better ways of doing things in my Common Fund program | 98 (75%) | 13 (10%) | 17 (13%) | 2 (2%) | 130 |

| | | | | | |
|---|---|---|---|---|---|
| d. My Common Fund program responsibilities makes good use of my skills and abilities | 107 (82%) | 13 (10%) | 8 (6%) | 2 (2%) | 130 |
| e. My Common Fund program responsibilities give me the feeling of personal accomplishment | 102 (78%) | 16 (12%) | 10 (8%) | 2 (2%) | 130 |
| f. The NIH recognizes and rewards Common Fund work that is well-done | 57 (44%) | 37 (28%) | 29 (22%) | 7 (5%) | 130 |
| g. Participation in-a Common Fund program has helped me to advance in my career at the NIH | 64 (50%) | 38 (30%) | 22 (17%) | 5 (4%) | 129 |
| h. There are adequate incentives to participate in the Common Fund programs | 53 (41%) | 36 (28%) | 33 (26%) | 7 (5%) | 129 |
| i. Please comment on the factors that encourage or discourage your participation in Common Fund programs | | | | | |

**SECTION - SATISFACTION** *(Answered by OSC Staff, IC Directors, WG Co-chairs, WG Coordinators, WG Project Team Leaders, WG Members (Highly Involved); Target Audience =138)*

**17. This section focuses on the information you receive and the time you spent on Common Fund program activities. Think about your role in one or more Working Groups, and your overall experience working with the Common Fund.**

| **Please rate your satisfaction with the following items:** | **Very Satisfied/ Satisfied** | **Neutral** | **Dissatisfied/ Very Dissatisfied** | **Not Applicable** | **Total** |
|---|---|---|---|---|---|
| a. The information you receive from senior management about what is going on with the Common Fund | 58 (44%) | 26 (20%) | 43 (33%) | 4 (3%) | 131 |
| b. The guidance you receive to do your work | 69 (54%) | 35 (27%) | 23 (18%) | 1 (1%) | 127 |
| c. Your workload related to Common Fund programs | 75 (57%) | 26 (20%) | 28 (21%) | 2 (2%) | 131 |

**SECTION - GRANTS MANAGEMENT PROCESSES** *(Answered by WG Coordinators, WG Project Team Leaders, Grants Management Officers, OSC Staff; Target Audience = 113)*

**18. This section focuses on the grants management processes of Common Fund programs. Think about your role in one or more Working Groups, and your overall experience working with the Common Fund.**

| **Please rate your agreement with the following statements:** | **Strongly Agree/ Agree** | **Neutral** | **Disagree/ Strongly Disagree** | **Not Applicable** | **Total** |
|---|---|---|---|---|---|
| a. The process for developing, approving, and issuing FOAs for the Common Fund is clear | 51 (54%) | 17 (18%) | 20 (21%) | 6 (6%) | 94 |
| b. The Chief Grants Management Officer at the lead IC is involved at an appropriate point in the FOA development process to contribute effectively | 40 (43%) | 25 (27%) | 14 (15%) | 14 (15%) | 93 |
| c. The guidance that OSC provides during the FOA development process is timely | 45 (48%) | 22 (23%) | 15 (16%) | 12 (13%) | 94 |
| d. The guidance that OSC provides during the FOA development process is clear | 43 (46%) | 22 (24%) | 16 (17%) | 12 (13%) | 93 |
| e. With respect to Common Fund FOAs, there are clear procedures for establishing the funding plan | 55 (58%) | 16 (17%) | 13 (14%) | 10 (11%) | 94 |
| f. The process to request Common Fund- supported administrative supplements is clear | 42 (45%) | 25 (27%) | 16 (17%) | 11 (12%) | 94 |
| g. The paylist sent by OSC provides adequate authority and information to award CF grants | 44 (47%) | 24 (26%) | 6 (6%) | 19 (20%) | 93 |

| |
|---|
| h. What is your overall impression of the Common Fund Grants Management processes? |
| i. What suggestions do you have for improving the Common Fund Grants Management processes? |

**SECTION - BUDGET MANAGEMENT PROCESSES** *(Answered by WG Coordinators, BOs, EOs, OSC Staff; Target Audience = 61 )*

**19. This section focuses on the budget processes of Common Fund programs. Think about your role in one or more Working Groups, and your overall experience working with the Common Fund.**

| Please rate your agreement with the following statements: | Strongly Agree/ Agree | Neutral | Disagree/ Strongly Disagree | Not Applicable | Total |
|---|---|---|---|---|---|
| a. The current budget management processes for Common Fund programs work well | 30 (52%) | 20 (34%) | 5 (9%) | 3 (5%) | 58 |
| b. The procedures used in developing the annual operating budget for a Common Fund program are clear | 25 (43%) | 17 (29%) | 14 (24%) | 2 (3%) | 58 |
| c. The procedures for FTE loans are clear | 22 (39%) | 15 (26%) | 10 (18%) | 10 (18%) | 57 |
| d. The guidance that OSC provides on the budget is timely | 28 (48%) | 18 (31%) | 7 (12%) | 5 (9%) | 58 |
| e. The guidance that OSC provides on the budget is clear | 30 (52%) | 14 (24%) | 9 (16%) | 5 (9%) | 58 |
| f. Common Fund reimbursement provided to ICs through Interagency Agreements for managing a Common Fund program works well for my IC | 25 (44%) | 11 (19%) | 3 (5%) | 18 (32%) | 57 |
| g. Common Fund Budget Reports currently available to the ICs are helpful | 28 (49%) | 13 (23%) | 7 (12%) | 9 (16%) | 57 |
| h. The Strategic Initiative Database allows Working Group members to easily access budget data for Common Fund programs | 20 (35%) | 12 (21%) | 11 (19%) | 14 (25%) | 57 |
| i. What is your overall impression of the Common Fund Budget processes? | | | | | |
| j. What suggestions do you have for improving the Common Fund Budget processes? | | | | | |

**SECTION - COMMON FUND RESOURCE USE** *(Answered by OSC Staff, WG Coordinators, WG Project Team Leaders, WG Members (Highly Involved), GMOs, BPOCs; Target Audience =138)*

| CF Resource Use | Yes | No | Don't Know | Total |
|---|---|---|---|---|
| Common Fund SharePoint | 66 (51%) | 55 (42%) | 9 (7%) | 130 |
| Common Fund Handbook | 50 (39%) | 66 (52%) | 12 (9%) | 128 |
| Common Fund website | 65 (50%) | 60 (46%) | 4 (3%) | 129 |
| Common Fund portion of QVR | 40 (31%) | 81 (63%) | 7 (6%) | 128 |
| All Hands Meetings | 78 (61%) | 45 (35%) | 5 (4%) | 128 |

| CF Resource Use | Very Helpful | Somewhat Helpful | Not Helpful | Total |
|---|---|---|---|---|
| SharePoint | 19 (29%) | 42 (65%) | 4 (6%) | 65 |
| Common Fund Handbook | 24 (48%) | 26 (52%) | 0 | 50 |
| Common Fund website | 35 (54%) | 29 (45%) | 1(2%) | 63 |
| Common Fund portion of QVR | 26 (65%) | 14 (35%) | 0 | 40 |
| All Hands Meetings | 22 (29%) | 44 (57%) | 11 (14%) | 77 |

Note: Only those who answered Yes to the questions above responded to these questions.

**5b. What suggestions do you have to improve the All Hands Meetings?**

**SECTION - IC Staff Working on Common Fund programs** *(Answered by EOs; Target Audience = 9)*
**This section is about your experience when a supervisor has approached you regarding their staff who work on CF programs.**

1. Please comment on whether supervisors receive adequate information for the activities of their staff in the following areas:
a. Travel approvals -
b. Performance reviews
c. Workload balance

2. Are supervisors of IC staff who are engaged in CF programs involved in the CF programs themselves?

**SECTION - CLOSING QUESTIONS** *(Answered by all groups; Target Audience = 326)*

1. How long have you worked at NIH?

| Number of Years | Frequency |
|---|---|
| Less than 1 yr. | 7 (2%) |
| 1 to 3 yrs. | 21 (7%) |
| 4 to 5 yrs. | 24 (8%) |
| 6 to 10 yrs. | 69 (23%) |
| 11 to 15 yrs. | 71 (24%) |
| 16 to 20 yrs. | 31 (10%) |
| 21 to 25 yrs. | 30 (10%) |
| 26 to 30 yrs. | 27 (9%) |
| 31+ yrs. | 17 (5%) |
| Total | 297 |

2. Have you been continually involved in the Roadmap/Common Fund programs since FY 2004?

| Continually Involved in CF | |
|---|---|
| Yes | 81 (27%) |
| No | 209 (71%) |
| I don't remember | 6 (2%) |
| Total | 296 |

3. Did you participate in the 2005 Roadmap Planning and Implementation Survey?

| 2005 Survey Participation | Frequency |
|---|---|
| Yes | 29 (10%) |
| No | 192 (65%) |
| I don't remember | 76 (26%) |
| Total | 297 |

4. Have you ever served in any of the following capacities for a Common Fund Award? *(Answered by Working Group Members; Target Audience =275 )*

5. In which Common Fund Programs have you been involved?

6. What is your IC?

# Appendix 2: 2014 NIH Common Fund Online Survey (With Do Not Know & Not Applicable Responses Factored Out)

**SECTION - MAIN SURVEY CONTENT**

**SECTION - OVERALL IMPRESSION OF STRATEGIC PLANNING PROCESS** *(Answered by IC Directors, P&E Officers, OSC Staff, and WG Members; Target Audience = 304)*

**7. This section focuses on your overall impression of the Common Fund strategic planning process and the scientific initiatives that resulted from the process. Please keep the process illustrated in the figure below in mind when responding to the questions.**


| **Please rate your <u>agreement</u> with the following statements:** | **Strongly Agree/ Agree** | **Neutral** | **Disagree/ Strongly Disagree** | **Total** |
|---|---|---|---|---|
| a. The process is guided by a clear set of goals, objectives, and procedures | 153 (56%) | 65 (24%) | 54 (20%) | 272 |
| b. The process provides adequate time to consider and develop scientific initiatives | 124 (47%) | 72 (27%) | 69 (26%) | 265 |
| c. The process results in a carefully considered prioritization of the proposed scientific initiatives | 120 (45%) | 77 (29%) | 70 (26%) | 267 |
| d. The process results in the NIH addressing areas of science that would not have been pursued otherwise, including research opportunities relevant to all ICs | 196 (69%) | 54 (19%) | 35 (12%) | 285 |
| e. The process results in the NIH identifying trans-NIH and trans-disciplinary initiatives that are relevant to all ICs | 198 (68%) | 53 (18%) | 38 (13%) | 289 |
| f. The process results in the NIH addressing research gaps relevant to all ICs | 141 (50%) | 87 (31%) | 55 (19%) | 283 |
| g. The process results in scientific initiatives that help advance the mission of my IC. | 164 (61%) | 68 (25%) | 38 (14%) | 270 |

| **How satisfied are you with:** | **Very Satisfied/ Satisfied** | **Neutral** | **Dissatisfied/Very Dissatisfied** | **Total** |
|---|---|---|---|---|
| a. Your level of participation in the planning process | 135 (52%) | 72 (28%) | 53 (20%) | 260 |
| b. The pace and length of time provided for the overall planning process | 106 (40%) | 94 (35%) | 66 (25%) | 266 |
| c. The overall Common Fund strategic planning process, considering everything from inception to Director approval | 96 (36%) | 95 (36%) | 76 (29%) | 267 |
| **Please rate your level of <u>satisfaction</u> with the following:** | **Very Satisfied/ Satisfied** | **Neutral** | **Dissatisfied/Very Dissatisfied** | **Total** |
| a. The process for soliciting ideas from the ICs | 106 (41%) | 90 (35%) | 60 (23%) | 256 |
| b. The initial one-page template to submit ideas for new programs | 134 (55%) | 83 (34%) | 26 (11%) | 243 |
| c. The prioritization process for selecting a few ideas for further development | 74 (30%) | 96 (39%) | 75 (31%) | 245 |
| d. The Council of Councils' role in concept clearance | 89 (37%) | 121 (50%) | 32 (13%) | 242 |
| e. The information you received on the outcome of concept clearance of ideas | 73 (30%) | 68 (28%) | 101 (42%) | 242 |
| **Please rate your level of <u>satisfaction</u> with the following:** | **Very Satisfied/ Satisfied** | **Neutral** | **Dissatisfied/Very Dissatisfied** | **Total** |
| f. Your individual level of participation in program planning after Working Groups are formed to refine cleared concepts into program proposals | 108 (71%) | 27 (18%) | 18 (12%) | 153 |
| g. Your IC's level of participation in program planning after Working Groups are formed to refine cleared concepts into program proposals | 110 (66%) | 34 (20%) | 22 (13%) | 166 |
| h. The process to refine the broad program ideas into a proposal containing specific initiatives | 105 (63%) | 42 (25%) | 20 (12%) | 167 |
| i. The length of the time provided to refine the broad program ideas into a proposal containing specific initiatives | 83 (50%) | 47 (28%) | 37 (22%) | 167 |
| j. The level of detail requested in the proposal that is submitted to OSC | 100 (61%) | 45 (27%) | 19 (12%) | 164 |
| k. The decision making process for approving proposals to become Common Fund programs | 60 (35%) | 56 (33%) | 54 (32%) | 170 |
| **Please rate your <u>agreement</u> with the following statements:** | **Strongly Agree/ Agree** | **Neutral** | **Disagree/ Strongly Disagree** | **Total** |
| a. It is critical to conduct portfolio analysis during the planning phase | 164 (90%) | 14 (8%) | 4 (2%) | 182 |
| b. The NIH resources (e.g., tools, staff, guidance) available to conduct portfolio analysis are adequate | 75 (44%) | 40 (23%) | 56 (33%) | 171 |
| c. The length of time to conduct portfolio analysis is adequate | 69 (43%) | 54 (34%) | 37 (23%) | 160 |
| d. The length of time to solicit input from the scientific community to further refine broad program ideas is adequate | 67 (42%) | 52 (32%) | 42 (26%) | 161 |
| e. The decision making process for approving Common Fund programs is transparent – everyone understands the process and how decisions are made | 32 (18%) | 36 (21%) | 106 (61%) | 174 |

| | | | | |
|---|---|---|---|---|
| f. The process for selecting new CF programs allows adequate input by IC Directors | 3 (33%) | 2 (22%) | 4 (44%) | 9 (Answered by IC Directors) |
| g. The process results in clearly articulated goals and milestones for CF programs | 78 (45%) | 55 (31%) | 42 (24%) | 175 |

**SECTION - COLLABORATION** *(Answered by all groups; Target Audience = 326)*

**10. This section focuses on your own work experiences or personal opinion about collaboration within NIH and the changing culture.**

| **Please rate your <u>agreement</u> with the following statements:** | **Strongly Agree/ Agree** | **Neutral** | **Disagree/ Strongly Disagree** | **Total** |
|---|---|---|---|---|
| a. The scientific mission of individual ICs benefits from working with other ICs on grants/projects | 274 (91%) | 22 (7%) | 5 (2%) | 301 |
| b. Collaborative work via the Common Fund involving multiple ICs is an effective use of NIH resources | 233 (80%) | 43 (15%) | 17 (6%) | 293 |
| c. Common Fund programs have increased the likelihood of collaborative, high-impact trans-NIH programs and activities | 214 (74%) | 51 (18%) | 24 (8%) | 289 |
| d. Since the Roadmap/Common Fund began, ICs are more willing to work together on additional Common Fund related grants/projects than they were in the past | 130 (54%) | 63 (26%) | 48 (20%) | 241 |
| e. Since the Roadmap/Common Fund began, ICs are more willing to work with other ICs on non-Common Fund related grants/projects than they were in the past | 82 (34%) | 101 (42%) | 59 (24%) | 242 |
| f. The Common Fund encourages a culture of change, shared resources, cooperation, and collaboration among ICs | 171 (60%) | 74 (26%) | 41 (14%) | 286 |

g. Please provide any comments you have about your own experiences or personal opinion about working with other ICs on CF programs.

**SECTION - PERCEPTION OF THE EXTERNAL COMMUNITY ABOUT THE COMMON FUND** *(Answered by IC Directors, P&E Officers, OSC Staff, WG members – high involvement; Target Audience = 240)*

**11. This section focuses on the perception of the external community about the Common Fund.**

| **Please rate your <u>agreement</u> with the following statements:** | **Strongly Agree/ Agree** | **Neutral** | **Disagree/ Strongly Disagree** | **Total** |
|---|---|---|---|---|
| a. In your view, the external scientific community is satisfied with Common Fund programming and activities | 57 (35%) | 58 (36%) | 46 (29%) | 161 |

**SECTION - OSC Organizational Structure and roles of OSC staff** *(Answered by OSC Staff, IC Directors, WG Co-chairs, WG Coordinators, WG Project Team Leaders, WG Members (Highly Involved) ; Target Audience =138)*

**12. This section focuses on communications and support you receive from OSC staff, not the Common Fund Working Groups.**

**The NIH Common Fund is overseen by the Office of Strategic Coordination (OSC). OSC is housed within the Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI), Office of the Director (OD), National Institutes of Health (NIH). DPCPSI was created as a result of the 2006 NIH Reform Act.**

| **Please rate your agreement with the following statements:** | **Strongly Agree/ Agree** | **Neutral** | **Disagree/ Strongly Disagree** | **Total** |
|---|---|---|---|---|
| a. The OSC organizational structure is clear to me and others | 36 (29%) | 30 (24%) | 59 (47%) | 125 |
| b. The OSC promotes communication among IC staff working on Common Fund programs | 67 (55%) | 42 (34%) | 13 (11%) | 122 |
| c. The OSC provides adequate governance for Common Fund programming and activities | 59 (48%) | 39 (32%) | 25 (20%) | 123 |
| d. The OSC promotes an environment supportive of NIH staff collaboration on Common Fund programming and activities | 70 (56%) | 32 (26%) | 22 (18%) | 124 |
| e. The role of DPCPSI Director is clear to me and others | 43 (35%) | 27 (22%) | 52 (43%) | 122 |
| f. The role of OSC Director is clear to me and others | 42 (34%) | 27 (22%) | 53 (43%) | 122 |
| g. The role of OSC Program Directors is clear to me and others | 56 (45%) | 26 (21%) | 42 (34%) | 124 |
| h. The role of the OSC Grants Management staff is clear to me and others | 40 (34%) | 24 (20%) | 54 (46%) | 118 |
| i. The role of the OSC Budget staff is clear to me and others | 53 (44%) | 25 (21%) | 41 (34%) | 119 |
| j. The role of the OSC Communication staff is clear to me and others | 47 (40%) | 27 (23%) | 42 (36%) | 116 |
| k. What aspects of OSC organizational structure are working well? | | | | |
| l. What suggestions do you have for improving the OSC organizational structure? | | | | |

**SECTION - WORKING GROUP STRUCTURE** *(Answered by OSC Staff, IC Directors, WG Co-chairs, WG Coordinators, WG Project Team Leaders, WG Members (Highly Involved); Target Audience =138)*

**13. This section focuses on the Common Fund Working Groups structure. When responding to this question, think about your overall experience as a member of one or more Working Groups.**

| **Please rate your agreement with the following statements:** | **Strongly Agree/ Agree** | **Neutral** | **Disagree/ Strongly Disagree** | **Total** |
|---|---|---|---|---|
| a. The Working Group structure (e.g., Co-Chairs, Coordinator, Budget Point of Contact, Communication Point of Contact, and Project Leader) is effective in meeting the scientific goals of the program | 95 (75%) | 24 (19%) | 7 (6%) | 126 |
| b. The Working Group structure (e.g., Co-Chairs, Coordinator, Budget Point of Contact, Communication Point of Contact, and Project Lead) is effective for managing the program | 87 (70%) | 25 (20%) | 12 (10%) | 124 |
| c. The roles and responsibilities of Working Group members are clear | 77 (61%) | 29 (23%) | 20 (16%) | 126 |
| d. The process for establishing Working Group membership is effective | 60 (49%) | 37 (30%) | 26 (21%) | 123 |

**14. This section focuses on communications between OSC and the Working Groups. Think about your role in one or more Working Groups, and your overall experience working with OSC.**

| **Please rate your <u>agreement</u> with the following statements:** | **Strongly Agree/ Agree** | **Neutral** | **Disagree/ Strongly Disagree** | **Total** |
|---|---|---|---|---|
| a. OSC guidance for the formation of Working Groups is sufficient | 44 (38%) | 45 (39%) | 26 (23%) | 115 |
| b. OSC programmatic/scientific guidance is relevant | 61 (51%) | 39 (33%) | 19 (16%) | 119 |
| c. OSC programmatic/scientific guidance is timely | 55 (46%) | 41 (34%) | 23 (19%) | 119 |
| d. OSC gives an appropriate amount of programmatic/scientific guidance | 55 (46%) | 36 (30%) | 29 (24%) | 120 |
| e. OSC programmatic/scientific guidance is clear | 49 (41%) | 40 (34%) | 30 (25%) | 119 |
| f. The OSC allows for a rapid response to changing scientific landscapes | 47 (40%) | 42 (36%) | 29 (25%) | 118 |
| g. Information conveyed from the Office of the Director to the Working Group is appropriate | 53 (47%) | 37 (33%) | 23 (20%) | 113 |
| h. Information conveyed from the Office of the Director to the Working Group is timely | 42 (37%) | 48 (42%) | 24 (21%) | 114 |
| i. OSC is available to answer questions when needs arise | 88 (75%) | 19 (16%) | 11 (9%) | 118 |
| j. Working Group feels comfortable asking OSC for programmatic/scientific guidance | 72 (60%) | 30 (25%) | 18 (15%) | 120 |
| k. OSC staff provide informative and useful answers to questions | 72 (60%) | 36 (30%) | 13 (11%) | 121 |
| l. OSC policies and procedures for managing Common Fund programs are clear | 42 (36%) | 36 (31%) | 38 (33%) | 116 |
| m. What is your overall impression of communication between OSC and the CF Working Groups? | | | | |
| n. What suggestions do you have for improving communication between OSC and the CF Working Groups? | | | | |

**15. This section focuses on your <u>personal experience with Common Fund programs.</u> Think about your role in one or more Working Groups, and your <u>overall experience</u> working with the Common Fund.**

| **Please rate your <u>agreement</u> with the following statements:** | **Strongly Agree/ Agree** | **Neutral** | **Disagree/ Strongly Disagree** | **Total** |
|---|---|---|---|---|
| a. I am enthusiastic about the science of the Common Fund program in which I am or have been involved | 116 (91%) | 8 (6%) | 4 (3%) | 128 |
| b. It is worth my effort to participate in a Common Fund program | 117 (91%) | 5 (4%) | 6 (5%) | 128 |
| c. I feel encouraged to come up with better ways of doing things in my Common Fund program | 98 (77%) | 13 (10%) | 17 (13%) | 128 |
| d. My Common Fund program responsibilities makes good use of my skills and abilities | 107 (84%) | 13 (10%) | 8 (6%) | 128 |
| e. My Common Fund program responsibilities give me the feeling of personal accomplishment | 102 (80%) | 16 (12%) | 10 (8%) | 128 |
| f. The NIH recognizes and rewards Common Fund work that is well-done | 57 (46%) | 37 (30%) | 29 (24%) | 123 |
| g. Participation in-a Common Fund program has helped me to advance in my career at the NIH | 64 (52%) | 38 (31%) | 22 (18%) | 124 |
| h. There are adequate incentives to participate in the Common Fund programs | 53 (43%) | 36 (30%) | 33 (27%) | 122 |
| i. Please comment on the factors that encourage or discourage your participation in Common Fund programs | | | | |

**SECTION - SATISFACTION** *(Answered by OSC Staff, IC Directors, WG Co-chairs, WG Coordinators, WG Project Team Leaders, WG Members (Highly Involved); Target Audience =138)*

**16. This section focuses on the information you receive and the time you spent on Common Fund program activities. Think about your role in one or more Working Groups, and your overall experience working with the Common Fund.**

| Please rate your satisfaction with the following items: | Very Satisfied/ Satisfied | Neutral | Dissatisfied/Very Dissatisfied | Total |
|---|---|---|---|---|
| a. The information you receive from senior management about what is going on with the Common Fund | 58 (46%) | 26 (20%) | 43 (34%) | 127 |
| b. The guidance you receive to do your work | 69 (54%) | 35 (28%) | 23 (18%) | 127 |
| c. Your workload related to Common Fund programs | 75 (58%) | 26 (20%) | 28 (22%) | 129 |
| d. Please provide any additional comments related to the information you receive and the time you spent regarding the Common Fund Program | | | | |

**SECTION - GRANTS MANAGEMENT PROCESSES** *(Answered by WG Coordinators, WG Project Team Leaders, Grants Management Officers, OSC Staff; Target Audience = 113)*

**17. This section focuses on the grants management processes of Common Fund programs. Think about your role in one or more Working Groups, and your overall experience working with the Common Fund.**

| Please rate your agreement with the following statements: | Strongly Agree/ Agree | Neutral | Disagree/ Strongly Disagree | Total |
|---|---|---|---|---|
| a. The process for developing, approving, and issuing FOAs for the Common Fund is clear | 51 (58%) | 17 (19%) | 20 (23%) | 88 |
| b. The Chief Grants Management Officer at the lead IC is involved at an appropriate point in the FOA development process to contribute effectively | 40 (51%) | 25 (32%) | 14 (18%) | 79 |
| c. The guidance that OSC provides during the FOA development process is timely | 45 (55%) | 22 (27%) | 15 (18%) | 82 |
| d. The guidance that OSC provides during the FOA development process is clear | 43 (53%) | 22 (27%) | 16 (20%) | 81 |
| e. With respect to Common Fund FOAs, there are clear procedures for establishing the funding plan | 55 (66%) | 16 (19%) | 13 (16%) | 84 |
| f. The process to request Common Fund- supported administrative supplements is clear | 42 (51%) | 25 (30%) | 16 (19%) | 83 |
| g. The paylist sent by OSC provides adequate authority and information to award CF grants | 44 (60%) | 24 (32%) | 6 (8%) | 74 |
| h. What is your overall impression of the Common Fund Grants Management processes? | | | | |
| i. What suggestions do you have for improving the Common Fund Grants Management processes? | | | | |

**SECTION - BUDGET MANAGEMENT PROCESSES** *(Answered by WG Coordinators, BOs, EOs, OSC Staff; Target Audience = 61 )*

**18. This section focuses on the budget processes of Common Fund programs. Think about your role in one or more Working Groups, and your overall experience working with the Common Fund.**

| Please rate your agreement with the following statements: | Strongly Agree/ Agree | Neutral | Disagree/ Strongly Disagree | Total |
|---|---|---|---|---|
| a. The current budget management processes for Common Fund programs work well | 30 (54%) | 20 (36%) | 5 (9%) | 55 |
| b. The procedures used in developing the annual operating budget for a Common Fund program are clear | 25 (45%) | 17 (30%) | 14 (25%) | 56 |
| c. The procedures for FTE loans are clear | 22 (47%) | 15 (32%) | 10 (21%) | 47 |
| d. The guidance that OSC provides on the budget is timely | 28 (53%) | 18 (34%) | 7 (13%) | 53 |
| e. The guidance that OSC provides on the budget is clear | 30 (57%) | 14 (26%) | 9 (17%) | 53 |
| f. Common Fund reimbursement provided to ICs through Interagency Agreements for managing a Common Fund program works well for my IC | 25 (64%) | 11 (28%) | 3 (8%) | 39 |
| g. Common Fund Budget Reports currently available to the ICs are helpful | 28 (58%) | 13 (27%) | 7 (15%) | 48 |
| h. The Strategic Initiative Database allows Working Group members to easily access budget data for Common Fund programs | 20 (46%) | 12 (28%) | 11 (26%) | 43 |

# Appendix 3: Comparison of Survey Results – 2005 vs 2014

**Table 1. Strategic Planning Process, Change of Culture, Collaboration among ICs, and Common Fund Responsibilities.[1]**

| Question | 2005 | | | | 2014 | | | |
|---|---|---|---|---|---|---|---|---|
| | Strongly Agree/Agree | Neutral | Strongly Disagree/ Disagree | Total | Strongly Agree/Agree | Neutral | Strongly Disagree/ Disagree | Total |
| The process is guided by a clear set of goals, objectives, and procedures | 128 (58%) | 42 (19%) | 51 (23%) | 221 | 153 (56%) | 65 (24%) | 54 (20%) | 272 |
| The process provides adequate time to consider and develop scientific initiatives | 82 (38%) | 39 (18%) | 95 (44%) | 216 | 124 (47%) | 72 (27%) | 69 (26%) | 265 |
| The process results in a carefully considered prioritization of the proposed scientific initiatives | 102 (48%) | 44 (21%) | 65 (31%) | 211 | 120 (45%) | 77 (29%) | 70 (26%) | 267 |
| The process results in the NIH addressing areas of science that would not have been pursued otherwise, including research opportunities relevant to all ICs | 132 (61%) | 26 (12%) | 56 (26%) | 214 | 196 (69%) | 54 (19%) | 35 (12%) | 285 |
| The process results in the NIH identifying trans-NIH and trans-disciplinary initiatives that are relevant to all ICs | 164 (75%) | 28 (13%) | 26 (12%) | 218 | 198 (68%) | 53 (18%) | 38 (13%) | 289 |
| The process results in the NIH addressing research gaps relevant to all ICs | 129 (60%) | 49 (23%) | 37 (17%) | 215 | 141 (50%) | 87 (31%) | 55 (19%) | 282 |
| The OSC promotes an environment supportive of NIH staff collaboration on Common Fund programming and activities | 210 (56%) | 109 (29%) | 56 (15%) | 375 | 70 (56%) | 32 (26%) | 22 (18%) | 124 |
| The process for developing, approving, and issuing FOAs for the Common Fund is clear | 62 (50%) | 30 (24%) | 33 (26%) | 125 | 51 (58%) | 17 (19%) | 20 (23%) | 88 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| With respect to Common Fund FOAs, there are clear procedures for establishing the funding plan | 73 (55%) | 27 (20%) | 32 (24%) | 132 | 55 (66%) | 16 (19%) | 13 (16%) | 84 |
| The Common Fund encourages a culture of change, shared resources, cooperation, and collaboration among ICs | 331 (61%) | 114 (21%) | 98 (18%) | 542 | 171 (60%) | 74 (26%) | 41 (14%) | 286 |
| The scientific mission of individual ICs benefits from working with other ICs on grants/projects | 492 (87%) | 57 (10%) | 17 (3%) | 566 | 274 (91%) | 22 (7%) | 5 (2%) | 301 |
| Common Fund programs have increased the likelihood of collaborative, high-impact trans-NIH programs and activities | 310 (63%) | 104 (21%) | 79 (16%) | 493 | 214 (74%) | 51 (18%) | 24 (8%) | 289 |
| Since the Roadmap/Common Fund began, ICs are more willing to work together on additional Common Fund related grants/projects than they were in the past | 167 (45%) | 137 (37%) | 67 (18%) | 371 | 130 (54%) | 63 (26%) | 48 (20%) | 241 |
| I feel encouraged to come up with better ways of doing things in my Common Fund program | 214 (44%) | 170 (35%) | 102 (21%) | 486 | 98 (77%) | 13 (10%) | 17 (13%) | 128 |
| My Common Fund program responsibilities make good use of my skills and abilities | 239 (49%) | 162 (33%) | 82 (17%) | 483 | 107 (84%) | 13 (10%) | 8 (6%) | 128 |
| My Common Fund program responsibilities give me the feeling of personal accomplishment | 202 (42%) | 159 (33%) | 120 (25%) | 481 | 102 (80%) | 16 (12%) | 10 (8%) | 128 |
| The NIH recognizes and rewards Common Fund work that is well-done | 150 (41%) | 132 (36%) | 84 (23%) | 366 | 57 (46%) | 37 (30%) | 29 (24%) | 123 |

Note: Actual numbers for specific categories for the 2005 survey are based on total counts and percentages in that report.

[1] "Do not know" and "Not applicable" responses are factored out of the 2014 results for comparison purposes.

**Table 2. Satisfaction with Participation in Strategic Planning Activities, and Length of Time of Planning, Guidance from Management, and Workload Related to Common Fund Programs.**

| Question | 2005 | | | | 2014 | | | |
|---|---|---|---|---|---|---|---|---|
| | Very Satisfied/ Satisfied | Neutral | Dissatisfied/ Very Dissatisfied | Total | Very Satisfied/ Satisfied | Neutral | Dissatisfied/ Very Dissatisfied | Total |
| Your level of participation in the planning process | 129 (59%) | 52 (24%) | 37 (17%) | 218 | 135 (52%) | 72 (28%) | 53 (20%) | 260 |
| The pace and length of time provided for the overall planning process | 78 (36%) | 45 (21%) | 93 (43%) | 216 | 106 (40%) | 94 (35%) | 66 (25%) | 266 |
| The overall Common Fund strategic planning process, considering everything from inception to Director approval | 92 (42%) | 61 (28%) | 65 (30%) | 218 | 96 (36%) | 95 (36%) | 76 (28%) | 267 |
| The information you receive from senior management about what is going on with the Common Fund | 228 (43%) | 149 (28%) | 154 (29%) | 531 | 58 (46%) | 26 (20%) | 43 (34%) | 128 |
| The guidance you receive to do your work | 189 (37%) | 200 (39%) | 123 (24%) | 512 | 69 (54%) | 35 (28%) | 23 (18%) | 127 |
| Your workload related to Common Fund programs | 189 (39%) | 228 (47%) | 73 (15%) | 495 | 75 (58%) | 26 (20%) | 28 (22%) | 129 |

## Appendix 6: Success of Proposals from Different Strategic Planning Methods

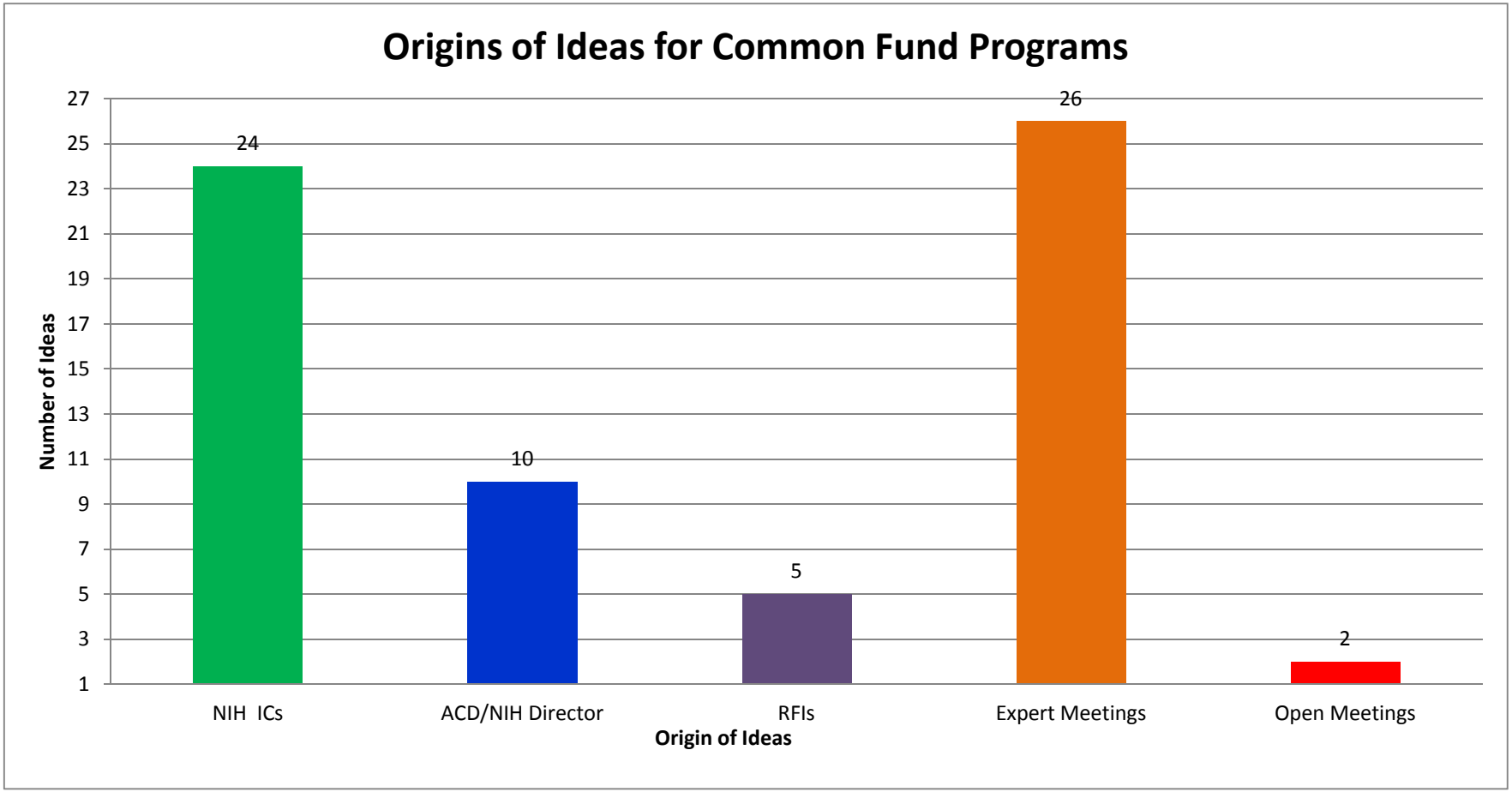
**Methods of Strategic Planning**

| Program Name | NIH ICs | NIH/OD | RFI | Expert Meeting | Open Meeting | Years of Idea |
|---|---|---|---|---|---|---|
| Big Data to Knowledge | **1** | **1** | **1** | **1** | **1** | 2012-13<br>2011-12<br>2010-11<br>2008-09<br>2006-07 |
| Bioinformatics and Computational Biology | **1** | | | **1** | | 2002-03 |
| Bridging Interventional Development Gaps (BrIDGs) (Formerly known as NIH-RAID) | **1** | | | **1** | | 2002-03 |
| Building Blocks, Biological Pathways and Networks | **1** | | | **1** | | 2002-03 |
| Enhancing the Diversity of the NIH-Funded Workforce | | **1** | | | | 2012-13 |
| Epigenomics | **1** | | | **1** | | 2006-07 |
| Extracellular RNA Communication | **1** | | | | | 2011-12 |
| Genotype-Tissue Expression (GTEx) | **1** | | | | | 2007-08 |
| Global Health | | **1** | | **1** | | 2010-11 (H3A)<br>2009-10 (MEPI) |
| Gulf Oil Spill | | **1** | | | | 2009-10 |
| HCS Research Collaboratory | | | | **1** | | 2010-11 |
| Health Economics | | | **1** | **1** | | 2010-11<br>2008-09 |

| | | | | | | |
|---|---|---|---|---|---|---|
| NIH Director's Early Independence Award (EIA) | | **1** | | **1** | | 2010-11<br>2009-10 |
| NIH Director's New Innovator Award | | | | **1** | | 2006-07 |
| NIH Director's Pioneer Award | **1** | | | **1** | | 2002-03 |
| NIH Director's Transformative Research Awards | | **1** | | | | 2007-08 |
| Human Microbiome Project | **1** | | | **1** | | 2006-07 |
| Illuminating the Druggable Genome | | | | **1** | | 2012-13 |
| Knockout Mouse Phenotyping | **1** | **1** | | | | 2009-10<br>2006-07 |
| Library of Integrated Network-Based Cellular Signatures (LINCS) | **1** | | | | | 2009-10<br>2008-09 |
| Metabolomics | | | | **1** | | 2010-11 |
| Molecular Libraries and Imaging | **1** | | | **1** | | 2002-03 |
| Nanomedicine | **1** | | | **1** | | 2002-03 |
| NIH Center for Regenerative Medicine (NIH CRM) | | **1** | **1** | | | 2009-10<br>2008-09<br>2006-07 |
| NIH Medical Research Scholars Program (Formerly known as CRTP) | **1** | | | **1** | | 2002-03 |

| | | | | | | |
|---|---|---|---|---|---|---|
| PROMIS: Patient-Reported Outcomes Measurement Information System | **1** | | | **1** | | 2002-03 |
| Protein Capture Reagents | **1** | | **1** | **1** | | 2009-10<br>2007-08<br>2006-07 |
| Regulatory Science | | **1** | | **1** | | 2009-10 (Reg Sci)<br>2011-12 (MPS) |
| Science of Behavior Change | **1** | | **1** | **1** | | 2009-10<br>2008-09<br>2006-07 |
| Single Cell Analysis | **1** | | | | | 2010-11 |
| Strengthening the Biomedical Research Workforce | | **1** | | | **1** | 2012-13 |
| Structural Biology | **1** | | | **1** | | 2002-03 |
| Undiagnosed Diseases | **1** | | | | | 2011-12 |
| Clinical and Translational Science Awards(CTSAs) | **1** | | | **1** | | 2002-03 |
| Clinical Research Policy Analysis and Coordination (CRPac) | **1** | | | **1** | | 2002-03 |
| Interdisciplinary Research | **1** | | | **1** | | 2002-03 |
| National Electronics Clinical Trials and Research (NECTAR) | **1** | | | **1** | | 2002-03 |

| NIH ICs | ACD/NIH Director | RFIs | Expert Meetings | Open Meetings |
|---|---|---|---|---|
| 24 | 10 | 5 | 26 | 2 |



## Appendix 7: Examples of Ideas Submitted Through Various Strategic Planning Methods

This document provides examples of ideas generated through the various strategic planning methods. Methods include meetings with invited thought leaders, public meetings, Requests for Information, and solicitation of ideas from IC Directors. Note that ideas generated through meetings with either invited thought leaders or with the general community involve discussion to result in "consensus" ideas. The process of group discussion tends to refine concepts submitted at the beginning of the meeting by individual attendees. These individual ideas were captured for meetings with thought leaders but not for meetings that were open to the community. This document also distinguishes between ideas generated through each method that were later deemed appropriate for Common Fund investment and those that were not. The documents are numbered for reference in the attachments folder on the SharePoint.

| Type of input | Suitable for CF support | Not suitable for CF support |
|---|---|---|
| **Thought Leader meetings** | | |
| *Individual ideas* | A U.S. National Cohort for Health, Genomics, and the Environment<br><br>Metabolomics for Clinical Medicine | Non-coding RNA and Brain Function<br><br>Incentivizing Sound Research Practices and Addressing the File Drawer Effect |
| *Consensus ideas* | Citizen Science<br><br>Deorphanizing the Druggable Genome | NIH Award Strategies<br><br>Expanding the Capabilities of Structural Biology |
| **Public meetings** | | |
| *Consensus ideas* | Glycomics<br><br>Mechanobiology | Fibrosis<br><br>Immunovariability |
| **Requests for Information** | | |
| | A Resource of Affinity Reagents for Analysis of the Human Proteome | Eradicate Lung Cancer<br><br>Human Papilloma Virus |

| | | |
|---|---|---|
| | Infrastructure for Very Large Data Repositories and Data Mining | |
| **NIH IC ideas** | | |
| | Undiagnosed Diseases Program<br><br>3D Nucleome (Idea ID #64) | Multidrug Resistant Gram Negative Bacterial Infections (Idea ID#39)<br><br>Understanding Medical Treatment in the Context of Pregnancy |

## Appendix 8: Summary of Common Fund Strategic Planning Activities By Year

This document lists the strategic planning methods used by year and phase. Phase 1 inputs are received from both internal (IC staff, IC Directors, NIH Director) and external sources (meetings, RFIs). Concepts are cleared by the Council of Councils and progress to Phase 2. Concepts are refined with the use of portfolio analysis, IC led workshops, and a Working Group proposal. The proposals are then sent to the NIH Director for approval to become Common Fund programs. This document demonstrates how the strategic planning process varies by year.

| Year | PHASE 1 | | | | PHASE 2 | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Internal Input | External Input | | | Refinement | | | Decision Making | |
| | NIH IC Staff, IC Directors (ICDs), NIH Director | Meetings | Request for Information (RFI) | Council of Councils | Portfolio Analysis | IC-led Meeting/ Workshop | Trans-NIH Working Group (WG) Proposals | Priority Setting | NIH Director |
| **2002-2003** | IC program staff and ICDs participate in external meetings | 5 external meetings, mostly senior PIs | No | N/A | Informal | No | WGs develop proposals for subset of ideas selected by ICDs and NIH Director | ICDs and WGs prioritize proposals | Approves 9 new programs |
| **2006-2007** | ICDs submit ideas for consideration | 5 external meetings, mostly senior PIs | Yes | N/A | Yes | No | WGs develop 11 proposals selected by ICDs | ICDs recommend 2 new programs | Approves 3 new programs |
| **2007-2008** | IC program staff provide ideas, self-assemble around specific topics/develop proposals | No | RFI ideas reconsidered | N/A | Yes | IC-led workshops to define research barriers and gaps | WGs develop proposals | ICDs refine proposals, recommend 6 for further consideration | Approves 1 new program, combines other 5 topics into one program (TR01) |
| **2008-2009** | IC Senior staff submit ideas | IC-led meetings | Yes | Concepts discussed during Phase 2 planning | Yes | WGs solicit public input on 3 ideas selected by IC Senior staff | WGs develop proposals | Concepts discussed at the NIH Council of Councils Meeting | Concepts on hold until NIH Director hired |
| **2009-2010** | External meetings focused on NIH Director's themes; ICDs and NIH Director select program areas for development | Series of small external meetings, some IC-led | No | Concepts discussed during Phase 2 planning | Informal | Ideas from IC-led meetings | WGs develop proposals | Concepts discussed at NIH Council of Councils meeting with ICD input | Approves 11 new programs |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **2010-2011** | ICDs attend external "Big Think" meeting | 1 external "Big Think" meeting | No | Concepts discussed during Phase 2 planning | Informal | IC-led workshops to define gaps and opportunity | WGs develop proposals | Concepts discussed at NIH Council of Councils meeting | Approves 2 new programs; 1 concept incorporated into existing program |
| **2011-2012** | ICDs/NIH senior staff submit ideas; ICDs attend external "Innovation Brainstorm" meeting | 1 external meeting "Innovation Brainstorm" | No; public comments solicited on ideas emerging from meeting and from ICs | Concepts discussed during Phase 2 planning | Yes | IC-led workshops | WGs develop proposals | ICDs help prioritize | Approves 2 new programs to start in FY13 |
| **2012-2013** | ICDs/NIH senior staff submit ideas; ICs attend external invited "Forward Focus" meeting | 3 external meetings (1 invited, 2 public) "Forward Focus" | No | Concepts cleared prior to entering Phase 2 | Yes | IC-led workshops | WGs develop proposals | ICDs help prioritize | Approves 4 new programs; 3 start in FY2013, 1 to start in FY2014. 2 concepts incorporated into existing programs. |
| **2013-2014** | ICDs/NIH senior staff submit ideas | N/A | No | Concepts cleared prior to entering Phase 2 | Ongoing | Ongoing | Ongoing | ICDs help prioritize | TBD |

Key: IC = Institute/Center; ICD = Institute/Center Director; PIs = Principal Investigators; WG = Working Group

## Appendix 9: Sample of Concepts Sent to Council of Councils

5

**Title:** Publicly Available siRNA Libraries for the Unrestricted Release of Screening Data and Corresponding Sequence Information

**Submitting Source:** NIH

**What is the major obstacle/challenge/opportunity that the Common Fund should address? What would the goals of the program be?**

siRNA screening has become a powerful tool to interrogate gene function. However, RNAi screening suffers from severe limitations that leave the promise of this technology woefully unfulfilled. For example, off-target effects dominate RNAi screens and make the data difficult to interpret. This is evidenced by the observation that there is little correlation between different siRNAs designed to target the same gene in any given assay. Recently, a number of studies have shown that off-target effects can be identified, and even interpreted, through a global understanding of how siRNA sequences influence an assay. Unfortunately, sequence data for commercial libraries cannot be released, rendering subsequent analysis of these data by the community of bioinformatics researchers impossible, and thus severely limiting the contribution of genome-wide siRNA studies to the understanding of genome function in health and disease. To overcome these obstacles, we propose the creation of publicly available siRNA libraries along with open access to corresponding sequence information. The goals of such a program would be to:

- Design and obtain siRNA libraries (beginning with human and mouse) built on a state-of-the-art understanding of RNAi biology and empirical data from actual large-scale screens. Custom libraries will allow for the unrestricted release of sequence information.
- Via NIH or third-party distributors, make the libraries available to the research community.
- Release and archive all screen data and corresponding sequences obtained with these libraries.

**Why is a trans-NIH strategy needed to achieve these goals? What initiatives might form the strategic plan for this topic?**

This type of program would benefit all areas of research and advance our understanding of gene function in the context of disease and fundamental biology. A broad, trans-NIH strategy is needed to gather the resources and expertise necessary to realize the benefits of such a program. This plan would require a consortium to help design and produce the libraries, and would nucleate a community to utilize and for the first time publically release the data generated.

**If a Common Fund program on this topic achieved its objectives, what would be the impact?**

It is sobering to realize that, 10 years after completion of the Human Genome Project and 6 years after the Nobel Prize was awarded for RNAi, there is no publically available compendium of genome-wide siRNA data, since the siRNA sequence data are proprietary. This program would solve that problem and thus catalyze a new field of bioinformatics based on these data, enabling secondary and meta-analyses of siRNA screens and thus delivering unprecedented insights in systems biology and an ever-improving understanding of how siRNA/miRNAs influence cellular processes relevant to physiology and disease.

**CoC Comments:**

**CoC Concept Clearance** **% Approving:** 83% **% Not Approving:** 17%

| | |
|---|---|
| Mitchell | the first issue is to work to overcome the proprietary issues. |
| Crabb | This would be transformative, and there are probably parallels with the protein capture reagents proposal we heard about 2 years ago. |
| Barnes | This seems to be analogous to problems that beset DNA microarrays where the sequences for each gene represented on the array were not available. So, setting up publicly available siRNA libraries has merit. As a pharmacologist, I retain some concern about the complexity of off-target effects and wonder whether a disruptive technology is in the works. |
| LeMasters | Definately needed and trans NIH |
| Wetle | Worthwhile effort |
| Okeefe | yes - will provide integrration across research fields and in different disease and help improve the design of new therapies. |
| Elias | Very very important |
| Lloyd | need to ensure sustainability of resource; provide support for pilot investigations using library to demonstrate proof of concept; provide support for web interfaces/wiki's that allow user access/contribution in real time. |
| Castellanos | enough with proprietary data already! |
| Lively | Possibly best suited for NHGRI; cluser with #2 |
| McSweeney | Not pertinent to all ics. |

| | |
|---|---|
| Crabb | I agree with Joyce's comments that the "value sets" that identify the various chronic illnesses will need to be defined and agreed upon by all participating trials, e.g., agreeing on how heart failure is defined/diagnosed, and the severity captured and updated with clinical changes. |
| Barnes | In order for this and many other NIH endeavors to work, there has to be a standardized data language. It is unrewarding even finding principal effects in complex clinical datasets, let alone the interactions being sought in this concept. |
| LeMasters | Meets requirements of common fund |
| Wetle | this is an important topic, is trans-institute and, in my opinion, meets criteria for common fund support. |
| Lively | Also an NCATS task? |
| Lloyd | seems a bit of a heavy, top-down approach, prescriptive, as opposed to a more informed, bottom-up and spontaneous effort…overall very good concept, but consider a way to incorporate into CTSA program in NCATS |
| Castellanos | important; feasible |
| Elias | I am not sure you can do this. I also believe the co-morbidities that are important will vry disease to disease. This is too vague. |
| Okeefe | yes - these conditions affect a large portion of the population - and should be considered in the context of clinical trials. |
| Hotez | How much already being done through the other Institutes? |

29 **Title:** Coordinating Data Collection

**Submitting Source:** Strategic Planning

**What is the major obstacle/challenge/opportunity that the Common Fund should address?**
Large sample sizes increase statistical power and can lead to greater reliability of research results, whereas comparable studies which rely on small samples often yield contradictory findings. Greater coordination and cooperation among investigators in collecting and pooling the data from studies has the potential to significantly increase knowledge in all fields. The development of a culture of collegiality among investigators coupled with technological advances in the storage and access to pooled data could break down barriers between labs and allow investigators greater flexibility to publish more reliable findings. For this model to be successful, however, issues of privacy with regard to data on individual human subjects and the use of these data in research would need to be addressed.

**What would the goals of the program be?**
The program would have 6 goals:

- Establish procedures to collect standardized data from diverse sets of investigators
- Standardize phenotypes
- Remove barriers to capturing and sharing data as a consortium when groups did not initially develop as consortia
- Expand the data pool to include school districts, state health care systems, and similar entities
- Establish interoperability standards and a data warehouse for data mining and sharing data
- Address the issues and ethics surrounding privacy

**Why is a trans-NIH strategy needed to achieve these goals?**
The cultural, technological, and privacy issues that form barriers to data coordination transcend the boundaries that separate the missions of the various ICs. These issues are relevant to data collection across disciplines and require the attention all parts of NIH.

**What initiatives might form the strategic plan for this topic?**
Goals that included a discussion of initiatives included the following:
Establish procedures to collect standardized data from diverse sets of investigators

- Develop a list of different issues that require an integrated approach
- Collect data from each human subject for use in studies across a variety of different domains

Remove barriers to capturing and sharing data as a consortium when groups did not initially develop as consortia

- Incentivize participation by investigators

Establish interoperability standards and a data warehouse for data mining and sharing data

- Build an NIH-housed data repository, analogous to PubMed, which is accessible to investigators both to input and access data

Address the issues and ethics surrounding privacy

- Create a stipulation in consent forms about the sharing of data in the data repository

**If a Common Fund program on this topic achieved its objectives, what would be the impact?**
A successful program to coordinate data collection could lead to more robust findings based on larger sample sizes, an outcome which will contribute to more rapid advancement across the fields of health. It could potentially standardize both the definitions and measures of variables of interest and create an infrastructure to capture findings from multiple studies in a manner that makes data accessible while it incentivizes collegiality among investigators and fosters collaboration between disciplines.

**CoC Comments:**

**CoC Concept Clearance** **% Approving:** 63% **% Not Approving:** 37%

| | |
|---|---|
| Crabb | Many goals could be linked with proposal 2, 27, and 7 |
| LeMasters | Do not see this as transformative and difficult to enforce and execute. |
| Geschwind | just one of the goals, such as standardizing phenotypes would be an enormous endeavor and worthwhile. But, I am not convinced as framed this is sufficiently focused. E.g. individual institutes could work on phenotype issues related to their focuses and could do so perhaps more efficiently. |
| Wetle | The overall goal to make data from various studies more useful for broader purposes is reasonable. the devil is in the details. This would be a complex and potentially contentious effort, but worthwhile if successful. |
| Barnes | Not transformative on its own. Has overlaps with Bioethics and Big Data. |
| Murphy | Not reasonably scoped. I agree with Dan that more focused projects could be done by institutes, and I think these are a prerequisite for something of the scope proposed here. |
| Greenwald | Also seems to be more policy and implementation based rather than scientific discovery. These type of projects are so important, and in my opinion, equal in importance to all the drug discovery efforts proposed. |
| Kaufman | Good only if part of 2, 4, 7, 23, 26 and/or 28 |

| | |
|---|---|
| Hotez | Overlap with Initiative 2. |
| Lloyd | must include regular ongoing QA, data correction and revision; also consider adding an automated "surveillance" function, in which data is automatically analyzed via preset surveillance parameters that, upon discovering statistical relevance, can send out alert for further, human-led analysis...this enables 24/7, real-time data query/mining...a tour de force. Potential cluster with #2. |
| Lively | Cluster with ID 2 |
| Okeefe | no - this needs to be accomplished on a smaller scale. At this point there is not even uniform outcome measures that are used. This is not a big science issue. |
| McSweeney | not quite ready; many IRB implications need to be worked out 1st. |

35 **Title:** Mechanobiology: An Emerging Frontier in Basic and Translational Research

**Submitting Source:** Strategic Planning

**What is the major obstacle/challenge/opportunity that the Common Fund should address?**
Mechanobiology is an emerging frontier in research, at the interface of biology and engineering, that involves the study of physical forces and changes in cell or tissue mechanics. Cells are exquisitely sensitive to mechanical stimuli, and their ability to detect mechanical cues is critical to stem cell biology, developmental biology, and a wide variety of diseases. A major challenge in the field is understanding mechanotransduction -the molecular mechanisms by which cells and tissues self-organize, and sense and respond to mechanical signals. At present, research in mechanobiology is rather piecemeal with different communities working on select diseases, cell types, and model organisms. Unifying approaches and datasets that could add much needed coherence to the field are simply not available. With support from the NIH Common Fund, new research foundations and insights into the mechanical basis of tissue regulation could lead to development of improved medical devices, biomaterials, and engineered tissues for tissue repair and reconstruction.

**What would the goals of the program be?**
This program would have 4 goals:

- Develop new techniques to measure mechanical forces in living organisms from nanometers to meters and milliseconds to years.
- Integrate understanding of mechanical signal transduction across log scales ranging from the cellular to the tissue to the organism level.
- Apply knowledge to the creation of complex bioengineered biomaterials (tissues and whole organs).
- Make engineered biomaterials available to the research community to advance development of new medical devices and tissues for reconstruction.

**Why is a trans-NIH strategy needed to achieve these goals?**
The Common Fund is uniquely positioned to drive progress across the NIH to coordinate the emerging field of mechanobiology into a coherent whole.

**What initiatives might form the strategic plan for this topic?**
Develop new techniques to measure mechanical forces in living organisms from nanometers to meters and milliseconds to years.

- Facilitate the development of new techniques for studying mechanotransduction in natural and bioengineered materials.

Establish datasets and analytical capabilities to integrate the understanding of mechanical signal transduction across log scales ranging from the cellular to the tissue to the organism level.

- Emphasize cellular unity.

Apply knowledge gained to the creation of complex bioengineered biomaterials (tissues and whole organs) and datasets for use by the broader research community.

- Create nature-inspired biomaterials using molecular self-assembly.

**If a Common Fund program on this topic achieved its objectives, what would be the impact?**
A successful project create coherent field of in mechanobiology. Since mechanobiology requires interdisciplinary knowledge, the project will develop a unified effort developed out of the marriage of powerful concepts from traditional fields of cell biology, mechanics, and materials.

**CoC Comments:**

**CoC Concept Clearance** **% Approving:** 76% **% Not Approving:** 24%

| | |
|---|---|
| Crabb | I think the impact may be somewhat more limited that that of some of the other proposals. Not all systems have a mechanical aspect to their function. |
| LeMasters | Could be very helpful for diseases where the nervous system is affected or after injuries. |
| Ehman | There has been growing recognition of the importance of biomechanical signaling on cell behavior in recent years. Mechanotransduction effects seem to have a central role in the development and function of normal tissues and in many pathological processes including inflammation, fibrogenesis, senescence, and neoplasia. An initiative to accelerate this emerging area should have broad relevance and transformational potential across essentially all NIH IC's. |
| Wetle | Worth additional work |
| Barnes | Like this concept since it cuts across much of NIH. Note that it is related to the previous concept - in vivo sensors |
| McSweeney | not trans NIH. |
| Lloyd | perhaps pilot in Musculoskeletal/arthritis institute. Potential cluster with #34. |
| Okeefe | no - already an pretty robust area of research in ICs where this is relevant. |
| Elias | A lot already being done at Institutes |

## Appendix 10: Dealing with Rapidly Emerging Challenges and Opportunities

Rapidly emerging challenges and opportunities can be addressed in a number of ways at the NIH, depending on the funds required and the complexity of the problem:

- Individual grantees may use their awards to go in new directions, with discussion with the grant's Program Officer as necessary. This is a critical feature of the Pioneer and New Innovator awards, but is also common within the context of R01s and other discovery-oriented awards.
- Supplements may be made to grantees to provide necessary funds, as long as the new work does not represent a change in scope from the original award. Supplements are widely used within the Common Fund to take advantage of new opportunities. An example is the expansion of the Knock-Out Mouse Phenotyping Program to include developmental phenotyping. The high rate of embryonic lethality (30%) of the mutants provided an opportunity to understand the contribution of these genes to early development, and the CF was able to take advantage of this opportunity.
- Intramural investigators have the flexibility to change their research plans as needed. Institutes and Centers may increase an individual PI's funds, as funds permit, to support critical research areas.

"Rapid response" in these situations assumes implementation of an action plan within days, weeks, or a few months. This compares to the required time for extramural award competition which typically takes nine months.

Common Fund programs have taken advantage of each of these rapid response mechanisms for specific needs within the context of larger programs. However, an entirely new program has only been implemented as a "rapid response" in one instance: the Gulf Long Term Follow-up (GuLF) Study.

The GuLF Study was prompted by the April 20, 2010 explosion of the Deepwater Horizon oil rig in the Gulf of Mexico. Concern over the safety of oil spill workers and volunteers led to an NIEHS-led effort to establish a longitudinal study of people exposed to oil and dispersants. On June 15, 2010, the NIH Director announced an investment of $10 Million to support the initial stages of the NIEHS launch of this research.

NIEHS, working with the OD and several federal agencies, developed a multi-faceted plan to address the health consequences of the oil spill. The GuLF study was one component of this plan. Enrollment began in February, 2011 with a goal of enrolling 55,000 people. By 2013, approximately 33,000 individuals had joined the study. More than 11,000 participants from the five Gulf coast states completed home examinations and contributed biological and environmental samples.

Other components of the NIEHS-led effort have included a multi-IC funded community-university consortium that aims to address the community health effects stemming from the oil spill, including seafood safety, impact on mental health, childhood development, respiratory diseases, rashes, headaches, etc. Support for these extramural awards began in June, 2011.

COMMON FUND PROCESS:

The implementation of the GuLF study through use of the Common Fund was initiated by the NIH Director, in recognition of the fact that the exposure could potentially affect all organ systems and that understanding the impact of the spill was a trans-NIH interest. Detailed plans for the project were developed by the NIEHS PI (Dr. Dale Sandler), through conversations with the OD/DPCPSI, extensive community outreach activities, and discussions with other federal agencies.

## Appendix 11: Extracellular RNA Program Evolution

**July-August 2011, Strategic Planning:** In July, NINDS and NCI submitted the initial idea for the Extracellular RNA (ExRNA) Communication program during the 2011-2012 strategic planning process. The program proposed to study Extracellular Space (ES) and how the cellular microenvironment contributes to health and disease. It was believed that Common Fund (CF) investment in this program would galvanize efforts towards a multidisciplinary approach towards determining the influence of the ES in health and disease. The NIH had some ongoing efforts investigating the biology of ES; however, this concept offered a more synergistic approach that would provide a more global and comprehensive understanding of ES physiology and function and how these are perturbed in disease. The concept, titled Exploring the Extracellular Space, was posted on a social networking website in August that OSC created for the community to comment. (Appendix 1. Initial Concept July-August 2011)

**October 13, 2011, IC Director Meeting**: The IC Directors met to discuss a few ideas that came in through Phase 1 of the Common Fund strategic planning process. During the discussion, Dr. Jim Anderson presented DPCPSI's recommendation that this concept move to Phase 2 strategic planning with a focus on exosomes. He felt that exploring the extracellular space was too broad, but that exosomes could be potentially transformative as diagnostics and as therapeutic delivery vesicles. The IC Directors agreed with this recommendation. (Appendix 2. ICD Mtg 10-13-2011 PowerPoint, slides 18-20)

**December 6, 2011, Portfolio Analysis:** An exosome portfolio analysis was conducted by DCPCSI Office of Portfolio Analysis. From FY2005 – FY2011, there were 38 projects with exosomes as the main focus and another 21 projects with exosome as one of several aims. Several of these projects were focused on the development of exosome-based biomarkers as diagnostic tools for diseases/conditions. Cancer and HIV pathogenesis were the most prominent categories. (Appendix 3. Exosome Portfolio Analysis 12.06.2011)

**January, 2012, International Society for Extracellular Vesicles (ISEV):** NIH staff contacted ISEV to have a plenary session about exosome research at their April 2012 conference. ISEV agreed and they also agreed to set up a social media site with their membership to gather input on needs and opportunities.

**March 7, 2012, Exosomes and Microvesicles Meeting:** The seven founding members of the American Society for Exosomes and Microvesicles offered to come to the NIH to share ideas that would amplify the input requested through the ISEV social media site. The members met with NIH staff and the discussion centered on responses to the 5 questions below:

- Obstacles: What are the major obstacles and challenges in exosome and microvesicle research? What is needed to overcome these obstacles and challenges?
- Characteristics of success: What fundamental characteristics of exosomes/microvesicles must be determined in order for the field as a whole to flourish?
- Tools for the research community: Is it feasible to catalog Extracellular Vesicles (EVs) by size, tissue of origin, target tissue, and cargo? What would this require? Are technologies limiting? Should other tools be developed?

- Nomenclature and Protocols: How can the Exosome community as a whole develop consensus nomenclature for EVs? What protocols need to be standardized for the community, and what would be required for that?
- Feasibility of timeline: Is it feasible, within 5 years, to engineer exosomes or other microvesicles to contain a defined cargo with a defined target to produce a defined response? If not, what has to be determined in the next 5 years to accomplish these goals what would be required to engineer exosomes as targeted drug delivery vesicles in the subsequent 5 years?

**April 19-21, 2012, International Society for Extracellular Vesicles (ISEV):** Representatives from NINDS, NCI, and OSC attended the conference and led an open discussion with all participants about the most pressing challenges and exciting opportunities in the field. Also, NIH staff met with ISEV leadership to further refine the most urgent research needs in exosome research.

**April 27, 2012, Proposal Submission:** NINDS and NCI submitted the proposal entitled, "Extracellular Vesicles in Health and Disease" to the Office of Strategic Coordination. The program goal was to develop a knowledge base, tools and resources to exploit the understanding and use of extracellular vesicles (EV) in human health and disease. The proposal included the results of the portfolio analysis. The five proposed initiatives and associated goals were:
Initiative 1: Tools and Technologies for Extracellular Vesicle Separation and Analysis
Goals: To enable the purification and characterization of homogenous EV populations from complex biological tissues and fluids, including, serum, urine, saliva, breast milk, CSF, and ingested food. The emphasis will be on identifying biomarkers that distinguish: subcellular and tissue of origin, trans-kingdom biomarkers.
Initiative 2: Data Management and Resource/Repository (DMRR)
Goals: The DMRR will establish a coordinating center and data repository, develop standards and harmonization for the type and format of data generated by the other initiatives, and provide comprehensive resource to the exosome community.
Initiative 3: Reference Profiles of Human Extracellular Vesicles
Goals: To identify signature profiles which differentiate between homeostatic "normal" and pathogenic EVs. In particular, vesicle-associated inflammatory, metastatic, immunosuppressive, or other pathogenic signatures associated with particular disease conditions will be determined.
Initiative 4: Extracellular Vesicle Biogenesis, Biodistribution, Uptake, and Effector Function
Goals: The goal of this initiative will be to develop the tools, technologies and bioreagents to characterize the fundamental molecular pathways that regulate EV biogenesis, biodistribution, uptake, and effector function.
Initiative 5: Clinical Utility of Extracellular Vesicle as Biomarkers and Therapeutic Delivery Vehicles
Goals: To combine our understanding of exosome biology (biogenesis, cargo loading, and targeting) with bioengineering approaches to accelerate preclinical development of EV-based therapeutics. (Appendix 4. Extracellular Vesicles CF Program Proposal)

**May 16, 2012, NIH Leadership Meeting:** Dr. Anderson, DPCPSI Director, Dr. Wilder, OSC Director, and a small group of IC Directors met with Drs. Collins and Tabak to review the proposal. During this discussion, the focus of the proposal shifted away from the extracellular

vesicles themselves to their RNA content as the most exciting opportunity for new biological paradigms. This shift was influenced by the fact that exosomal proteomics is well established, and by the possibilities presented for stable genetic impact from RNAs that are delivered to recipient cells. Since secreted RNAs may represent an important and long lasting mechanism for one cell to influence another, the focus of the program became understanding the mechanisms through which these RNAs are secreted, their biological impact, and the extent to which they may be manipulated or tracked for novel therapeutics and diagnostics. The impact of extracellular RNAs that are protein-bound but not secreted via vesicles was considered to be of equal importance as those found in vesicles, so the title shifted to focus on "Extracellular RNAs". Drs. Collins and Tabak supported the proposal, but noted it needed to be cleared by the Council of Councils in June 2012. (Appendix 5. Decision on Program 05.16.2012)

**June 5, 2012, Council of Councils Meeting:** The Extracellular RNA Communication proposal was submitted to the Council of Councils for clearance. The presentation focused on the program's transformative potential to create a new paradigm for intercellular and inter-organismal information exchange. It would lay the groundwork for many future investigator-initiated projects that will explore the function of specific exRNAs by providing tools for reliable isolation and analysis of exRNAs and by providing hypothesis-generating data. It would also provide a new avenue for therapeutic delivery of exRNAs by developing methods for engineering and establishing the principles that govern target cell selection. The overarching goals for this program were to establish principles of exRNAs as endocrine signals and to demonstrate the potential for clinical utility. Specific goals included:

1. Develop tools/technologies/methods for isolation and analysis of various classes of exRNAs.
2. Establish a central repository for data collection and analysis for the community at large.
3. Develop profiles for human exRNAs in many tissues and body fluids to serve as reference data for analyses of exRNAs in disease conditions.
4. Support coordinated analyses to define fundamental biological principles of exRNA biogenesis, distribution, and uptake.
5. Support projects that demonstrate possible clinical utility of exRNAs as biomarkers or therapeutic delivery vehicles.

The Council of Councils reviewed the concept and voted 56 to 44 percent to approve it as a Common Fund initiative. (Appendix 6. FY13-14 Cleared CF Ideas with CoC Comments 06.05.2012)

**June 2012, Detailed Plans**: The Working Group submitted the detailed program plans to the Office of Strategic Coordination. Initiatives would be headed by four different ICs: NIDA, NHLBI, NCI, and NINDS. The overall program goals were:

1. To establish fundamental biological principles of extracellular RNA secretion, delivery, and impact on recipient cells.
2. To describe exRNAs in human biofluids and the extent to which exRNAs from non-human cells are present.
3. To test clinical utility of exRNAs.
4. To provide a data/resource repository for the community at large.

These goals would be achieved through four different initiatives:

1. Data management and resource/repository (DMRR)

2. Reference profiles of human extracellular RNAs (ER2)
3. ExRNA biogenesis, biodistribution, uptake, and effector function (ER3)
4. Clinical utility demonstration projects (ER4)

(Appendix 7. Detailed Plans - Extracellular RNA Communications Approved 07-14-2012)

**July 2012, Program Approval**: Dr. Wilder, OSC Director, sent an email to the NINDS and NCI staff indicating that the detailed plan submitted by the group for the program had been approved. The plans would guide the program for the next five years. The exRNA program had been officially established. (Appendix 8. Email Stating ExRNA Plans are Approved 07.14.2012.docx)

## Appendix 12: Epigenomics Program Evolution

**July - September, 2006, Roadmap Strategic Planning:** The Epigenomics program grew from ideas submitted during the strategic planning process to determine the second cohort of Roadmap (RM) programs which would begin funding in FY 2008. The first phase of this process involved soliciting ideas for new programs. Ideas were solicited from IC staff, external expert scientists during five meetings, and the public through a Request for Information (RFI).

During the meeting with experts held on September 21, 2006, an idea entitled, "Epigenetic Modifications in Health and Disease" was suggested. The idea focused on the development of better tools to identify different epigenetic modifications that take place during development, aging, stress, cancer, and exposure to different environmental conditions. The concept aimed to improve existing methodology and/or develop new technologies for epigenetic analysis that would allow improved throughput, data content, data quality, and cost efficiency.

Additionally, five other ideas were offered by NIH ICs:

- Exploration of Epigenetics in Normal Physiology and Disease - NIAAA
- Epigenomic Targets and Disease Outcomes - NIEHS
- Developmental Epigenetics - NICHD
- Understanding the Epigenetic Basis of Human Health and Disease - NIA
- Exploring the Epigenome in Normal Development and Disease - NCI

Most of these ideas reiterated parts of the "Epigenetic Modifications in Health and Disease" idea. One idea in particular, "Epigenomic Targets and Disease Outcomes," aimed to identify specific genomic targets associated with exposure-induced epigenetically modified gene expression in the etiology or progression of diseases for which there is a known or suspected exposure component. This goal would be realized through the development of reference epigenomes that define normal human cells and tissues, providing opportunities to identify altered epigenetic marks in diseased cells and tissues. (Appendix 1. Epigenetic Modifications in Health and Disease; Appendix 2. Epigenomic Targets and Disease Outcomes)

**October 6, 2006, IC Directors' Mini-Retreat:** There was an IC Directors' mini-retreat to review the ideas gathered from ICs and consultation meetings with experts, and to explain the next steps in the strategic planning process.

**October - November 2006, Portfolio Analysis:** In 2006, Roadmap (RM) staff, in collaboration with other NIH program staff, consolidated 384 ideas into two broad categories: research enabling ideas, and research ideas. Within these broad categories, the ideas were further sorted into smaller clusters, including the epigenetics cluster. NIH staff piloted a rapid portfolio analysis process that used the Knowledge Management and Disease Coding (KMDC) software. The software extracted terms from the thesaurus that appeared in the ideas. Program staff then modified these ideas and generated a report using the KMDC search tool.

The epigenetics cluster focused on ideas for unveiling the epigenome in humans in normal, developmental, and a wide-variety of diseased states. Portfolio analysis using the KMDC software identified 14,977 grants for 2005. An arduous manual analysis of this portfolio by NIH

staff found that the current state of epigenetics science supported by NIH did not align well with the specific areas of interest within the epiegentics RM cluster. A vast majority of the projects were basic epigenetic research in model organisms with little focus on the contribution of epigenetics to diseases or aging, which was one of the primary research areas in the epigenetics cluster. Very few genome-wide analyses were being conducted, and the capacity to do this type of analysis was limited.

Genome-wide assessment of epigenomic contributions to health and human disease was considered sporadic with minimum overlap with the current ideas as proposed (mapping of epigenome in various diseased states). (Appendix 3. Portfolio Analysis Summary: Epigenetics Cluster)

**December 28, 2006, Prioritization of Ideas:** IC Directors were asked to vote on the ideas that should move forward into initiative concept development phase. The idea, "Epigenetic Modifications in Health and Disease," was one of the highest scoring ideas. (Appendix 4. New Roadmap Ideas & Analysis in Preparation for the IC Directors Retreat, pp. 1-2)

**January 4, 2007, IC Directors Retreat:** The agenda for the meeting was set based on the outcome of the IC Directors' votes on the ideas in December. IC Directors led the discussions and at the end of the day, the Epigenetics cluster of ideas was selected to move forward for further development (Phase 2 strategic planning).

**March 19-20, 2007, Epigenetics Workshops:** A CF supported workshop on Epigenetics of Human Health and Disease brought together leaders in the field with an interest in further developing approaches to epigenetics. Participants heard a wide-ranging series of talks related to epigenetics. These presentations were focused in two areas, applications to human health and disease and the state of epigenetic technology. Following the sessions, participants broke into groups to discuss the talks and provide suggestions for moving forward. (Appendix 5. Epigenetics Workshop Agenda)

**March - May 2007, Portfolio Analysis:** In preparation for proposal submission, the NIH research portfolio on "epigenetics" was evaluated by IC staff to determine scientific strengths, areas of current investment, and research opportunities. Focus areas included: disease, organ, epigenetic mechanism, biological process, model system, technology development, bioinformatics, exposure type, and clinical research. NIH had invested $231 million in related areas of research, with 584 extramural awards and 46 intramural awards. There had been limited disease-focused research except for projects relating to cancer. The portfolio analysis identified the following as opportunities for collaboration: (1) establish international standards for epigenomic research; (2) develop reference epigenomic maps and computational infrastructure to enable researchers world-wide; and (3) accelerate the understanding of epigenetic mechanisms in human health and disease. (Appendix 6. Epigenetics Portfolio Analysis)

**May 3, 2007, Proposal Submission:** Drs. Volkow (NIDA) and Schwartz (NIEHS) submitted the Epigenetics proposal to the Office of Strategic Coordination. The proposal included three supporting documents: proposal summary, portfolio analysis results, and Epigenetics workshop agenda. The overall goal of the initiative was to transform the understanding of the etiologic

basis of human health and disease by providing fundamental resources for the scientific community to use in conducting basic and translational research in human health and disease. To accomplish this goal, the initiative proposed to: (1) create an international consortium; (2) establish a set of comprehensive reference epigenomes, integrating multiple epigenetic marks in human ES cells, cell lines, and tissues; (3) develop standardized platforms, procedures and reagents for epigenomics research; (4) conduct demonstration projects to evaluate how the epigenome changes with disease and aging, development, and response to environmental exposures (physical, chemical, behavioral, and social environments); (5) develop new technology for comprehensive epigenomic analysis; and (6) create a public data resource to accelerate the application epigenomics approaches to understanding human health and disease.

The four proposed initiatives and associated goals were:
Initiative 1: Epigenomic Mapping Centers
Goals: Reference epigenomic maps in human ES cells, differentiated ES cells, selected cell lines, and human tissue; antibodies for epigenomics

Initiative 2: Epigenetics of Human Health and Disease
Goals: Evaluate epigenomic changes for IC-specific diseases or conditions of development, aging, or response to exposures (physical, chemical, behavioral, and social)

Initiative 3: Data Management Center for the Epigenomic Mapping Centers
Goals: Data storage, quality control, dissemination of raw/processed data to PIs (RFA #1 & #2); Data transfer to NCBI for public release; Import data from related projects; New methods for data summary/analysis/integration

Initiative 4: Technology Development in Epigenetics
Goals: Develop/validate new/improved existing technology to comprehensively measure/ integrate diverse data sets of multiple epigenomes within single cells/cell lines/tissues; Development of remote imaging of epigenetic activity in cells/tissues/whole animal

(Appendix 7. Email Correspondence: May 3, 2007 Proposal Submission; Appendix 8. Epigenetics Proposal Summary; Appendix 9. Epigenetics Proposal Template; Appendix 5. Epigenetics Workshop Agenda; Appendix 6. Epigenetics Portfolio Analysis)

**May 18, 2007, 2008/2009 NIH OPASI Roadmap Retreat:** NIH senior leadership convened to vet the proposed set of Roadmap FY 2008 initiatives with the following objectives: (1) identify initiatives to move forward as Requests for Applications (RFAs); (2) decide on approximate program size and start dates (FY 2008 or FY 2009); and (3) identify fundable pilot initiatives. NIH Director Dr. Elias Zerhouni encouraged the group to expand thinking "beyond Roadmap," to identify and clarify overarching themes for the NIH. Because the Roadmap is an intellectual venture space, its initiatives should be crafted through non-pedestrian thinking to meet grand challenges in biomedicine. He stressed the need for keeping a broad view and avoiding projects that are overly specific. Overall, the goal should be to define ideas by virtue of a "scientific excitement index."

The Epigenetics of Human Health and Disease program was presented by Drs. Volkow (NIDA) and Schwartz (NIEHS). The presentation stated that a modest Roadmap investment in infrastructure would be catalytic since there remained a large gap between basic and clinical research. Analyses of the NIH portfolio and international activities revealed that the field of epigenetics lacked integration, organization, standardization, and leadership. Particular gaps included the lack of a reference epigenome data set and a limited investment in disease-focused research (except cancer, which appears to be well-funded). It was believed the proposed Roadmap initiative would establish an NIH-led international consortium to create reference epigenomes, a publicly available epigenetic database, and other tools and resources. Four Requests For Applications (RFAs) were proposed to establish: (1) epigenomic mapping centers; (2) a data management center; (3) epigenetics demonstration projects (co-funded by ICs); and (4) new technologies.

When the proposed initiative was discussed, participants felt that as a fundamental mechanism, epigenetics had wide relevance to health and disease. Many believed that biological applications flowed naturally from ongoing basic studies of universal processes (e.g., senescence, differentiation, development). A critical mass of research interest existed in the field of epigenetics, fostering great enthusiasm within the community. The proposal's broad relevance to health and disease, ability to study across life stages, and filling a basic clinical gap were all seen as positive aspects of the initiative. However, it was noted that not all the needed technology was ready and the chromatin modification universe was incomplete. Despite these drawbacks, NIH Senior Leadership voted on the proposed initiative and the project was selected to proceed with development in FY 2008. (Appendix 10. Roadmap Retreat 2007 Summary, Epigenetic Excerpt)

**July 9, 2007, Detailed Plans:** Drs. Schwartz (NIEHS) and Volkow (NIDA) submitted the detailed program plans. During this time the program's name was changed from "Epigenetics" to "Epigenomics" to reflect the scope and comprehensiveness of the analyses the program would be supporting. The following four initiatives were included: (1) epigenomic mapping centers; (2) epigenomics of human health and disease; (3) data coordination and analysis center; and (4) technology development in epigenomics. (Appendix11. Epigenomics Detailed Plans)

## Appendix 13: Single Cell Analysis Program Evolution

**May 7, 2010, "The Big Think" Meeting:** The initial idea for the Single Cell Analysis Program (SCAP) was discussed during the 2010 strategic planning meeting with invited thought leaders, entitled "The Big Think. This meeting focused on three themes: (1) application of high throughput technologies, (2) translation of basic research, (3) utilization of science to benefit health care reform. Two ideas related to single cell analysis were discussed: tools for single cell biology proposed by NIMH and high-throughput platforms for molecular theranostics proposed by NIBIB. The idea of single cell analysis was identified as a crosscutting theme, which, if developed further, would help define and resolve biological phenotypes as well as disease processes at a level not fully realized. (Appendix 1. Big Think- NIMH Tools for Single Cell Biology; Appendix 2. Big Think- NIBIB Molecular Theranostics)

**June, 2010:** OD Leadership met to discuss the outcome of the Big Think and had sufficient enthusiasm for the ideas pertaining to Single Cell Analyses to warrant further planning. This preceded the decision by DPCPSI to involve the Council of Councils at this stage of planning; therefore, concept clearance was not conducted at this point.

**December 16, 2010, Trans-NIH Workgroup Convenes:** On December 16, 2010 a Single Cell Analysis Working Group comprised of 24 different members from various ICs held a kick-off meeting. The Working Group was created to develop the Single Cell Analysis concept into a proposal for a Common Fund (CF) program. Dr. Richard Conroy from NIBIB provided background information on the Working Group, which reflects a merging of the two IC concepts submitted to the Big Think. (Appendix 3. Single Cell Analysis WG 12-16-10 Minutes)

**February 8, 2011, RFI Published**: A Request for Information (RFI) was published to collect information from the broader research community to determine how best to accelerate research in single cell analysis. The Single Cell Analysis Working Group requested information on the following topics: (1) major themes in basic and/or clinical research for which additional focus on single cell analysis may provide the most significant and broadest impact, (2) current conceptual, technical, and/or methodological challenges in single cell analysis, (3) major biomedical research opportunities that can be addressed by single cell analysis, (4) the 5 highest priority tools and resources needed to seize these opportunities and overcome these challenges.

The RFI was open until March 18, 2011. There were 75 responses to the RFI. The major themes were: (1) map and understand cell state, importance of cell variability at tissue / system level, clinical impact, interpreting "noise", (2) imaging technologies, models & data analysis, sample handling, "-omic"analysis, (3) single cell profiling, linking cells to tissue / system phenomena, cell development, cell-cell interactions, clinical screening, (4) imaging technologies, community resources, sample manipulation, sensitive & quantitative "-omics", measurement technologies. (Appendix 4. NOT-RM-11-007 RFI- Single Cell Analysis for Biomedical Research; Appendix 5. Summary of Single Cell RFI)

**April 28-29, 2011, Workshop on Single Cell Analysis**: A CF supported Workshop on Single Cell Analysis brought together 21 leaders in the field including prominent academics, NIH

Intramural researchers, and national and international representatives from industry, all with an interest in further developing single cell approaches. The free-ranging discussion also involved more than 70 remote participants via webcast. From the four sessions the following themes emerged: (1) understanding and manipulating single cells *in situ* requires new biological paradigms and novel approaches, (2) a deep understanding of single cell function requires multimodal analysis that integrates disparate "–omics" datasets with sub-cellular spatial and temporal measures, (3) technologies currently exist that provide insight into single cell function; however, these need to be validated and be made available to the broader biological and clinical communities. (Appendix 6. Single Cell Analysis Workshop Summary)

**March-May 2011, Portfolio Analysis:** Working with staff from the DPCPSI/Office of Portfolio Analysis, the Working Group analyzed current spending in the field of Single Cell Analysis. The Portfolio Analysis report showed there had been a significant but uncoordinated, increase in NIH investment in the field from FY05 to FY10. It is a very broad reaching and multidisciplinary field, with
22 institutes awarded grants to conduct related research from FY05 to FY10. A majority of these individual awards focused on standard biology using conventional approaches. (Appendix 7. Portfolio Analysis of Single Cell Research; Appendix 8. Summary of SCAP Portfolio Analysis)

**May 4-6, 2011- "Innovation Brainstorm: Transforming Discovery into Impact" Meeting**: Discussion at this CF strategic planning meeting highlighted recent papers on the significance of heterogeneity at the single cell level. The investigators expressed the need to analyze and control genetic, epigenetic and environmental factors to understand complex populations and that the concept of phenotypes and subpopulations is plastic. Investigators determined that multi-disciplinary teams are best suited to overcoming technology hurdles, understanding the complexity of the data produced, and translating discoveries for more widespread use in biomedical research or the clinic.

As part of the "Innovation Brainstorm", the Single Cell Analysis concept was posted on the CF strategic planning website for the community to comment. Two comments indicated that analyzing various parameters of single cells would be truly transformative and lead to many breakthroughs in the way we study biological systems as well as serve as a platform for testing interventions and enable the development of personalized medicine. (Appendix 9. Summary of Single Cell Innovation Brainstorm; Appendix 10. CF Strategic Planning Social Media Comments, pg. 1, 21, 22)

**June 2, 2011, Proposal**: The Working Group, led by NIMH and NIBIB, submitted to the Office of Strategic Coordination (OSC) the proposal for the SCAP. The proposed initiatives and goals were: Initiative 1: Transformative Research Projects in Single Cell Analysis (R01)
Goal: To promote highly innovative approaches in single cell analysis. Involving, for example developing a complete taxonomy of human cell types.

Initiative 2: Accelerating the Integration and Translation of Technologies to Characterize Biological
Processes at the Single Cell Level (R01)
Goal: To accelerate new integrated and multiplexed approaches in single cell analysis.

For example, integrating "-omics" or following dynamical properties.
Initiative 3: Discovery of Exceptionally Innovative Tools and Technologies for Single Cell Analysis (R21)
Goal: To support the development of innovative tools and novel capabilities for single cell analysis.
Initiative 4: Single Cell Challenges or targeted opportunity
Goal: To provide well-defined resources and challenges for the field to address specific opportunities and attract new approaches and researchers to the field.
The working group presented the proposal to OD Leadership and a small group of IC Directors. Dr. Collins did not feel that that the plans were specific enough and asked the group to bring more details to him to reconsider at the end of the summer. (Appendix 11. Single Cell Proposal For Dr. Collins)

**June 29, 2011, Council of Councils Meeting:** Dr. Richard Conroy of NIBIB presented and stressed that the initiative met CF criteria. The program was transformative because it focused on the discovery and translation of multiplexed *in situ* approaches for the spatiotemporal analysis of a heterogeneous population of cells. The SCAP program sought to advance the individual missions of the NIH ICs because cells are at the center of biomedical research and the initiative would build synergy between ICs already active in the field. Understanding the link between cell states and tissue-level function is central to understanding the emergence and progression of many diseases and disorders. Through a coordinated effort by the NIH to promote scientific advancement this initiative would be something no other entity would be likely to do. The goals of the program were presented as follows:

1. To accelerate the discovery of tools that can be used to characterize individual cells including methods that preserve cell viability, methods that capture spatiotemporal information, and methods that allow for evaluation of cells *in situ*.
2. To specifically explore and examine technical and analytical challenges derived from and associated with, cell heterogeneity in healthy and diseased tissues.
3. To accelerate the validation and translation of new technologies using single cell approaches for use in clinical settings.
4. To engage investigators and interdisciplinary teams not typically funded through the NIH, in order to confront defined challenges in the field of single cell analysis.

Discussion by the Council members highlighted that there is a need to study a single cell within the context of a heterogeneous cell population in a parallel format that interrogates many parameters simultaneously. It was felt that studying cells in the context of external environmental influences is critical and it may be feasible as a result of this CF initiative in 5 to 10 years. It was also noted that heterogeneity is a term that can be used to describe a mixed population of cells, but can also be used to describe different stages of differentiation or activation of one cell type. The Council of Council members voted on the SCAP and approved the initiative unanimously without modification (Appendix 12. Council of Council Meeting Minutes 6-29-11; Appendix 13. Single Cell Analysis, Proposal for CF Program, 24 slides; Appendix 14. Single Cell Concept Clearance Proposal)

**September, 2011, Updated Plan to Dr. Collins:** During August, the Working Group met with staff from DPCPSI to flesh out the details of the proposal. Dr. Collins asked for these details to be shared with the IC Directors who reviewed the proposal in June. The biggest shift that

occurred was the articulation of the goal for a consortium of investigators funded via the program to collectively determine new fundamental paradigms of biology through the examination of many types of cells, each studied as individual cells in different complex environments. To achieve this goal, awards would be U01s rather than R01s, so that NIH could help the investigators focus on these cross-cutting fundamental principles and work as a group to develop them. All IC Directors were supportive and Dr. Collins approved the program. (Appendix 15. Single Cell Analysis Synopsis Sept 1 2011)

**September 29, 2011 Detailed Plans**: The detailed plan submitted by the Working Group was approved with a revised overall program goal - to accelerate the development of improved research capabilities in single cells and promote basic, translational, and clinical applications using single cell approaches. A description of the four program initiatives and their corresponding goals and milestones is below. These Detailed Plans still did not provide specific milestones for the program or elaborate on the plans to establish new paradigms. Instead of having the Working Group resubmit the document, the OSC asked them to explain specific goals and milestones in the first annual report, which was due at the end of October 2011.

Initiative 1. An initiative to support transformative research projects in single cell analysis
Goal: To promote highly innovative approaches in single cell analysis involving, for example, developing a complete taxonomy of human cell types.
Milestone: Fund XX projects applying highly innovative approaches by FY2013.

Initiative 2. A development initiative to accelerate the validation and translation of new technologies

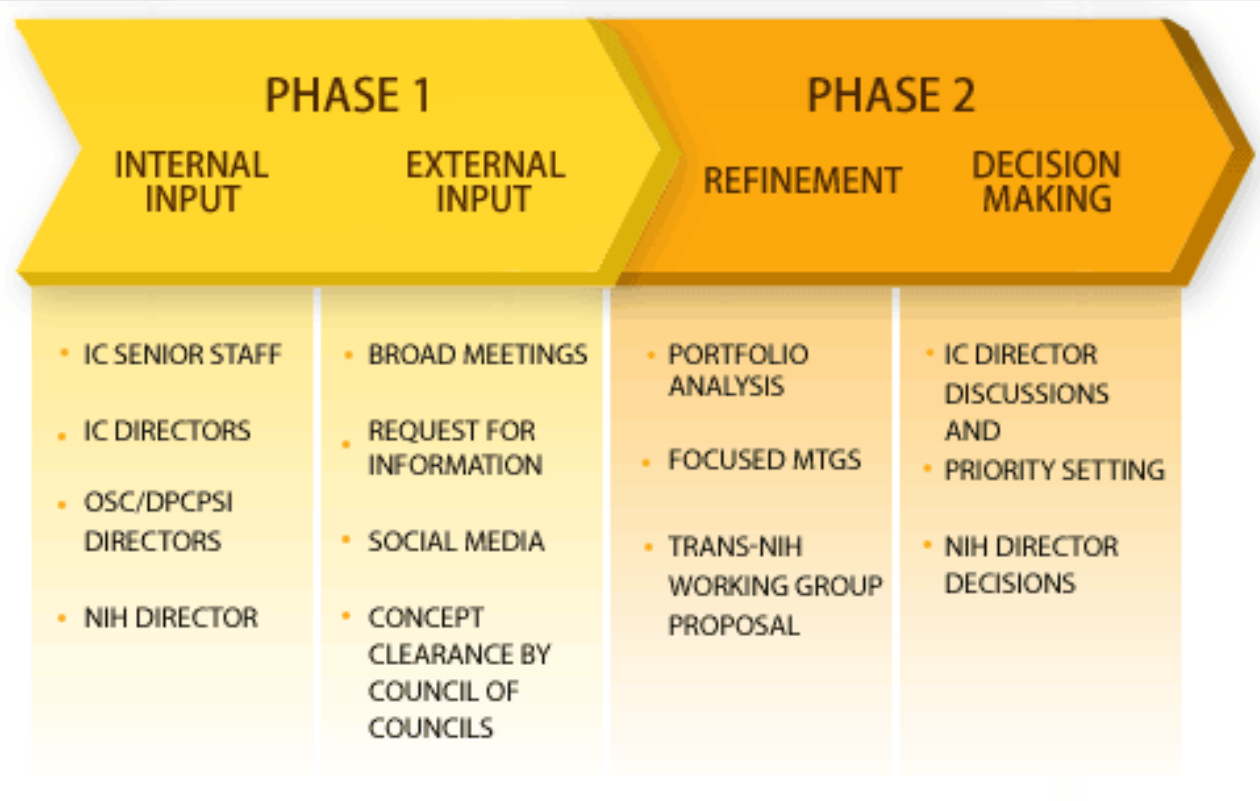
Goal: To accelerate new integrated and multiplexed approaches in single cell analysis. For example, integrating "-omics" or following dynamical properties.
Milestone: Fund XX projects that accelerate the validation and translation of new technologies by
FY2013.

Initiative 3. A high-risk, high-reward initiative for discovery of new approaches in single cell analysis Goal: To support the development of innovative tools and novel capabilities for single cell analysis. Milestone: Fund 5 projects by FY2012 that foster new approaches and identify and fund new priorities by FY2015.

Initiative 4. Single Cell Challenge or other targeted opportunities
Goal: To provide well-defined resources and challenges for the field to address specific opportunities and attract new approaches and researchers to the field.
Milestone: Encourage new approaches and new investigators by funding XX projects and XX researchers new to the field by FY2015. (Appendix 16. Detailed Plans Single Cell Analysis v3)

# Appendix 14: Detailed Strategic Planning Slides

# Common Fund Strategic Planning Process




- Two phases are required because CF has no defined area of science it covers
- The “mission” has to be defined every time a new program is developed
- A new round of Common Fund strategic planning is initiated annually
- The entire process (Phase 1 through Phase 2) lasts 18 months so there is overlap

# Strategic Planning Phases

PHASE 1: Identification of Broad Needs - 9 Months (Nov – Jul)

*Concepts are Developed*

- Broad topic areas that address the biggest challenges and greatest opportunities in biomedical research are identified through various activities.
  - Internal sources:
    - Internal meetings and discussions occur with IC Directors, IC staff, OSC Directors, and NIH Director to solicit ideas for concepts (Dec – Mar).
  - External sources:
    - Workshops occur to solicit feedback (Mar)
      - ICDs nominate participants for workshops (Nov)
      - Staff assist in leading sessions
      - Logistics are determined for the meetings
    - Requests for Information are sent to solicit feedback
      - RFI text is developed
      - Distribution is determined
      - RFI is distributed
      - Feedback is collected and analyzed

# Strategic Planning Phases

PHASE 1: Identification of Broad Needs - 9 Months (Nov – Jul) (Continued)

*Concepts are Reviewed and Referred to Council of Councils (CoC) (Apr – May)*

- Concepts are characterized and addressed accordingly
  - Referred to an existing Working Group if the idea relates to a current program
  - Removed if the idea is redundant with other ideas or previous programs
  - Otherwise, referred to the Council of Councils

*Concepts are Cleared (Jun)*

- CoC determines if concepts are consistent with CF criteria
- Cleared concepts are reviewed by OD
- Selected concepts are sent to ICDs to discuss

*Decision* (Jul)

- ICDs discuss cleared and forwarded concepts
- Determine if additional concepts should be included
- Decision is made by NIH and DPCPSI Directors which concepts to pursue
- Final concepts proceed to Phase 2

# Strategic Planning Phases

PHASE 2: Refinement into Specific Initiatives - 9 Months (Aug – Apr)

*Concepts are refined*

- Trans-NIH Working Groups are formed for each concept (Aug-Sep).
  - 2-3 IC Directors nominate themselves or senior staff as Co-Chairs and Coordinators of the program.
  - IC Directors nominate staff to participate as members or initiative leaders.
- Working Groups refine the concepts (Oct – Mar)
  - Portfolio analysis
  - Additional meetings/workshops
- IC Directors and CoC are updated (Jan)
  - Provide guidance to Working Groups

*Final Decision*

- Proposals due to and reviewed by OSC (Mar)
- Proposals presented to Dr. Collins and group of IC Directors (Apr)
- Working Groups follow-up on questions/changes requested at meeting (Apr)
- Final decisions are made to funds program by Dr. Collins (Apr)

## Appendix 15: Intramural Research Program – Planning

Most Common Fund (CF) award solicitations are open to applicants from all organizations, including the NIH Intramural Research Program (IRP), with the goal of supporting the best science regardless of where the research is conducted. This document provides an examination of occasions when the IRP has been determined to be uniquely positioned to address key roadblocks in biomedical research as part of the CF. In these cases, funds are allocated to the IRP without competition with extramural applicants and are thus considered IRP-only programs or initiatives (an initiative is one component of a multi-component program). This analysis of five IRP-only CF programs or initiatives is intended to provide insight into the criteria for determining that the IRP is uniquely positioned to meet the goals of the program or initiative, and the process through which these activities are planned. A document describing the oversight and management of IRP-only programs/initiatives will be provided at a subsequent stage of the CF evaluation.

### HISTORY

From Fiscal Years 2004-2006, the NIH Roadmap programs were supported by combined funds from each of the ICs, with each IC providing 1% of its appropriation to the pool. Since these funds "came off the top," i.e., before funds were allocated to intramural or extramural programs, both intramural and extramural investigators were intended to benefit from the programs and to be eligible to receive funds. During the planning stages for the initial set of Roadmap programs, initiatives were designed exclusively for either intramural or extramural; competition between the two did not occur. However, as additional programs were planned in 2006, the NIH Leadership questioned whether programs or initiatives should be developed exclusively for one or the other.

In 2007, a group of Institute and Center (IC) Directors which advises the NIH Director on trans-NIH operational activities (the NIH Steering Committee) provided guidelines that would determine how the NIH IRP should be involved in CF programs. Recognizing that certain strategic objectives might best be met by the IRP, while others might be suitable only for investigators in the Extramural Research Program (ERP), it determined that the IRP-ERP contribution to each program or initiative should be considered on a case by case basis. The expectation was that goals might generally be achieved by investigators in either the IRP or the ERP and that awardees should therefore be selected via competition with peer review; clear justifications for IRP-only or ERP-only programs or initiatives would be required.

### CRITERIA

At the time of the Steering Committee review, the following criteria for Intramural-only programs were articulated. These criteria continue to be used.

- The goals of the initiative are to develop a resource that is "inherently governmental" because it needs to be in the public domain, and, if successful, will require stable, ongoing support.
- The goals of the initiative benefit from access to the unique patient populations or resources that are available in the NIH Clinical Center or other facilities within the IRP.
- The goals of the initiative or program must be implemented rapidly. (See document entitled "Dealing with Rapidly Emerging Challenges and Opportunities" for a separate discussion of this type of program.)

The planning of IRP-only programs and initiatives has been variable, as described below for 5 representative initiatives.

- **PubChem (2004):** The Molecular Libraries and Imaging program was designed to provide the capability and data management resources for small molecule assay development and screening, chemical library development, and imaging probe development to intramural and extramural investigators. The creation of a coordinated set of initiatives was outlined in numerous NIH Roadmap Planning meeting reports from 2002, with certain components to be established within the IRP as stable government resources if they proved useful to the community. PubChem was spawned by the need for a long-term, publicly available inventory of NIH chemical databases such as NCI's Developmental Therapeutics Program, NIMH's Psychoactive Drug Screening Program, and NLM's ChemID along with other databases at FDA, NIST, and the Protein Data Bank. In addition, PubChem was designed to link other online resources (e.g., NLM's Medline) while serving as a central repository for organic-molecule chemical structures from the ML program, public sector, and commercial vendors. This positioned PubChem as a "one of a kind" comprehensive chemical database. The very uniqueness of this endeavor made housing this public database at NIH NCBI the most feasible option due to the need for "link out" access to numerous internal and external databases and continuing these activities in perpetuity.

- **Imaging Probe Development Center (IPDC, 2004):** A second ML component, IPDC, was created to address the dearth of probes available for molecular imaging. A 2004 NIH Roadmap Workshop involving public/private sector and academic experts along with potential "consumers" further elucidated the challenges surrounding molecular probe synthesis. This helped shape the IPDC into a core facility that provides imaging probes not available through a commercial supplier and generates novel imaging probes (e.g., optical, PET, SPECT, and MRI). The core facility was also intended to serve as counterpoint to extramural initiatives (P20 RFA; R21 RFA) focused on improving probe detection sensitivity 10x – 1000x. The IPDC would support the efforts of these extramural multi-PI teams while the extramural investigators would drive corresponding changes in the IPDC. In this way the two initiatives were intended to function synergistically. Although plans called for the IPDC to generate reagents for both

intramural and extramural communities eventually, it was initially established as a core serving only IRP investigators. Interaction of the IPDC with the ERP never developed. The IPDC Center Director was not involved in the planning for the Center; he was recruited after plans for the Center were approved.

- **Re-Engineering the Clinical Research Enterprise – Clinical Research Training Program (CRTP):** The Roadmap Re-engineering the Clinical Research Enterprise program began as a series of complementary initiatives that would facilitate clinical research and that emphasized training clinician scientists. As part of a goal to increase the number of clinician scientists dramatically, the CRTP – an existent, successful training program for medical and dental students within the NIH IRP – was expanded to double the number of trainees each year from 15 to 30. The CRTP, now known as the Medical Research Scholars Program, matches visiting medical and dental students with participating IRP principal investigators (PIs) who mentor these students as they conduct clinical or translational research in an area of their choosing. Expanding the CRTP was one component of a larger clinical research training effort that also included training at extramural sites. The need for clinical research training was strongly voiced during planning workshops held prior to the launch of the Roadmap.

- **Epigenomics – Data Management (2007):** The CF Epigenomics Data Management Center was created specifically to provide public access to the data generated by the Epigenomics Program along with data from other NCBI resources, NIH ICs, and the international community. This public resource required the development and harmonization of data tools in addition to transfer protocols facilitating global data integration. As such, NCBI was seen as uniquely capable of developing and implementing a publicly accessible, long-term data repository in support of the international epigenetics research community.

- **NIH Center for Regenerative Medicine (NIH CRM, 2010):** As part of Dr. Collins' vision for translational medicine, he asked OSC and IC partners to consider challenges for the development of cell therapies using induced pluripotent stem cells (iPSCs). Recognizing the unique clinical and translational resources that the IRP could bring to this effort, he asked that a Center be developed within the IRP to identify and overcome the translational challenges for iPSC therapies. Early planning for the CRM and recruitment of a Director was led by two IC Scientific Directors, who held a workshop to consider translational challenges and opportunities and began recruitment for a Center Director. The early plans called for the CRM to support a group of translational projects which would involve collaborations with the Center Director but would be conducted in multiple ICs. While a Director was being recruited, pilot projects were begun to establish a critical mass of stem cell investigators within the IRP. Later details of the activities of the Center were to be developed by the Center Director, with the expectation that the

following IRP resources could be brought to bear on the therapies to be developed: the Clinical Center's cellular GMP facility and experience with clinical studies; the Chemical Genomics Center's high-throughput molecular screening facility; the Stem Cell Unit's non-human primate facility; the Bone Marrow Stromal Cell Transplantation Center. In addition, the CRM Director was expected to address procedural and policy issues associated with stem cell therapy development, working closely with the FDA to facilitate regulatory clearances.

**Appendix 16: Funding Opportunity Announcements (FOAs) for Five Programs with Hyperlinks**

This document pertains to Management/Oversight question I, "Are expectations for programs clearly articulated in funding announcements, program kick-off documents, websites, and program materials? Are the goals and responsibilities clear?" It provides the FOAs for the following five programs: Epigenomics, Human Microbiome Project (HMP), Molecular Libraries and Imaging, NCBC, and PROMIS. The title and the year for each FOA are listed along with the link to that specific FOA. The goals of the relevant program should be discussed in the "Funding Opportunity Description" portion of each FOA. Additional information such as expectations around resource and data sharing may also be found in "Application and Submission Information" section of each FOA.

Epigenomics:

- Functional Epigenomics - Developing Tools and Technologies for Cell-type, Temporal, or Locus-specific Manipulation of the Epigenome (R01) (2013): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-12-026.html
- Epigenomics of Human Health and Disease (R01) (2008): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-08-017.html
- Reference Epigenome Mapping Centers (U01) (2007): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-07-013.html
- Epigenomics Data Analysis and Coordination Center – EDACC (U01) (2007): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-07-014.html
- Developing Technologies for Improved *In Vivo* Epigenetic Imaging or Analysis (R01) (2009): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-09-016.html
- Technology Development in Epigenetics (R21) (2007): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-07-012.html
- Technology Development in Epigenetics (R01) (2007): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-07-011.html
- Discovery of Novel Epigenetic Marks in Mammalian Cells (R21) (2007): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-07-016.html
- Discovery of Novel Epigenetic Marks in Mammalian Cells (R01) (2007): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-07-015.html

Human Microbiome Project:

- Evaluation of Multi-'omic Data in Understanding the Human Microbiome's Role in Health and Disease (U54) (2012): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-12-021.html
- Human Microbiome Demonstration Projects (UH2/UH3) (2007): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-08-012.html
- Construction of a Reference Sequence Data Set for the Human Microbiome Project (U54) (2007): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-08-001.html

- Studies of the Ethical, Legal, and Social Implications (ELSI) of Human Microbiome Research (R01) (2008): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-08-030.html
- Studies of the Ethical, Legal, and Social Implications (ELSI) of Human Microbiome Research (R01) (2007): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-08-006.html
- A Data Analysis & Coordination Center (DACC) for the Human Microbiome Project (U01) (2007): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-08-007.html
- Development of New tools for Computational Analysis of Human Microbiome Project Data (R01) (2009): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-09-020.html
- Development of New Tools for Computational Analysis of Human Microbiome Project Data (R21) (2009): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-09-021.html
- Development of New Technologies Needed for Studying the Human Microbiome (R01) (2009): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-09-008.html
- Development of New Technologies Needed for Studying the Human Microbiome (R21) (2009): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-09-009.html
- Development of New Technologies Needed for Studying the Human Microbiome (R01) (2008): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-08-026.html
- Development of New Technologies Needed for Studying the Human Microbiome (R21) (2008): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-08-027.html
- Development of New tools for Computational Analysis of Human Microbiome Project Data (R01) (2007): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-08-008.html
- Development of New Technologies Needed for Studying the Human Microbiome (R01) (2007): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-08-010.html
- Development of New Technologies Needed for Studying the Human Microbiome (R21) (2007): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-08-011.html

Molecular Libraries and Imaging

***Molecular Libraries Screening Centers and Small Molecule Repository***

- NIH Small Molecule Repository Solicitation Number: HHS-NIH-NIDA(MH)-12-029: https://www.fbo.gov/index?s=opportunity&mode=form&id=4b98cce7cb35c5ad08e53d5d005c0b59&tab=core&_cview=1
- Assays for High Throughput Screening (HTS) to Discover Chemical Probes in the Molecular Libraries Probe Production Centers Network (MLPCN) (X01) (2012): http://grants.nih.gov/grants/guide/pa-files/PAR-12-108.html
- Solicitation of Assays for High Throughput Screening (HTS) in the Molecular Libraries Probe Production Centers Network (MLPCN) (R03). This is a reissue of PAR-08-035 (2009): http://grants.nih.gov/grants/guide/pa-files/PAR-09-129.html
- Molecular Libraries Probe Production Centers Network (MLPCN) (U54) – Limited CompetitionRFA-RM-08-005 (2007): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-08-005.html

- Molecular Libraries Screening Centers Network (MLSCN) RFA-RM-04-017 (2004): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-04-017.html
- Solicitation of Assays for High Throughput Screening (HTS) in the Molecular Libraries Probe Production Centers Network (MLPCN) (X01) PAR-08-034 (2007): http://grants.nih.gov/grants/guide/pa-files/PAR-08-034.html
- Solicitation of Assays for High Throughput Screening (HTS) in the Molecular Libraries Probe Production Centers Network (MLPCN) (R03) PAR-08-035 (2007): http://grants.nih.gov/grants/guide/pa-files/PAR-08-035.html
- Solicitation of Assays for High Throughput Screening (HTS) in the Molecular Libraries Screening Centers Network (R03/X01) PAR-06-259 (2007): http://grants.nih.gov/grants/guide/pa-files/PAR-06-259.html
- Solicitation of Assays for High Throughput Screening (HTS) in the Molecular Libraries Screening Centers Network (R03) PAR-06-545 (2006): http://grants.nih.gov/grants/guide/pa-files/PAR-06-545.html
- Solicitation of Assays for High Throughput Screening (HTS) in the Molecular Libraries Screening Centers Network (X01) Reissue of PAR-05-147PAR-06-259 (2007): http://grants.nih.gov/grants/guide/pa-files/PAR-06-259.html
- Solicitation of Assays for High Throughput Screening (HTS) in the Molecular Libraries Screening Centers Network (MLSCN) (X01) Reissue of PAR-05-060 PAR-05-147 (2005): http://grants.nih.gov/grants/guide/pa-files/PAR-05-147.html
- Solicitation of Assays for High Throughput Screening (HTS) in the Molecular Libraries Screening Centers Network (MLSCN) (R03) PAR-05-060 (2005): http://grants.nih.gov/grants/guide/pa-files/PAR-05-060.html

***Technology Development***

- Assay Development for High Throughput Molecular Screening (R21) PAR-08-024 (2008): http://grants.nih.gov/grants/guide/pa-files/PAR-08-024.html
- Assay Development for High Throughput Molecular Screening (R21) This is a reissue of RFA-RM-07-001 RFA-RM-07-008 (2007): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-07-008.html
- Assay Development for High Throughput Molecular Screening (R21) Reissue of RFA-RM-06-004, which was previously released November 2, 2005 RFA-RM-05-011; Reissue for FY2005 of RFA-RM-04-012 RFA-RM-07-001 (2007):http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-07-008.html
- Assay Development for High Throughput Molecular Screening (R03/R21) Reissue for FY2006 of RFA-RM-05-011 RFA-RM-06-004 (2005): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-06-004.html
- Assay Development for High Throughput Molecular Screening (R03/R21) Reissue of RM-04-012 RFA-RM-05-011 (2004): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-05-011.html
- High Throughput Molecular Screening Assay Development (R03) RFA-RM-04-012 (2004): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-04-012.html
- Exploratory Centers for Cheminformatics Research (P20) RFA-RM-05-012 (2004): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-05-012.html

- Pilot-Scale Libraries (PSL) for High-Throughput Screening (P41) RFA-RM-09-007 (2009): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-09-007.html
- New Methodologies for Natural Products Chemistry (R01) RFA-RM-09-005 (2008): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-09-005.html
- Pilot-Scale Libraries for High-Throughput Screening (P41) RFA-RM-06-003 (2005): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-06-003.html
- Pilot-Scale Libraries (PSL) for High-Throughput Screening (P41) This is a reissue of RFA-RM-05-014 RFA-RM-08-003 (2007): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-08-003.html
- Pilot-Scale Libraries for High-Throughput Screening (P41) RFA-RM-05-014 (2004): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-05-014.html
- New Methodologies for Natural Products Chemistry (R01) This is a reissue of RFA-RM-05-013 RFA-RM-08-004 (2007): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-08-004.html
- New Methodologies for Natural Products Chemistry (R01) RFA-RM-05-013 (2004): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-05-013.html
- Molecular Libraries Screening Instrumentation (R01) RFA-RM-08-020 (2008): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-08-020.html
- Molecular Libraries Screening Instrumentation (R01) RFA-RM-04-020 (2004): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-04-020.html
- Novel Preclinical Tools for Predictive ADME-Toxicology (R21) RFA-RM-04-023 (2004): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-04-023.html

***Development of High Resolution Probes for Cellular Imaging***

- Innovation In Molecular Imaging Probes (R21) RFA-RM-04-021 (2004): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-04-021.html
- Development of High Resolution Probes for Cellular Imaging (P20) RFA-RM-04-001 (2003): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-04-001.html

NCBC

- National Centers for Biomedical Computing U54 RFA-RM-09-002 (2009): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-09-002.html
- National Centers for Biomedical Computing (Re-issuance of RFA-RM-04-003) (U54) RFA-RM-04-022 (2004): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-04-022.html
- National Centers for Biomedical Computing (U54) RFA-RM-04-003 (2003): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-04-003.html

PROMIS

- Patient-Reported Outcomes Measurement Information System™ (PROMIS) Network Center (U54) RFA-RM-08-022 (2003): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-04-006.html

- Patient-Reported Outcomes Measurement Information System™ (PROMIS) Research Sites (U01) RFA-RM 08-023 (2008): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-08-023.html
- Patient-Reported Outcomes Measurement Information System™ (PROMIS) Technology Center (U54) RFA-RM-08-024 (2008): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-08-024.html
- Patient-Reported Outcomes Measurement Information System™ (PROMIS) Statistical Center (U54) RFA-RM-08-025 (2008): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-08-025.html
- Dynamic Assessment of Patient-Reported Chronic Disease Outcomes (U01) RFA-RM-04-011 (2003): http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-04-011.html

## Appendix 17: PROMIS Program Summary

**Why This Program was Selected for Review**

PROMIS is included for review because of the distinct challenges it has faced with respect to transition. Its goal was to develop a tool that would be useful in diverse clinical situations in which patient reported outcomes must be assessed quantitatively and reproducibly. The transition of the program therefore involves questions of dissemination and use more than continued funding, although questions of continued support are also an issue. The PROMIS Working Group provides a model for working with other federal agencies, the private sector, NIH extramural staff, NIH intramural investigators, and others to inform them about the utility of new tools for operating within a clinical setting. Future funding for PROMIS also offers an alternate model for continued support of research tools. These items are highlighted in this document.

**Common Fund Support**

**Phase I: 2004-2008**

FY 2004 Actual: $6,010,000
FY 2005 Actual: $6,318,643
FY 2006 Actual: $6,198,286
FY 2007 Actual: $8,930,706
FY 2008 Actual: $9,435,548

**Phase II: 2009- 2014**

FY 2009 Actual: $11,068,766
FY 2010 Actual: $9,395,762
FY 2011 Actual: $8,214,135
FY 2012 Actual: $8,840,631
FY 2013 Actual: $4,144,438
FY 2014 Budgeted: $319,220

**Common Fund Criteria**

PROMIS met the criteria for Common Fund programs because it was deemed transformative, cross-cutting, unique, catalytic, and synergistic from the outset. Historically, clinical research and care has suffered from the lack of comprehensive tools to measure self-reported health for comparisons across the age spectrum and in both healthy populations and disease groups. PROMIS was unique in that it represented the first major attempt to incorporate Item Response Theory (IRT) and Computer Adaptive Testing (CAT) into biomedical research and clinical care. The patient burden was reduced, as the CAT generated questions based on previous responses, so the patient only had to reply to a few items in a bank. By addressing the chronic disease missions of multiple Institutes and Centers (ICs), PROMIS stood out as a program that cut across many of the ICs.

PROMIS intended to develop more precise, efficient, and easy to use measures of quality of life and symptom indices to enhance clinical research and patient care. Researchers would be able to measure clinical outcomes from preventative, rehabilitative, and curative interventions more precisely and compare them across diseases and populations, an approach that would transform the paradigm in assessing patient-reported outcomes (PROs). The resulting repository and supporting technology would permit the direct comparison of results, even from different instruments with different questions, a result that synergistically enhances the mission of the ICs in benefiting health. By developing these measures and tools within the funding time frame it was hoped the PROMIS would yield catalytic results.

## Program Description

The NIH Roadmap planning process identified a need for improved assessment of symptoms and other patient-centered outcomes in clinical research.[1] In response, the NIH initiated PROMIS, a 10-year Common Fund project to develop and test item banks measuring PROs across diseases, create a CAT for efficient and psychometrically robust PRO assessment, and create a publicly available and evolving measurement system that allows access to both a common item repository and computerized administration.[2] PROMIS instruments are designed to provide clinical researchers, patients, and clinicians with efficient, reliable, and valid assessments of adult and child self-reported health including ability to function, symptoms, feelings, and perceptions. PROMIS measures are particularly important to evaluating the effectiveness of health care for chronic conditions because, for these, the goals of therapy are to improve patients' abilities to function and to reduce symptoms associated with the condition. PROMIS uses CAT, which provides increased precision while reducing patient burden, to measure what patients are able to do and how they feel. The data are accumulated into reports that can be used by clinical researchers to assess the effectiveness of experimental treatments and by patients and clinicians to manage disease.

## Goals

### Phase I

The overall goal of PROMIS is to become a widely accepted, standardized PRO measurement tool that will allow greater comparability of studies, with reduced burden on patients.

Milestones[3]

- To establish a domain framework and develop candidate items for an initial set of adult and pediatric item banks
- To administer the candidate items to a large sample of individuals suffering from a variety of chronic diseases
- To analyze the data to calibrate the items to build the PROMIS v1.0 item banks
- To initiate validation studies of the PROMIS v1.0 measures as well as a mode of administration study
- To build a web–based resource for administering computerized adaptive tests and other patient–reported instruments, track accrual, score and export data for clinical research
- To conduct feasibility studies to evaluate the utility of PROMIS and promote widespread use of the instrument for clinical research and clinical care
- To link with external scientists to share PROMIS methodology, instruments, and software

### Phase II

The goals are to validate the PROMIS domains in the context of clinical studies and to develop PROMIS to facilitate adoption by clinical researchers.

Milestones[3]

- To develop new items and domains

- To translate current and future items and domains into other languages, such as Spanish and Chinese, to facilitate international studies
- To conduct validation studies in large-scale clinical trials in a variety of clinical populations
- To make PROMIS tools accessible to a wider range of clinical researchers and patient care communities and to optimize their usability for rapid adoption
- To provide ongoing education and outreach to familiarize users with new developments in PROMIS
- To improve PROMIS tools to allow for better outcomes in clinical trials and, potentially, for better individual and clinical decisions
- To engage stakeholders at all levels, by continuing interactions with other health-related Federal agencies, forging new relationships with patients and patient organizations, and establishing public-private partnerships to sustain PROMIS once NIH Roadmap for Medical Research funding ends

**Management**

The first phase of PROMIS was managed by a trans-NIH working group, chaired by an IC Director and comprised of program staff from nearly every IC.[4] The NIH Science Officers (SOs), representing seven ICs, had substantial scientific and programmatic involvement with the conduct of these awards, through technical assistance, advice, and coordination, above and beyond normal program stewardship for grants. The NIH Project Officer (PO) was responsible for normal program oversight and stewardship of the award. The role of the Office of Strategic Coordination (OSC) (then called "OPASI") staff was minimal prior to 2008 because the new office had not yet been fully staffed.

A steering committee (SC) composed of NIH SOs and PROMIS extramural investigators provided coordination and scientific direction, with input from an External Scientific Board (ESB). SC voting membership included the SOs and the Principal Investigators (PIs) of each cooperative agreement. The PO appointed the SC chair, served as a non-voting member of the SC, conducted continuous review of all activities, and recommended support levels.[2] The ESB, which consisted of ten scientists appointed by the NIH, also evaluated the awardees' progress in relation to the goals of this program and made recommendations to the NIH regarding improving the project.[5]

In the second phase of PROMIS, a large group of ICs staff from many ICs continues to manage the program via a working group chaired by two IC Directors.[6] OSC staff members have provided increased input and oversight since March 2008, when the office expanded. A SC continues to function as the main governing body for all projects awarded, and as the mechanism for NIH interactions and collaborations with the awardees. There has not been a standing ESB in the second phase of PROMIS.[7]

**Panel Review and/or Formal Evaluation Conducted**

A panel review was conducted in 2007[5] and a formal evaluation was conducted in 2012[8] (see next section for recommendations).

**History and Evolution**

The PROMIS network was funded in late September 2004 as a group of seven U01 grants including one Statistical Coordinating Center and six Primary Research Sites.[9] For the first few years, activities focused on organizing PROMIS into a functional, cooperative network, developing the domain framework, creating the item banks, initiating data collection for item bank testing and validation, initiating software development, disseminating project information, and initiating plans for project sustainability.[3]

In 2007, a review panel of external experts was convened to conduct a mid-course evaluation of PROMIS that would inform a decision as to whether and how the program should continue to receive Common Fund (then "Roadmap") support. The panel concluded that the program had met its goals for the first three years.[5] The panel also commented that the ultimate success of the project would depend on:

- Validation of the PROMIS instruments for clinical research
- Implementation of the CAT system
- Adoption of PROMIS products by the clinical research community.

"Roadmap" funding was approved for Phase II – 2009 through 2012.[9]

In response to the panel review, the PROMIS Working Group requested applications for clinical validation studies because demonstration of the utility of PROMIS in the clinic would be necessary before clinical researchers would adopt PROMIS. Another way it promoted the adoption of PROMIS by clinical researchers was by working to have PROMIS instruments incorporated into assessments by a number of large organizations. These organizations include EPIC, the Center for Disease Control and Prevention (CDC), the Department of Defense (DOD), the Center for Medicare and Medicaid Services Centers (CMS) and the NIH Clinical Center (see sections below on outputs and outcomes). For the second funding phase of PROMIS, the NIH held open competitions for three types of centers- a Technology Center to implement the CAT tool and house the item banks, a Statistical Center to coordinate data collection and manage quality, and a Network Center for overall coordination and dissemination. In addition, there were 11 research sites focused on translating item banks into different languages, developing new item banks (including some for women and children), conducting clinical validation studies, increasing dissemination and uptake of PROMIS measures, and advancing plans for sustainability.[3,8]

A formal evaluation was conducted in 2012.[8] Interviews were carried out and a panel of external experts was convened from March 2012 through November 2012 to review PROMIS II. The outcomes and recommendations reported by the expert panel and documented in a December 2012 report include the following:

- The PROMIS Principal Investigators have conducted a number of well-run validation studies. However, there is concern that no domain has completely met all the criteria to establish validity in general and specific populations, availability in different formats and languages, and concurrent and predictive validity so that it reached a maturity model. A metric for success for when a domain is complete should be developed.
- The majority of PROMIS users could identify ways in which the PROMIS measures helped their research (80%) and planned or knew a colleague who planned to use PROMIS in the future (85%). It is clear that clinicians and investigators find PROMIS

items valuable, but their utility is impeded by the lack of education and publications on the measures. There should be a well-defined plan for dissemination.
- Regarding data collected from the Technology Center, the investigators report 800 launched studies using PROMIS. The independent literature searches and examination of the clinicaltrials.gov website found less than 30 registered trials currently using PROMIS measures. While the Panel recognizes many of the ongoing studies using PROMIS may not be captured on this site, the number of studies the Technology Center reported is significantly higher and how they define launched studies should be operationalized.
- Some concrete steps have been taken toward creating a structure for sustainability, but additional work is needed to maintain CAT and the Technology Center. Partnerships to maintain CAT and the Technology Center should be explored.

In the ten months since it received the report from the 2012 review, the PROMIS SC has refined its metrics for when a domain is complete and made this document public.[10] In addition, it developed a matrix of the psychometric work accomplished and the population on which it has been tested.

The PROMIS SC's subcommittee on outreach has enhanced its dissemination efforts in several ways. It developed a list of frequently asked questions and put them on the PROMIS website; [11] it started a quarterly newsletter; [12] and it developed a Twitter account that now has 225 followers.[13] It also formed a working group with industry representatives. To date, the PROMIS program has produced over 200 publications.[14] The Technology Center has held workshops and established on-line tutorials and a help desk.[15]

Regarding the criteria for active studies, the Technology Center has defined an active study as one that:
- Is launched for data collection (they do not count pre-launch field testing which typically takes place at the beginning of a study)
- Includes at least five consenting participants who have provided at least one data point each at any point in time
- Has accrued at least one participant who provided at least one data point in the identified time period
- Is NOT a study created by a member of the PROMIS Technology team unless clearly identified as a true data collection study
- Is NOT the CAT demonstration available through the PROMIS website

Regarding sustainability, the PROMIS SC has launched a long-term sustainability plan and created a new non-profit organization, currently called the PROMIS Health Organization (PHO), which will gradually assume management of PROMIS resources, such as the instruments and scientific standards, as public sponsorship of the program is phased out. In addition, the PROMIS steering committee is discussing with the Patient-Centered Outcomes Research Institute (PCORI) the development of a program that would support clinical investigations using PROMIS.

## Notable Challenges

### Managerial

In 2008, to facilitate improved communication among members of the trans-NIH working group, a discussion with OSC staff resulted in a second IC Director being appointed to help co-chair the program and ensure that program staff members from that IC were included in decisions.[16] Over time, this addition has resulted in enhanced transparency and communication among the program staff from the different ICs.

The PROMIS intellectual property is held by the multiple institutions of the participating investigators, a situation that has delayed many plans for public private partnerships.[17] The PROMIS Working Group has been working with the Office of General Counsel to consolidate the intellectual property and trademarks.

**Scientific**

PROMIS has faced several scientific challenges. A present challenge is pharmaceutical companies' adoption of PROMIS as a drug development tool when it has not been qualified as such by the FDA.[16] For several years, the PROMIS PIs and NIH staff members have discussed the design of PROMIS with the FDA. However, there has been a conceptual gap between the two groups. In contrast to the disease-specific approach of the FDA, NIH envisioned PROMIS as a trans-disease measurement system to foster data harmonization. Discussions have led to agreement on a way to bridge this difference and the PROMIS investigators are working on an FDA qualification application for use of the fatigue items.[18]

## Selected Outputs Through 2013

Progress toward Phase II Goals (note: a close-out report will be written at the end of the funding period after July 2014). Selected outputs follow.

To develop new items and domains

- Over 50 item banks and scales have been developed and posted on the Technology Center's "Assessment Center" website[19]

To translate current and future items and domains into other languages, such as Spanish and Chinese, to facilitate international studies

- All PROMIS banks have been translated into Spanish and other translations projects (including Chinese) are ongoing[17]
- PROMIS investigators and staff have joined international PRO investigators to form "PROMIS International"[18]
- The Office of General Counsel is helping ensure the PROMIS® trademarks are recognized internationally [17, 18]
- The PROMIS Network Center assisted in development of a website for PROMIS in the Netherlands[20]

To conduct validation studies in large-scale clinical trials in a variety of clinical populations

- Three large validation studies were funded as part of PROMIS Phase II and are ongoing[9]
- PROMIS is beginning to publish its validation studies[21]

To make PROMIS tools accessible to a wider range of clinical researchers and patient care communities, and to optimize their usability for rapid adoption

- The PROMIS Assessment Center has over 3,000 registered users and 6.5 million patient responses[18]

- Over 600 research projects have used the Technology Center's Assessment Center in the past year[17, 22]
- In 2013, the NIH Clinical Center, in collaboration with PROMIS Technology Center, will launch an intramural version of the Assessment Center for use by NIH intramural investigators and other HHS agencies[17, 18]
- The Technology Center now supports item bank use and development in both Spanish and German[17]

To provide ongoing education and outreach to familiarize users with new developments in PROMIS

- In Phase II, PROMIS developed a new website to appeal to patients, clinicians and researchers[23]
- PROMIS has published over 200 publications[14]
- The Technology Center has an ongoing series of educational workshops for interested users [17]

To improve PROMIS tools to allow for better outcomes in clinical trials and, potentially, for better individual and clinical decisions

- PROMIS investigators are beginning to integrate PROMIS item banks into the electronic health record[17]

To engage stakeholders at all levels, by continuing interactions with other health-related Federal agencies, forging new relationships with patients and patient organizations, and establishing public-private partnerships to sustain PROMIS once NIH Roadmap for Medical Research funding ends

- An FDA/NIH Interagency Clinical Outcomes Assessment Working Group (ICOAWG) was established to coordinate PRO and other clinical outcome efforts between the agencies. PROMIS is currently working on a qualification application for the fatigue bank for use in Multiple Sclerosis, Chronic Fatigue Syndrome, or Rheumatoid Arthritis patients[17, 18]
- The DOD is developing an electronic clinical management system for chronic pain patients and has been consulting with PROMIS on the use of selected PROMIS banks for measuring outcomes in clinical populations[17, 18]
- PROMIS has been in discussion with the CMS Centers for Clinical Standards and Quality over the past year regarding the use of PROMIS instruments as quality performance measures[17, 18]
- The PROMIS Principal Investigators established the PHO, a 501 c3 non-profit organization, to facilitate formation of a public private partnership to sustain PROMIS[17, 18]
- A subgroup of the PROMIS NIH Working Group developed a trans-NIH, IC-supported Funding Opportunity Announcement for Person-Centered Outcomes Research to support the use and enhancements of PROMIS® and three related measurement information systems[17, 18, 24]
- PCORI has formed an NIH-PCORI task force to explore opportunities to stimulate research to use PROMIS to improve patient-centered outcomes[25]

**Notable Reported Outcomes**:

In 2010, CDC used PROMIS in the National Health Interview Survey as a health related quality of life (HRQOL) measure in their survey of 35,000 households.[18]

In 2012, DOD began working with PROMIS to incorporate its item banks into a new electronic clinical management system for chronic pain patients called the Pain Assessment Screening Tool and Outcomes Registry (PASTOR). Although initially involving only the Army, the PASTOR project is expanding to include other military branches. [17, 18]

In 2012, EPIC incorporated PROMIS into its newly created PRO application. These instruments included both adult and pediatric PROMIS item banks as part of MyChart. [17, 18]

In 2013, the CDC is testing PROMIS in the Behavioral Risk Factor Surveillance System (BRFSS). If the test is successful, PROMIS items will be incorporated as the HRQOL measure for the BRFSS in all 50 states and administered to over 350,000 adults nationwide each year. [17, 18]

## Transition Out of the Common Fund

The Common Fund is providing funding in FY13 and FY14 to help PROMIS transition to a multi-IC model that will start in late FY14. This model is based on a trans-NIH, IC-supported Funding Opportunity Announcement (FOA) for a Patient-Centered Outcomes Research Resource (PCORR) [24] to maintain the core infrastructure, and integrate under a single platform, all the functionalities of PROMIS, NIH Toolbox, Neuro-QOL, and ASCQ-Me. The goal is for the PCORR to be self-sustaining by the end of the funding period in 2017. Full support will be provided by NIH for years 1 and 2 with 25 to 50 percent reductions in years 3 and 4. The ICs are committed to funding individual PROMIS research relevant to their missions, and there are several potential opportunities for future support of PROMIS research efforts outside the NIH (e.g., through PCORI).

## References


1. PROMIS Proposal Sept RICC Deb Alder document
2. PROMIS FOA Website: http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-04-011.html
3. Common Fund PROMIS overview webpage: http://commonfund.nih.gov/promis/overview.aspx
4. PROMIS Update to Dr. Kington- June 11, 2008 PowerPoint Presentation
5. PROMIS Mid-Course Review Final Report September 12, 2007
6. Common Fund PROMIS WG Webpage: http://commonfund.nih.gov/promis/members.aspx
7. PROMIS Annual Progress Report FY2011-2012
8. PROMIS Second Round Funding Review December, 2012
9. Common Fund Funded Research Webpage: http://commonfund.nih.gov/promis/fundedresearch.aspx
10. PROMIS Website: http://www.nihpromis.org/Documents/PROMISStandards_Vers2.0_Final.pdf
11. PROMIS Website: http://www.nihpromis.org/insfaq.aspx
12. PROMIS Website: http://www.nihpromis.org/newsletters/2013_issue4.html
13. PROMIS Website: https://twitter.com/promisNIH
14. PROMIS Website: http://www.nihpromis.org/science/PublicationsYears
15. PROMIS Assessment Center Website: http://www.assessmentcenter.net
16. PROMIS Teamwork Meeting Minutes October 10, 2008

17. PROMIS Annual Progress Report FY 2012-2013
18. NIH Report on PROMIS to PCORI July 16, 2013
19. PROMIS Assessment Center Website: https://www.assessmentcenter.net/documents/InstrumentLibrary.pdf
20. PROMIS Network Center Report, Dr. San Keller, Principal Investigator, PROMIS Network Center, PROMIS Steering Committee meeting, October 22, 2013
21. Hinds, et al., 2013. PROMIS pediatric measures in pediatric oncology: valid and clinically feasible indicators of patient-reported outcomes. *Pediatric Blood & Cancer*, 402-408, Volume 60, no. 3 [March].
22. PROMIS Technology Center Report, Dr. Richard Gershon, Principal Investigator, PROMIS Technology Center, PROMIS Steering Committee meeting, October 22, 2013
23. PROMIS Website: http://www.nihpromis.org/
24. PROMIS FOA Website: http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-13-008.html
25. Personal communication, Mary Perry, OSC Program Leader for PROMIS

## Appendix 18: Molecular Libraries (ML) Program Summary

**Why This Program was Selected for Review:**

This is the largest program ever supported by the Common Fund, with an annual budget of over $100M at the height of the program. It consisted of several initiatives and was managed by a multi-IC Working Group that has worked together well for the life of the program. The transition of the program from its pilot phase to the full production phase was accompanied by considerable discussion among the NIH Leadership, with long term sustainability being a key concern. While the daily management of this program provides an excellent model for trans-NIH Working Group operations, the program has led to an important consideration for Common Fund programs: should they be designed to accomplish defined goals and then to end with minimal or no ongoing support required, or should they build and test novel types of infrastructure or awards, which, if valuable enough, will be taken over by one or more ICs? This program summary is intended to provide sufficient information for the Evaluation Working Group to consider the transition planning challenges that the Molecular Libraries program underwent and to provide recommendations for future programs. Highlighted text in the document points to information about program management practices that helped the program to be successful and to information about transition-relevant issues.

**Common Fund Support**

**Phase I: 2004-2007**

FY 2004 Actual: $31,572,000
FY 2005 Actual: $66,610,833
FY 2006 Actual: $96,951,833
FY 2007 Actual: $114,734,973

**Phase II: 2008-2014**

FY 2008 Actual: $117,939,414
FY 2009 Actual: $112,337,391
FY 2010 Actual: $113,241,251
FY 2011 Actual: $103,234,546
FY 2012 Actual: $92,178,162
FY 2013 Actual: $46,392,447
FY 2014 Budgeted: $555,544

**Common Fund Criteria**

As part of the NIH Roadmap theme, Pathways to Discovery, the Molecular Libraries Program (MLP) was intended to take advantage of major advances in biomedical research that together provided a tremendous opportunity to expand the number of small molecular research tools (probes) available to public sector biomedical laboratories. First, the human genome project had revealed that there may be up to a million human proteins. Second, the use of robotics and other advanced technology allowed the cost-effective testing of thousands of chemicals in a single laboratory. Third, powerful computer-based information retrieval systems facilitated the storage and sharing of complex information. These three areas of research had converged to provide an opportunity to expand the number of chemical probe tools available to decipher protein function. The MLP was designed to provide a scientific resource that would accelerate the discovery of protein functions that control processes critical to health and to any disease. The MLP was expected to have a very high impact by facilitating the understanding of basic biological mechanisms, identifying new biological targets for evaluation in disease models, and shortening the timeline for ligand and tool discovery. For the MLP to facilitate the use of small molecules in public sector biomedical research laboratories, three hurdles had to be overcome. First, there would need to be an increase in the number of small molecule probes known to bind to proteins of interest or to alter cellular processes. Second, information about these probes would need to be

made freely available to the research community. Third, the small molecules would need to be stored and distributed appropriately.[1] The MLP was designed to overcome these hurdles by generating and providing open access to information about the structure and biological activity of such small molecules. The expectation was that the MLP would transform biomedical research by catalyzing the adoption of chemical biology approaches by the broad academic research community.

## Program Description

A coordinated set of ML initiatives has been funded by the Common Fund since 2004.[2] The major ML initiative is comprised of the ML Small Molecule Repository (MLSMR) and a network of research centers charged with screening the many compounds in this repository to identify potent new small molecule probes. The centers use advanced technology to screen hundreds of thousands of small molecules for their ability to activate or inhibit protein activity or cellular processes of interest to the biomedical research community. Assays are nominated by the community and peer reviewed prior to acceptance for screening at the centers.[3] Emphasis is placed on assays that provide insight into proteins and cellular processes that have not been accessible with current methods and probes, including those that conventionally have been considered "nondruggable."[4] The centers and assay providers agree on the characteristics of the desired small molecule probes before the centers adapt the screens to their ultra-high throughput technologies, screen against a large number of compounds from the repository, and then perform medicinal chemistry to improve the utility of the probe candidates.[5] All of the information derived from the assays is deposited in a public database, PubChem[6], which was created by the ML cheminformatics initiative. Complementary ML initiatives have been focused on 1) assay designs for screening and predictive toxicology, chemical libraries, and assay instrumentation (Technology Development) and 2) imaging agents (Development of High Specificity / High Detectability Probes for Imaging, the Imaging Probe Development Center [IPDC], and the Molecular Imaging and Contrast Agent Database [MICAD]).[1]

## Goals

### Phase I

The overall goal of the MLP is to provide high-throughput screening (HTS) and chemistry resources to discover and optimize small molecules that can serve as chemical probes for research and starting compounds for drug discovery. In Phase I, the program consisted of the six initiatives listed below with their milestones.

Milestones[4]

Initiative 1: Small Molecule Library and Screening Centers

- Assemble initial collection of 50,000-100,000 small molecules by May 2004, including synthetic molecules and natural products
- Establish a central compound repository facility by September 2004 that configures, maintains, and distributes arrayed sets of small molecules for screening at the ML centers
- Establish an intramural screening center in 2004 to accept assays from academic investigators (extramural and intramural) for screening
- Establish a network of extramural centers in 2005

- Put in place master agreements to protect the rights of all parties when submitting assays to screening centers and obtaining compounds from the repository
- Resolve intellectual property treatment of NIH compounds and assay positives with the NIH Office of Technology Transfer

Initiative 2: Cheminformatics

- Establish a National Center for Biotechnology Information (NCBI) database as an open repository for organic-molecule chemical structures that will provide a "link out" to depositor web sites with additional information
- By 2004, establish initial capacity in extramural cheminformatics centers for virtual synthesis, virtual screening, and related high-intensity computing applications
- Establish substantial research component in extramural cheminformatics centers for development of new cheminformatic tools

Initiative 3: Technology Development

Sub-initiative 3.1: Chemical Diversity Technology Development

- Develop both entirely novel chemical structures and structural elements of bioactive natural products

Sub-initiative 3.2: Assay Technology Development

- Fund the early stage development of approximately 30 novel assays via R03 awards
- Test all funded assays against a bioactive compound collection
- Automate and screen selected assays at Roadmap screening centers with large compound library
- Publish successful outcomes of moderate or high throughput screening of funded assays to demonstrate the value of screening of non-traditional targets
- Implement approximately 5-10 novel assays from the pool supported by this effort in each Molecular Libraries Screening Center every year starting in FY 2005
- By 2006, create a set of "compound evaluation assays" that will be used to evaluate new chemical libraries created in the Chemical Diversity Technology Development initiative

Sub-initiative 3.3: Robotics/Instrumentation Technology Development

- Develop innovative instrumentation to accelerate the pace of HTS[7]
- Develop innovative instrumentation to maximize the efficiency of molecular library HTS

Sub-initiative 3.4: Predictive Absorption, Distribution, Metabolism, Excretion (ADME)-Toxicology Technology Development

- Identify assay models and datasets which could predict toxicity of drug candidates
- Identify major barriers to developing predictive toxicology models that can be used in the drug development process
- Develop predictive models of pharmacokinetic properties and drug-induced toxicity
- Develop in *silico* and in *vitro* assays and high throughput screens for predictive pharmacokinetic and toxicology modeling

Initiative 4: Development of High Specificity / High Detectability Probes for Imaging

- Develop new probes that achieve a 10 – 100 fold improvement in detection sensitivity

Initiative 5: Imaging Probe Database

- Develop, manage and maintain an up-to-date database that will be available to extramural and intramural researchers

- By September 2005, populate the database with chemical and biological data on > 2000 imaging probes that are relevant to diseases and applications across all organ systems
- Integrate the imaging database with the proposed NCBI chemical structure database

Initiative 6: Core Synthesis Facility to Produce Imaging Probes

- Establish two components of the Core Synthesis Facility: receptor modeling/biophysical chemistry and organic synthesis to generate novel probes for various imaging modalities (e.g., optical, PET, SPECT, and MRI imaging) to the intramural and extramural community for cellular and clinical applications
- Design novel probes utilizing technology that will permit very flexible detection or binding schemes for particular applications
- Coordinate efforts of the Core Synthesis Facility with the ML screening centers by 1) depositing molecules synthesized by the Core Synthesis Facility in the ML compound repository and 2) labeling compounds identified in ML center screens to convert them into imaging probes

**Phase II**

The overall goal of the ML program was the same in the second phase, but the focus changed to a production mode for the generation of high quality probes. Several sub-initiatives (e.g., Development of High Specificity/High Detectability Probes for Imaging and Predictive ADME-Toxicology Technology Development) had accomplished their goals and were transitioned out of the ML program. In Phase II, the program consisted of the five initiatives listed below with their milestones.

Milestones[8]

Initiative 1: Bioactive Small Molecule Library and Screening Centers (formerly known as Small Molecule Library and Screening Centers)

- Acquire, maintain, and distribute the collection of > 350,000 compounds
- Increase the novelty and diversity of the collection in FY 2010 and beyond
- Provide efficient distribution of compound collection and orders to support the needs of the MLPCN centers
- Implement a steady-state level of HTS assays with a milestone of 50 new small molecule probes per year

Initiative 2: Cheminformatics

- Provide information on chemical structures and link the structural information to biological activities and the biomedical literature
- Increase capacity to manage large chemical genomic data sets, including data quality control and maintenance
- Integrate with the NCBI gene and protein databases
- Develop and provide data mining tools

Initiative 3: Technology Development

Sub-initiative 3.1: Library Enrichment (formerly known as Chemical Diversity Technology Development)

- Pilot Scale Libraries - Deposit novel small molecule libraries and natural products from top academic chemistry labs in the MLSMR

- New Methodologies in Natural Products - Develop novel methods to produce new natural products for the MLSMR

Sub-initiative 3.2: Assay Development Program (formerly known as Assay Technology Development)

- Support assay development from lab-based to fully validated HTS-ready format
- Support entry into the MLPCN through the Fast Track mechanism

Sub-initiative 3.3: Instrumentation (formerly known as Robotics/Instrumentation Technology Development)

- Develop breakthrough instrumentation technologies
- Test new instruments in MLPCN centers

Initiative 5: Molecular Imaging and Contrast Agent Database (MICAD) (formerly known as Imaging Probe Database)

- Continue addition of curator-added entries of imaging agents

Initiative 6: Imaging Probe Development Center (IPDC) (formerly known as Core Synthesis Facility to Produce Imaging Probes)

- Synthesize imaging probes that are not available commercially

**Management**

During the pilot phase of ML, this complex program had several layers of management. A large trans-NIH working group, chaired by three IC directors and led by two coordinators, managed the initiatives. A unique aspect of the MLP was the central involvement of staff from the NIH intramural program (IRP) on the MLP working group. While most Roadmap/Common Fund working groups were comprised of staff from the extramural research program (ERP), the MLP group was joined by IRP staff who led some of the initiatives. There were monthly meetings of the entire WG. There were also weekly meetings of the MLPCN Coordination Work Group, a subset of the trans-NIH working group composed of NIH staff involved specifically with ML initiative 1. In addition, an NIH Scientific Officers Working Group (SOWG), which coordinated and monitored the progress of assays through the centers, met monthly.[1] A Steering Committee (SC) of investigators and NIH staff, was in place to oversee the ML program. The SC met quarterly and an External Scientific Panel (ESP) attended one of the SC meetings each year to provide feedback to the NIH working group.[1] OSC staff became more involved with the program when an OSC program director for the MLP was named in summer 2007. The involvement of IRP staff in coordination of the MLP emerged as a management issue when the IRP screening center competed for Phase II of the MLP.

For the production phase, a similar management structure is in place. The ESP continues to provide input and feedback on the initiatives. The SC meets twice a year and the ESP attends one of the SC meetings each year and provides feedback on an as needed basis.[8]

**Panel Review and/or Formal Evaluation Conducted**

A midcourse review of the ML program was conducted in December, 2006 by an expert panel.[1]
A midcourse review of the IPDC was conducted in April, 2009 by an expert panel.[9]

In 2006, an expert panel reviewed progress of the program to inform an NIH decision on whether it should continue to a second phase. The panel noted that some of the initiatives had been operational for less than two years, making their progress difficult to assess. However, one

decision that needed to be made in the spring of 2007 was whether to scale up the MLSCN from the pilot phase to a full-scale enterprise; reviewers examined the timing and goal of such a scale-up. The major outcome of the review was a set of recommendations:[2]

- Focus the MLP on difficult or unique problems as an organizing theme to drive innovation and differentiation from drug discovery screening efforts in industry
- Manage the MLP as a diversified portfolio of initiatives
- Reassess the MLP and chart the overall direction at the 5-year point

In response to this review, a second phase of the program began, termed the production phase. Shortly thereafter, NIH staff conducted a needs assessment of the program by interviewing stake holders, conducting a Request for Information and documenting progress.[10] The needs assessment found that the MLSMR, MLPCN and PubChem were meeting their goals for productivity. For example, by July 2009, the SMR had grown to 300,000 compounds, PubChem had grown to 44,000 users per weekday and the centers had produced 68 probes at a decreasing cost. Those surveyed compared the MLP centers favorably to other screening centers, but mentioned several areas of improvement including increased support for assay development, a better review process for assay projects, and increased chemistry capacity. Users of PubChem suggested improvements in the database to make it more user-friendly. Each of these suggestions was being addressed by the changes in the production phase.

In 2009, the IPDC was reviewed. The panel found that the IPDC appeared to be a useful resource for the NIH IRP, but was not set up to reach its original milestones. It was decided that the initiative could remain a useful resource for the NIH IRP and that it should transition to IRP support over the next few years. In FY 2010, the Common Fund provided a year of transition funding and the IRP committed to providing ongoing support for the IPDC.[9]

In 2010, the ESP suggested using an external evaluation process to assess the quality of the ML probe reports. It was also suggested that library numbers be assigned to ML-generated probes so that they could be cited in publications and tracked. Both of these suggestions were implemented.[11]

**History and Evolution**

The MLP was approved as one of the original Roadmap programs in 2003. Its goals were deemed to have potential synergy with a proposed Imaging program, so the two were merged. MLP began in 2004 with establishment of an intramural screening center at NIH. It was joined by nine extramural centers a year later, forming the Molecular Libraries Screening Center Network (MLSCN). The small molecule repository (MLSMR) was also established in 2005 and by the end of 2006 had assembled 111,479 compounds.[12] The academic research community began nominating assays in 2005, and by the end of the pilot phase, over 200 assays had been screened and 75 probes had been developed.[1] The PubChem database was launched at NCBI in 2005 and by the end of 2006 contained over 12 million chemical structures and 300 assays, linked to all other National Library of Medicine (NLM) databases.[12] The Technology Development initiative and imaging initiatives also got underway as planned, with the exception that the IPDC was delayed due to the length of time taken to recruit a director.

In response to recommendations from the 2006 panel review, the NIH decided to continue the MLP into a production phase (FY2008-2012) with an improved plan that could be updated following a reassessment at the 5-year point.

In addition to concerns about future funding, NIH leadership raised additional concerns about the program that needed to be addressed:[13,14,15]

- Length of time for probe development and specificity of probes
- Stability of the repository that housed the compound library
- Quality of the information in PubChem

In response to these concerns and to input from the panel review, the MLP working group planned several changes for the second phase.

- To increase the focus on difficult or unique problems to drive innovation and differentiation from drug discovery efforts in industry, applicants for the center grants would be asked to propose "center driven aims" to develop innovative proposals to attack difficult or unique problems in chemical genomics.[16] Also, the center applicants would be invited to specialize in either innovative screening technologies or medicinal chemistry approaches to develop more useful probes from initial hits. To reach these aims, ML reduced the number of comprehensive centers from 10 to four and funded smaller centers specializing in chemistry or in screening (e.g., for phenotypic assays for which the target of the probe was unknown).[1]
- To better manage the MLP as a diversified portfolio set of initiatives, the NIH decided to eliminate some sub-initiatives and refocus others to increase synergy within the program. Instead of renewing the cheminformatics centers, the cheminformatics efforts would become the responsibility of the new screening and chemistry centers. The chemical diversity of the compound library would continue to be enhanced through *de novo* library synthesis initiatives. It was planned that instrumentation developed within the MLP would be tested in the screening and chemistry centers. The toxicology sub-initiative would not continue, since its mission was felt to be beyond the scope of the MLP.[17] In addition, two of the imaging initiatives would no longer be part of the MLP.[1]
- Several processes were implemented for the MLP working group to help the assay providers and the centers to plan, monitor and redirect or end each project. First, the centers were given more responsibility for the successful adaptation and implementation of the assay projects. Second, the assay providers, center staff and SOWG improved the process for establishing expectations specific to each probe. Third, the MLP established an automated reporting system for the center to report progress to NIH staff. Fourth, the new network structure allowed increased collaboration between the centers such that a stuck project could be rescued. Fifth, the NIH asked the ESP to review the value of each probe candidate before it was accepted as an MLP probe.[1]
- The length of probe development was approximately 18 months, so few had been developed by the time of the review in 2006. However, to attempt to shorten the length of time for the production of probes, the centers were asked to spend more time on outreach to educate potential assay providers and a new mechanism for accepting advanced high throughput assays from investigators with NIH grants was established (the Fast Track mechanism). The specificity of the probes would be increased by 1) providing additional support for "extended characterization" of the probes beyond those agreed upon by the

center and assay provider, and 2) requiring an external review of the probe's characteristics prior to acceptance by the NIH.
- The stability of the repository that housed the compound library was of concern because the company that oversaw the MLSMR had been sold. Although operations continued uninterrupted, it was decided to revisit movement of the MLSMR to the NIH intramural program in the future.
- The quality of the information in PubChem was uneven, in part due the fact that this database has open deposition and therefore the biological data were not curated or annotated using standardized assay nomenclature. The MLP working group and steering committee decided to work with NLM to improve the bioassay component of PubChem.

In Phase II, the production phase was launched to provide the biomedical research community access to high quality, small molecule screening facilities that would perform approximately 80 high throughput assays a year against 300,000-500,000 compounds. It would then follow up "hits" by enhancement so that they would become useful probes for investigating biological function.[1] The Molecular Libraries Probe Production Centers Network (MLPCN) was established with four comprehensive screening and chemistry centers, two specialized chemistry centers and three specialty screening centers.[18]

In early 2011, NIH Leadership and the MLP working group began to develop a plan for transitioning the MLPCN from Common Fund support. They formulated a plan to gradually reduce the number of centers over the next few years. In addition, they identified synergies between the mission of the newly proposed National Center for Advancing Translational Sciences (NCATS) and several components of the MLP.[19] Extra monies from the Common Fund were committed to the program in FY 2012 and FY 2013 to aid the transition.

In 2013, six of the MLPCN centers launched the new BioAssay Research Database (BARD)[20] to allow scientists to efficiently develop and test hypotheses on the influence of different chemical probes on biological functions.[8] BARD enables mining of data on more than 35 million compounds, 4,000 assays and over 300 probe projects, including MLP assay data curated by the MLPCN centers. To facilitate searches, it has established guidelines for standardized language and assay organization.

## Notable Challenges

### Managerial

The transition of the MLPCN centers from Common Fund support has been the greatest management challenge to the program. Although most of the MLP initiatives will have transitioned successfully from Common Fund support, the ICs have not committed funds to work together to support probe discovery by a network of centers. (See "Transition Out of the Common Fund" section.)

Management of the centers had to balance the freedom for innovation with the strict milestones for productivity. Some projects were inherently more interesting than others, and center personnel often were tempted to follow the most exciting science rather than work on problematic assays that might not pay off. NIH staff worked to ensure each assay project received a fair chance of success.

The involvement of the IRP in the MLP led to numerous managerial challenges. For example, in 2007, NIH leadership decided that the IRP should compete with the ERP for Common Fund dollars when both the IRP and ERP are capable of meeting the goals of the program.[21] Therefore the IRP screening center was required to compete against ERP screening centers for a spot in the production phase. This change precipitated several changes to the management of the program in the production phase as the IRP screening center staff had been integral members of the working group. In addition, both PubChem and the IPDC were led by IRP investigators whose professional rewards structures were not always compatible with the mission of the MLP. In both cases, the IRP investigators often preferred to focus on issues of scientific interest rather than those of importance to the program.

**Scientific**

The primary emphasis of PubChem was on the storage of chemical information, but this led to limitations in its ability to provide the types of browsing, searching, and analysis tools that the biological scientific community would find useful. After much debate within the MLP steering committee, the MLP decided to undertake an initiative to create BARD, an open-source public resource to provide this service.[22]

The impact of the MLSMR could have been broadened by making the compound library available to other NIH-funded initiatives as well as academic screening labs. Full scale implementation would require additional funding to support infrastructure, increased compound demand and resupply, and informatics upgrades. It was determined that making the compound collection available to a limited number of NIH-supported screening initiatives using a fee-for-service model could be implemented with little to no increase in cost. However, recent guidance on contract policies has prompted NIH to reconsider the fee-for-service model.[23]

**Selected Outputs Through 2013**

Progress toward Phase II goals: (note: a close-out report will be written at the end of the funding period after July 2014). Selected outputs follow.

Initiative 1: Bioactive Small Molecule Library and Screening Centers

Acquire, maintain, and distribute the collection of > 350,000 compounds

- The MLSMR collection contained over 387,543 highly annotated compounds at the end of FY 2013[8]

Increase the novelty and diversity of the collection in FY 2010 and beyond

- The MLSMR added 10,000 probes, analogs and diversity compounds in FY 2013[8]

Provide efficient distribution of com`pound collection and orders to support the needs of the MLPCN centers

- The MLSMR supported the MLPCN by continuing to provide efficient distribution of the collection to the MLPCN centers[11]

Implement a steady-state level of HTS assays with a milestone of 50 new small molecule probes per year

- As of September 2012, over 650 projects had been accepted into the centers and over 200 probes had been produced. Forty-eight new probes were generated in FY 2013[8]

Initiative 2: Cheminformatics

Provide information on chemical structures and link the structural information to biological activities and the biomedical literature

- The PubChem open access database has over 35 million chemical structures and 60,000 daily users

Increase capacity to manage large chemical genomic data sets, including data QC and maintenance

- As of 2012, more than 200 scientific groups uploaded data into PubChem and depositions of individual substances surpassed 100 million[22]

Integrate with the NCBI gene and protein databases

- In 2012, PubChem added to the PubChem BioAssay summary pages and began to display the Gene Ontology (GO) classification of the gene/protein target(s) that were tested by the bioassay and protein structure and other information from the Therapeutic Target Database

Develop and provide data mining tools

- In 2013, added Pubchem Bioactivity DataDicer: a new, efficient search engine that allows both novice and expert scientists to search and subset the greater than 200 million bioactivity outcomes from the PubChem BioAssay database

Initiative 3: Technology Development

Sub-initiative 3.1: Library Enrichment

Pilot Scale Library - Deposit novel small molecule libraries and natural products from top academic chemistry labs in the MLSMR

- By the end of 2013, the pilot scale libraries initiative had generated greater than 24,904 novel compounds and deposited them in the MLSMR[23]

New Methodologies in Natural Products program - Develop novel methods to produce new natural products for the MLSMR

- By the end of 2010, this initiative had developed new methods for extracting or scaling up the production of natural products or compounds derived from natural products[23]

Sub-initiative 3.2: Assay Development Program

Support assay development from lab-based to fully validated HTS-ready format

- By the end of 2011, 284 projects had been awarded for assay development.

Support entry into the MLPCN through the Fast Track mechanism

- A total of 165 Fast Track assay projects have been approved through 2013[8]

Sub-initiative 3.3: Instrumentation

Develop breakthrough instrumentation technologies

- In 2012, a new flow cytometric technology was shown to be capable of analyzing samples in the MLPCN's HTS format of 1536 wells[24]

Test new instruments in MLPCN centers

- The flow cytometer described above was beta tested in one of the MLPCN specialized screening centers

Initiative 5: MICAD

Continue addition of curator-added entries of imaging agents

- MICAD has curated information on 1445 imaging agents through summer, 2013[25]

**Notable Reported Outcomes**:

In 2007, the European Union began planning for a European infrastructure for open screening

platforms for chemical biology, EU-OPENSCREEN. This international effort is exploiting the MLP experience in setting up a distributed network of screening facilities.[26]

In 2009, Janssen Pharmaceuticals and Vanderbilt University formed a drug development partnership that leveraged the infrastructure, capacity, and key personnel that had been supported by the MLSCN at Vanderbilt.[27, 28]

In 2010, the National Cancer Institute launched the Chemical Biology Consortium (CBC) program to "facilitate the discovery and development of new agents to treat cancer" by providing medical chemistry support to develop candidates for NCI's drug development pipeline. NCI adopted the organizational structure of the MLPCN. Like the MLPCN, the CBC was designed as an integrated research consortium of three types of centers: comprehensive centers with cores for assay development, assay implementation, and medicinal chemistry; specialized, screening centers to perform high content screens; and specialized, chemical diversity centers to provide medicinal chemistry support to follow up on hits from the screening centers. Six of the twelve CBC centers are present (MLPCN) or former (MLSCN) MLP centers.[29]

In 2010, staff from the journal Nature Chemical Biology asked an international panel of experts in chemical biology to share their thoughts on the scientific and cultural evolution of the field, to identify the major scientific contributions of chemical biology over the past decade and to outline current challenges for the field. They concluded that the MLP had a major role in catalyzing changes in culture that have significantly broadened the impact of chemical biology in the wider scientific community. They concluded, "First, the enhanced visibility of chemical biology in the scientific literature has brought the breadth and utility of studies at the chemistry-biology interface to a wider audience… Second, the rapid expansion of access to chemical compound libraries and high-throughput screening facilities has made it possible for researchers of any background to identify chemical probes and apply them to biological questions with greater success… Initiatives such as the US National Institutes of Health Roadmap for Medical Research greatly supported such efforts in the United States and served as catalyst for broader efforts worldwide." [30]

By 2011 over 95 compounds had been moved into preclinical development.[11]
In 2013, a new chemical entity based on an ML probe (ML007) was entered into Phase III clinical trials for multiple sclerosis. The compound, which is a selective sphingosine-1-phosphate 1 receptor (S1P1R) modulator, has also been entered into Phase II clinical trials for ulcerative colitis.[31]
Several key personnel in the MLPCN Centers have been recruited to leadership positions at top pharmaceutical companies, most notably:

- Dr. John Reed, Sanford Burnham CEO and Director of the MLPCN Sanford Burnham Center for Chemical Genomics became Global Head of Roche Pharma Research and Early Development in March, 2013.
- Dr. Peter Hodder, Associate Director of Lead Identification at The Scripps Research Institute joined Amgen as an Executive Director of Discovery Research in November, 2013.
- Dr. Min Li, Director of the Johns Hopkins Ion Channel Center joined GlaxoSmithKline as Senior Vice President of Neurosciences in January, 2014.

## Transition Out of the Common Fund

Transition of MLP initiatives from Common Fund support by 2012 has been considered since the pilot phase. This timeline coincided with the establishment of the National Center for Advancing Translational Sciences (NCATS). As this Center was envisioned, it would provide a permanent home for trans-NIH services and research that would hasten the development of new therapies. Molecular screening was considered a natural fit for this mission, as a result, NCATS has committed to supporting the MLSMR, the NIH intramural comprehensive screening center, and BARD.[32] As planned since 2008, Common Fund support for the center network has been reduced. Although ICs did not commit continued support of the MLPCN, multiple ICs support screening activities through IC-specific funds. To decide the best plan for the final three years of CF support, the MLP working group obtained feedback from a panel of six external scientists who recommended funding fewer centers and focusing on completing accepted projects. Following this recommendation, the MLP began phasing out three specialized screening centers in FY 2011 and one comprehensive center in FY 2012.[11] The remaining three comprehensive centers and two specialized chemistry centers are presently supported with additional FY 2013 funds provided by the Common Fund to ease the transition.[22] In 2011, the National Library of Medicine committed to continue to support PubChem as an active database.

Some of the Technology Development sub-initiatives are continuing without Common Fund support. Library enrichment and instrumentation have ended, but assay development continues with IC support. Several ICs now coordinate to support assay development, high throughput screening, and medicinal chemistry projects without Common Fund support.

The sub-initiative for Development of High Specificity/High Sensitivity Probes to Improve Detection transitioned to support by the National Institute of Biomedical Imaging and Bioengineering and other ICs in 2009.[8] The IPDC has been supported by the intramural program of the National Heart, Lung and Blood Institute since 2011.[8] In 2013, the National Library of Medicine committed to continue supporting MICAD as a reference on the NLM Bookshelf after active curation ended.[25]

## References


1. The Molecular Libraries Briefing Book, July 2008
2. NIH Molecular Libraries Program Proposal for Formal Phase and Transition, March 2007
3. ML FOA Website: http://grants.nih.gov/grants/guide/pa-files/PAR-05-060.html
4. ML Implementation Plans, September 2003
5. ML FOA Website: http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-04-017.html
6. PubChem Website: http://www.ncbi.nlm.nih.gov/pccompound
7. ML FOA Website: http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-04-020.html
8. ML Annual Progress Report FY 2013-2014
9. IPDC Midcourse Review PowerPoint Presentation
10. Executive Summary of Molecular Libraries Needs Assessment Website: http://commonfund.nih.gov/sites/default/files/Executive_Summary_ML_Needs_Assessment.pdf
11. ML Annual Progress Report FY 2011-2012

12. IPDC Midcourse Review Executive Summary
13. Roadmap Implementation Coordination Committee (RICC) Meeting, March 2007
14. RICC Follow-up Questions for Molecular Libraries Roadmap Formal Phase & Budget: Response to RICC Questions Presentation, March 2007
15. RICC Follow-up Questions for Molecular Libraries Roadmap Formal Phase & Budget: Detailed Responses to RICC Questions Presentation, March 2007
16. ML FOA Website: http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-08-005.html
17. Austin et al. 2012. NIH Molecular Libraries Initiative. *Science,* 1138-1139, Volume 306 [November]. http://www.sciencemag.org/content/306/5699/1138
18. Common Fund Molecular Libraries Funded Research Website: http://commonfund.nih.gov/Molecularlibraries/fundedresearch
19. NIH News and Events Website: http://www.nih.gov/news/health/dec2011/od-23.htm
20. BARD Database: https://bard.broadinstitute.org/BARD/bardWebInterface/index
21. NIH Notice http://grants.nih.gov/grants/guide/notice-files/NOT-RM-07-011.html
22. ML Annual Progress Report FY 2012-2013
23. ML Annual Progress Report FY 2010-2011
24. Edwards et al. 2012. Cluster cytometry for high-capacity bioanalysis. *Cytometry,* 419-429, Part A [May]. http://www.ncbi.nlm.nih.gov/pubmed/22438314
25. MICAD Database: http://www.ncbi.nlm.nih.gov/books/NBK5330/
26. EU-OPENSCREEN European Infrastructure of Open Screening Platforms for Chemical Biology: http://www.eu-openscreen.de/fileadmin/user_upload/PowerPoint/EU-OPENSCREEN_flyer_for_website.pdf
27. Wang, Shirley S. 2009. J&J, Vanderbilt Team Up on Schizophrenia Drugs. *The Wall Street Journal*. January 9. www.mc.vanderbilt.edu/labs/lindsley/documents/WSJ_20090108.pdf
28. Snyder, Bill. 2005. Network to Boost Discovery Efforts. *Vanderbilt University Medical Center's Weekly Newspaper*. June 17. http://www.mc.vanderbilt.edu/reporter/index.html?ID=4040
29. The NCI Chemical Biological Centers Website: http://next.cancer.gov/discoveryResources/cbc.htm
30. Bucci, et al. 2010. A decade of chemical biology: With insights from a panel of experts, the Nature Chemical Biology editors examine the evolution and current era of chemical biology. *Nature Chemical Biology,* Volume 6 [December]. http://www.nature.com/naturechemicalbiology
31. Multiple Sclerosis Discovery Forum, Drug Pipeline Website: http://www.msdiscovery.org/research-resources/drug-pipeline/337-rpc1063
32. NCATS Funding Justification: http://www.ncats.nih.gov/files/justification-2014.pdf

## Appendix 19: National Centers for Biomedical Computing (NCBC) Program Summary

**Why This Program was Selected for Review**:
The NCBC Program was intended to establish a national consortium of centers that would collectively address some of the most pressing computational challenges facing biomedical researchers. These challenges were not identified through an NIH-led strategic planning process but were intended to be identified by the Center PIs and by their collaborators on "Driving Biological Problems." The NCBCs were also intended to be a major resource for the nation with respect to training in computational biology. The investigator-initiated problems addressed by these Centers minimized the need for the Centers to collaborate to achieve their goals: each Center worked largely in isolation on the challenges identified. Consortial goals were not identified, and the program as a whole was not developed as an integrated community resource and each Center followed its own course with respect to outreach and dissemination. An external advisory panel for the overall NCBC program was not engaged until 2012 to discuss issues of sustainability. This model for program management was established before DPCPSI/OSC existed and provides an alternative, more hands-off planning and oversight model. This program also highlights the issue of transition after Common Fund support ends. As independent Centers, individual ICs had little enthusiasm for continuing these centers. As a networked group of Centers, they are envisioned to continue via the Big Data to Knowledge program, with IC funding. Highlights within the summary text call attention to these issues.

**Common Fund Support**

**Phase I: 2004-2009**
FY 2004 Actual: 12,000,000
FY 2005 Actual: 23,755,000
FY 2006 Actual: 23,884,996
FY 2007 Actual: 30,272,689
FY 2008 Actual: 23,010,181
FY 2009 Actual: 26,577,683

**Phase II: 2010-2013**
FY 2010 Actual: 19,360,626
FY 2011 Actual: 13,231,307
FY 2012 Actual: 8,425,331
FY 2013 Actual: 3,435,935

**Common Fund Criteria**
The 1999 Biomedical Information and Science Technology Initiative (BISTI) report noted that scientists were increasingly using computers to analyze data and model biological processes.[1] BISTI recommended that the NIH increase efforts in promoting and supporting computational biology. Historically, individuals in laboratories and small groups had developed algorithms to serve their particular research needs. The aim of the NCBCs was to create a computational infrastructure for biomedicine, providing tools that were robust, efficient, easy to use, widely disseminated, and in conformance with software engineering standards. This goal was to be accomplished by building a larger, more coordinated enterprise with a mix of computer scientists and biomedical scientists covering a range of expertise required to produce bioinformatics and computational tools.[2]

The ultimate products that were envisioned were data sources, models, and model validation tools integrated within and across domains through the use of standards and ontologies. This effort intended to create an integrated national biomedical computing environment and associated Centers. In addition to carrying out fundamental research, it was expected that the

Centers would play a major role in educating and training researchers to engage in biomedical computing.[3]

It was felt the NCBCs were poised to address several of the Roadmap themes: (1) "New Pathways for Discovery" - as part of the focus on new tools and methods; (2) "Research Teams of the Future" - developing sites where training of cross disciplinary researchers occurs; and (3) "Re-engineering the Clinical Research Enterprise" - where NCBC advances in informatics and biomedical computing provide critical support to that research arena as well as computational tools that facilitate the delivery of its findings to clinical practice.[4]

## Program Description

The National Centers for Biomedical Computing (NCBCs) were intended to be part of the national infrastructure in Biomedical Informatics and Computational Biology. They are cooperative agreement awards. There are currently six Centers supported by the ICs in this, their final year of funding, but which were initiated through Common Fund support: biophysical modeling, biomedical ontologies, information integration, tools for gene-phenotype and disease analysis, systems biology, image analysis, and health information modeling and analysis. The Centers create innovative software and other tools that enable the biomedical community to integrate, analyze, model, simulate, and share data on human health and disease.[5] Each NCBC Center is required to perform or facilitate six different core functions: (1) conducting significant research in relevant computational science, such as algorithm creation and optimization, development of hardware architectures applicable to the solution of biomedical problems, and conducting significant research and development in biomedical computational science by developing and deploying tools designed to solve particular biomedical problems; (2) establishing Driving Biological Projects (DBP) to allow experimental and clinical biomedical and behavioral researchers to interact with and drive computational research in the Center; (3) providing infrastructure to serve the needs of the broad community of biomedical and behavioral researchers seeking access to the Center's tools and resources; (4) enhancing the training for a new generation of biomedical researchers in appropriate computational tools and techniques; (5) disseminating newly developed tools and techniques to the broader biomedical research community; and (6) providing an administrative core to ensure that the Center achieves its goals within the proposed grant period of the NCBC.[6]

Additionally, in 2008 and 2011 Funding Opportunity Announcements (FOAs) were released to provide support for investigators working in collaboration with the NCBC using the R01 mechanism.[7, 8]

## Goals

### Phase I

The overall goal of the program is to provide the computational infrastructure for biomedical computing in the nation.[3]

Milestones[9]

- Establishment of the National Centers

- Establishment of collaborative relationships between the Centers and other biomedical researchers
- Development of integrated computational environments in support of specified areas of biomedical research
- Integration of computational environments across broad areas of biomedical research

**Phase II**
The goals are to build a computational infrastructure, common software tools, and networks for biomedical computing that allow for analysis and sharing of data.

Milestones[10]

- Establishment of National Centers
- Develop a process to assess the impact of software tools (usability, evaluation)
- Continue and extend training focus of NCBC program
- To develop sophisticated and long-term software, as well as design and implementation of hardware that couples stochastic and continuous methods to quantitative multi-large/scale modeling
- Predictive personalized medicine that leads to individualized optimal therapy
- Create a continuously updatable semantic website/tool for answering complex queries and for providing a one-stop shop for computational tools
- Establishing a resource for advancing and maintaining software valuable for biomedical research and applications

**Management**
In the implementation plan for FY 2004, the Working Group proposed strategies related to coordination, staffing, and ongoing improvements within the Centers. The plan was to have annual scientific meetings to facilitate coordination among the Centers. It was also in the initial plan to have program directors from the participating Institutes and Centers (ICs) meet regularly to assess progress, address obstacles, and promote interactions among participants. Over time, these meetings were discontinued, although NIH staff with interests in each individual Center continued to interact with the PI for that Center. The role of OD staff was minimal because DPCPSI/OSC (or OPASI, as it was initially called) was not established until 2007, and new programs were the initial priorities for staff.[9]

In the 2012-2013 Annual Progress Report, the Working Group described the strategy of how the Centers were managed: *"The Project Team managed the grant in the following manner: Each Center had PO [Program Officer], Lead Science Officer, and team of Science Officers. The resulting teams were expected to play an active role in regular phone calls with PI [Principal Investigator] team, they were expected to contribute to a through computational scientific review of the progress reports. The SOs were chosen on the basis of their expertise and also to represent the interests of their ICs. Thus they helped to guide the PIs to maintain relevance to the goals of the ICs."* [Page 6] They also noted that plans and goals were assessed against the reported outcomes as presented in the individual progress reports.[11]

In preparation for the transition of the program out of the Common Fund, the NCBC Working Group established a 12 member Scientific Advisory Board (SAB) in 2012 to provide guidance to the PIs on outreach and sustainability. Also, individual Centers reported that their own SABs met in 2012 and provided feedback on the Centers activities, assessed progress, and discussed future funding opportunities.[11]

As a result of SAB guidance, the NCBC PIs established four Working Groups: Biositemaps; DBP Interactions and Impact; Software and Data Integration; and Dissemination. Representatives from each Center began working together to ensure that software development and dissemination are coordinated to the fullest extent possible, resources are broadly available, and dissemination mechanisms allow for the evaluation of impact.[5]

The SAB also informed additional dissemination activities: a special issue of Journal of the American Medical Informatics Association (JAMIA) with highlights of all Centers, joint presentation by the Centers at Intelligent Systems for Molecular Biology (ISMB) in July, and the NCBC Showcase meeting in November. The main goals of the showcase meeting were to highlight research, training, and outreach in computational science, as well as the connections with related research programs such as the Clinical and Translational Science Awards (CTSA), National Technology Centers for Networks and Pathways (TCNP), Computational P41, and the BISTI consortium.[11, 12]

In contrast to SABs for other CF programs, which advise the NIH in ongoing program management, the NCBC SAB was established to advise the PIs as they planned for continued funding after Common Fund support ends. They functioned as advocates as well. They wrote a letter to NIH management in support of the NCBC activities, and helped generate the template for the NCBC one-pagers, which highlight the impact of the Centers over the life of the program.[11, 12]

**Panel Review and/or Formal Evaluation Conducted**

The program has not been formally evaluated.[4] There were discussions in 2005 related to conducting an evaluation of the program. However, since the program launched in 2004, it was believed that measurement of the outcomes were still several years away and an evaluation was not pursued.[13]

In 2007, a review panel of external experts was convened to conduct a mid-course review of NCBC that would be used to inform a decision by NIH leadership as to if and how the program should continue to receive Common Fund support. The panel was asked to address the following seven questions and make recommendations.

1) To what extent does the vision and direction of the NCBC program promote biomedical computing?
2) In what ways has the NCBC initiative advanced biomedical computing?
3) Are the NCBCs interfacing appropriately?
4) What new collaborations have been formed through the NCBC initiative?
5) What new training opportunities have the Centers provided?
6) What changes could make the program more effective in the future?

7) What lessons have been learned from the NCBC initiative that can guide future NIH efforts in biomedical computing?

The panel felt that establishing the seven Centers was only the beginning of the investment required for the creation of a stable computational platform to sustain biomedical research. The panel reported that the Centers were *"meeting the challenge of developing a national network of research centers in biomedical computing."* [Page 2] The panel recommended the following actions to ensure the success of this important effort:

1) Continue the support of biomedical computing as a key part of the NIH research portfolio.
2) Develop a process to sustain and expand this effort now to anticipate support beyond the 10 year Roadmap funding horizon. The panel was concerned that the viability of this program, and of biomedical computing in general, depended on the relatively unstructured cooperative interactions of different NIH ICs.
3) Focus research within and across the NCBC Centers on ambitious problems that other programs are

unlikely to support, such as the development of cheaper, safer drugs, or new methods for multi-scale modeling importance, by taking advantage of longer more stable funding periods not possible within the biotech industry. Coordinate tool development with industry, since this is where the tools may have their biggest impact.

4) Continue to support the model of multidisciplinary, team-based, collaborative research within the NCBCs. Extend the reach of the individual centers to collaborators outside the centers to increase the impact of the Centers on the community. Do not require interaction between NCBC Centers where there is no obvious programmatic advantage. Continue the All Hands Meeting as an effective means for sharing best practices among the Centers and for fostering high impact Center-wide activities.
5) Develop an additional approach beyond the R01 and R21 collaborative grant program for developing and supporting collaborations with the Centers.
6) Develop a process to assess the impact of the software tools developed by the Centers.
7) Continue to support the NCBCs and other programs in training multi-disciplinary researchers through collaborative research and outreach to the community. Leverage the efforts of the NCBCs and expand the educational programs designed to foster the education and training of computational biologists.

The panel also identified grand challenges that they felt existed in the field of biomedical computing which were not being addressed by any of the NCBC.[4] The grand challenges were:

- Quantitative multiscale modeling
- Predictive personalized medicine
- Methods for answering complex queries over a continuously updatable semantic web
- Working towards developing cheaper, safer drugs
- Creating comprehensive, integrated computational modeling/statistical/information systems
- Establishing a resource for advancing and maintaining software valuable for biomedical research and applications
- Training the next generation of computational scientists.

Notably, these grand challenges were not emphasized as goals in the RFA for the second phase of the NCBC program. No specific computational goals were established. The 2009 FOA for the NCBC program required applicants to include plans for dissemination of their software and findings. The FOA also asked for applicants to provide specific and detailed plans to ensure that graduate students and postdoctoral fellows received broad relevant training beyond the specific contributions they make to the infrastructure and research projects of the Center. In addition, the FOA asked for plans to include workshops or other activities to train the larger biomedical community about the new tools and techniques that the Center was developing.[6]

**History and Evolution**

Dr. Harold Varmus, (NIH Director from 1993-1999), charged a Working Group of the Advisory Committee to the Director (ACD) *"to investigate the needs of NIH-supported investigators for computing resources, including hardware, software, networking, algorithms, and training."* [1] The BISTI Report had four recommendations, one of which was to create National Programs of Excellence in Biomedical Computing. The BISTI Working Group reported that, *"It is in the context of those National Programs that the best opportunities can be created for doing and learning at the interfaces among biology, mathematics, and computation."* [1] This need for an intellectual fusion of biomedicine and information technology was reaffirmed by the NIH Roadmap, initiated by Dr. Zerhouni (NIH Director 2002-2008), and Bioinformatics and Computation Biology became one of the areas for funding.[14]

The program started with seven Centers. A FOA was released in 2003 and in 2004 four Centers were funded: Physics based Simulation of Biological Structures (Simbios) from Stanford University, National Alliance for Medical Imaging Computing (NAMIC) from Brigham and Women's Hospital, Informatics for Integrating Biology and the Bedside (i2b2) from Brigham and Women's Hospital, and Center for Computational Biology (CCB) from University of California Los Angeles.[3] In 2004, the FOA was reissued and in 2005 three centers were funded: National Center for Integrative Biomedical Informatics (NCIBI) from University of Michigan At Ann Harbor, National Center for the Multiscale Analysis of Genomic and Cellular Networks (MAGNet) from Columbia University Health Sciences, and National Center for Biomedical Ontology (NCBO) from Stanford University.[15]

The results of the 2007 panel review were presented to the IC Directors in August 2007. They agreed that support of the program should continue, but that future funding for each award should be split between the Common Fund and the ICs most closely associated with that award so that Common Fund support would be gradually decreased each year. This would provide a means of transitioning the Centers out of the Common Fund and would facilitate the uptake of the program by ICs who were benefitting from the computational approaches being developed. This means of funding reflected the fact that each Center had an emphasis that aligned with a given IC or small group of ICs. However, it reinforced this focus such that from 2009-2013, the NCBCs became increasingly IC-specific.

A total of six Centers were funded in 2010, five of the original seven Centers and one new center. The Centers funded were: Integrating Data for Analysis, Anonymization, and Sharing (iDASH) from University of California San Diego; NCBO from Stanford University; i2b2 from

Brigham and Women's Hospital; NAMIC from Brigham and Women's Hospital; MAGNet from Columbia University Health Science; and Simbios from Stanford University.

The NCBCs maintain active software repositories that freely distribute user-friendly software applications. These resources are aggregated in the joint web portal.[5] In addition, the Centers developed and adopted Biositemaps, a mechanism for computational biologists and bioinformaticians to openly broadcast and retrieve meta-data about biomedical resources.[17] As of November 2012, there were 580 annotated resources of which 252 were developed by NCBCs. The search tool for Biositemaps is the Resource Discovery System which is maintained by a consortium of researchers from within the NCBC as well as the broader community.[18] There is also a Wiki site.[19]

Each NIH NCBC provides and develops tools and resources that biomedical and behavioral researchers can use. To ensure that these tools are useful and responsive to the needs of the biomedical and behavioral community, several mechanisms exist within the NCBC program itself to promote collaborations between an NIH NCBC and these communities. These mechanisms include: DBP, FOAs, and also the training and dissemination activities of each NIH NCBC. The DBPs help to maintain the biomedical focus of the scientific computational research of each NCBC. Two FOAs were released to provide support for investigators working in collaboration with the NCBC using the R01 mechanism.[6] Over the course of the program 32 collaborative projects have been awarded using individual IC funds.[12]

The conclusion of the NCBC program coincided with the onset of the Big Data to Knowledge (BD2K) program, which is a trans-NIH effort that extends well beyond the Common Fund, and is expected to continue via IC funds for the indefinite future. BD2K was developed in recognition that computational challenges have gotten increasingly complex, are not IC-specific, and that a stable source of coordinated, trans-NIH funding is required. Extensive networking among computational biologists, clinicians working in many disease areas, and basic scientists will be required. Training must be expanded to become part of standard training grant curricula. These goals represent an extension and expansion of the goals established for the NCBCs, and lessons learned from the NCBCs will presumably be brought to bear as this program is implemented.

## Notable Challenges

### Managerial

The establishment of specific computational goals for the program in the absence of input from the broad user community contributed to the sense, at the end of the first funding phase, that the NCBC program was tailored to the interests of the funded investigators. Networking activities were not critical. Indeed, network-wide goals were not a feature of the first phase of the program and had not contributed to the achievements. Rather, individual Centers were providing substantial benefit to a restricted portion of the biomedical research community, and these users tended to cluster in IC-specific research areas. This led to the decision that the Centers should transition to those Centers for continued support. A goal to create a nationally networked group of Centers was therefore de-emphasized in the second phase, but the Program Coordinator maintained hope for a national network. Referring to the transition of each Center's budget to the relevant IC, the NIH Working Group noted in the 2010-2011 Annual Report, *"This requirement has encouraged the Centers to focus on their primary funding IC rather than on the cross-cutting*

*research that was the heart of the originally envisioned program."* [Page 5][10] This points to a lack of clarity for the vision of the program and how to achieve that vision.

The NCBCs were formed under a cooperative agreement mechanism, and the expectation was that they would work as a network; however, this expectation did not materialize. In the 2013-2014 Annual Report, the NIH Working Group noted there were two important lessons learned in the administration of the NCBC program. First, "*the NCBCs had a mandate to create a 'networked' set of Centers. However, no funds were specifically allocated [to] achieve this. The NIH Program assigned funds to the Centers with the expectation that, once funded, the PIs would work with NIH staff under the cooperative agreement mechanism. Experience shows that this is not effective since there is no leverage for leadership both among the PIs and on the program side*." [Page 6] Although the NIH Working Group had the ability to adjust funding via the cooperative agreeement mechanisms, they elected not to do this. Secondly, "*the NCBCs had no coherent vision for scientific validation, for software and tool user feedback, or for program evaluation*." [Page 6][12]

Since there was limited coordination across Centers at the NIH program level, the PI Working Groups that were formed were not as effective as they could have been in coordinating activities. The Data and Informatics Working Group (DIWG) noted in the June 2012 report to the Advisory Committee that there was virtually no overlap of focus among the Centers which resulted in limited opportunities for synergy and complementary approaches that could benefit the research community.[21]

**Scientific**

The DIWG pointed out that because only a small number of Centers were funded, all relevant areas of need for biomedical computation were not effectively covered. The Working Group listed three of the seven biomedical computing challenges identified in the Mid-course Review of 2007 that had not been addressed by the NCBC:

- Establishing a large-scale concerted effort in quantitative multi-scale modeling
- Developing methods for "active" computational scientific inquiry by tying them to modeling, visualization and ontologically-based argumentation, helping researchers pose problems in entirely new ways, and checking their conjectures against a synthesis of existing knowledge
- Creating comprehensive, integrated computational modeling/statistical/information systems

These shortcomings of the NCBC program were attributed to limited funding.[21]

**Selected Outputs Through 2013** [22]

Establishment of National Centers

- Eight Centers have been established since 2003 (two were retired after the first round of five years)

Develop a process to assess the impact of software tools (usability, evaluation)

- Outputs are presented across the various milestones

Continue and extend training focus of NCBC program

- The NCBCs have graduated and trained thousands of computational scientists who are now contributing to basic research and the nation's economy.

- NCBO attracted 16 visiting scholars, trained 18 graduate students and 16 post-doctoral fellows, organized 59 educational workshops and conferences as well as 25 webinars
- NAMIC mentored 55 software engineers, 35 doctoral students, and 20 post-doctoral fellows and trained over 2,000 investigators in use of the 3D slicer in 63 workshops
- i2b2 established the Summer Institute in Bioinformatics and Integrative Genomics that has graduated 94 students (42 are now in MD, PhD, or MD/PhD programs), attendance at annual User's Conference exceeds 125
- MAGNet has over 100 pre-doctoral students and post-doctoral fellows working in their labs, 61 of which received MAGNet funding
- iDASH trained 65 individuals, sponsored 16 free webinars and organized and provided support for several other workshops
- Simbios trained over 48 graduate students and postdoctoral fellows and trained more than 1,000 people in using Simbios software
- CCB taught 58 graduate and undergraduate courses and mentored 251 graduate and undergraduate students
- NCIBI supported 16 Ph.D. students and 4 postdoctoral trainees

Continue maintenance of the NCBCs.org web site as a one-stop shopping portal for information about NCBCs and their resources

- NCBO has created BioPortal, which stores 350 biomedical ontologies and controlled terminologies, and has 65,000 visitors per month

Establishing a resource for advancing and maintaining software valuable for biomedical research and applications

- NAMIC 3D slicer has been downloaded 41,000 times in the past 12 months
- i2b2 platform has been adopted by over 84 academic health Centers internationally
- MAGNet algorithms and tools have been broadly adopted, the geWorkbench platforms has been downloaded more than 10,000 times by more than 800 unique users. The top five most popular tools have been downloaded more than 38,000 times
- iDASH hosts the hub for five University of California health systems encompassing 11 million patients. It has 22 data sets from different studies and 11 software tools for privacy protection, analysis, and annotation
- Simbios has several software applications: OpenSim has been downloaded by over 9000 individuals including 30 hospitals, Simbody has been downloaded by 1,200 users, and OpenMM has been downloaded by over 9000 users, Simtk.org is a webportal with more than 22,000 users who share and develop biocomputational tools and data
- CCB designed and disseminated over 53 complementary software packages
- NCIBI software tools have had nearly 1 million web hits in the past year

**Notable Reported Outcomes** [22]

The eight software repositories of the Centers now continue to provide permanent resources that will support biomedical informatics and computational biology for years to come. Summarizing data from the set of one-pagers from all NCBCs (2012) indicates that the combined Centers have accumulated in excess of 140,000 users and downloads. This is important since software is the main 'product' of the NCBCs.

Centers have published over 2,250 papers and proceedings that have been over 15,000 times.

In 2010, Columbia University approved creation of a new department of Systems Biology to streamline and consolidate the research and educational activities of MAGNet.

i2b2 at Brigham and Women's Hospital with Harvard CTSA have created the broadly disseminated SHRINE software pipeline and database which is instrumental in pulling research-grade data out of electronic health records in major hospitals.

Simbios provided the foundation for a new company, Heartflow, which offers a new approach to non-invasive diagnosis of coronary artery disease.

**Transition Out of the Common Fund**

Funding for NCBC will end in FY 2014, though Common Fund support of the program ended in FY 2013. On September 5, 2012, the Chair of the NCBC SAB sent a letter to Drs. Collins, Anderson, and Green (then Acting Director of Data Science) referring to the ACD DIWG. The DIWG suggested the NIH consider the natural evolution of the NCBCs into a more focused activity to integrate the experimental and the computational sciences. They also indicated that the NIH should encourage and enable more overlap between Centers to facilitate collaboration.

In the 2013-2014 Annual Report that the NIH Big Data to Knowledge (BD2K) initiative could provide opportunities for many of NCBC PIs. However, because the Common Fund only supports programs for up to ten years, any option that includes continuously funding the NCBCs from the Common Fund would be problematic.

**References**


1. 1999 BISTI Report- http://www.nih.gov/about/director/060399.htm
2. Computational biology article summer 2005
3. NCBC FOA Website: http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-04-003.html
4. National Centers for Biomedical Computing Midcourse Program Review Report
5. NCBC Website: http://ncbcs.org/summary.html
6. NCBC FOA Website: http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-09-002.html
7. NCBC FOA Website: http://grants.nih.gov/grants/guide/pa-files/PAR-12-001.html
8. NCBC FOA Website: http://grants.nih.gov/grants/guide/pa-files/PAR-08-184.html
9. Bioinformatics and Computational Biology Roadmap, Implementation Plan for FY 2004- September 9, 2003
10. NCBC Annual Progress Report FY 2010-2011
11. NCBC Annual Progress Report FY 2012-2013
12. NCBC Annual Progress Report FY 2013-2014
13. FINAL REPORT Roadmap NCBC Evaluation Meeting July, 2005
14. Roadmap Planning Meeting, August 16, 2002
15. NCBC FOA Website: http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-04-022.html
16. IC Directors Meeting for Roadmap, August 2007
17. Biositemaps Website: http://biositemaps.ncbcs.org/
18. Biositemaps Resource Discovery Website- http://biositemaps.org/rds/
19. SDIWG Website: http://namic.org/Wiki/index.php/SDIWG:Software_and_Data_Integration_Working_Group

20. NCBC Annual Report OSC Summary 2010-2011
21. Data and Informatics Working Group; Draft Report to the Advisory Committee to the Director
22. Appendices NCBC Progress Report 2013, Appendix C: Set of ‘One Pagers’ which summarize achievements of NCBC Centers over their lifetime

## Appendix 20: Human Microbiome Project (HMP) Program Summary

**Why This Program was Selected for Review**

The MP provides an example of a program that was envisioned from its outset to accomplish defined goals within a 6 year timeframe (with an initial year of "jumpstart funding") and then to end, as the community at large expanded microbiome research by using the tools and data that the program was to develop. The program was highly successful, meeting or exceeding all its milestones, and the broader community has rapidly expanded microbiome research in many new and exciting ways. At the end of the initial funding period, the OD was faced with a question of whether to end the program as originally envisioned, whether to continue to provide support at a similar or higher level of funding in recognition of the success of the initial phase and to take advantage of the opportunities that the first phase had provided, or whether to provide support for a more focused question or problem. This program summary is intended to illustrate management processes that ensured the success of the program and to provide context for the consideration of when/how to provide continued support for successful Common Fund programs and how to plan for their transition to ongoing support by the ICs. Highlighted text is intended to draw attention to the most salient portions for these issues.

**Common Fund Support**

**Phase I: 2007 - 2012**

FY 2007 Actual: $8,973,000
FY 2008 Actual: $10,014,831
FY 2009 Actual: $39,387,587
FY 2010 Actual: $38,188,507
FY 2011 Actual: $ 25,363,896
FY 2012 Actual: $ 23,648,800

**Phase II: 2013 - 2016**

FY 2013 Actual: $6,145,085
FY 2014 Budgeted: $5,357,618
FY 2015 Budgeted: $5,000,000
FY 2016 Budgeted: $93,000

**Common Fund Criteria**

The Human Microbiome Project (HMP) embodied the Common Fund criteria: transformative, cross-cutting, unique, catalytic, and synergistic. Prior to the start of the program, the importance of pathogenic microbes had been well established, whereas the significance of the often beneficial, commensal human microbes was only beginning to be understood. The HMP was timely and unique because, even though the microbes on the human body outnumber human cells by a ratio of ten to one, very few had been amenable to cultivation in the laboratory, and therefore only a small number had been identified or characterized. Although there were hints that the microbiome played a role in health, as well as in conditions as varied as obesity and cancer, microbiome research was hindered by the lack of descriptions of the many microbes that inhabit the human body. When the HMP was proposed, genomic sequencing technology and bioinformatics had just advanced to a stage that allowed researchers to discover and characterize individual microbes from complex mixtures such as those found on the human body. The HMP was designed as a community resource project that would transform research by defining the components of the healthy human microbiome and by demonstrating links between changes in the microbiome and changes in human health. The fundamental questions the program would address and the resources it developed would cut across all body sites and many complex diseases. The ability to characterize and manipulate the human microbiome would catalyze new

approaches to monitoring health status, understanding disease etiology and developing new preventive strategies through the maintenance or re-establishment of a healthy microbiome.[1]

## Program Description

To take advantage of recent technological advances and to develop new ones, the HMP was established in 2007 as a six-year Common Fund program with the mission of generating resources enabling comprehensive characterization of the human microbiome and analysis of its role in human health and disease. The program aimed to characterize the microbial communities found at several different sites on the human body, including the nasal passages, oral cavity, skin, gastrointestinal tract, and urogenital tract, and to analyze the role of human microbes in health and disease. It defined the healthy human microbiome, sequenced hundreds of new reference strains, developed new methods of sequencing and analyzing complex genomic information, developed new methods for analyzing the biological properties of the microbiome, and demonstrated links between changes in the microbiome and health status.[2] In 2013, the HMP was continued for three years to develop a dataset that the community can utilize to explore whether study of the human microbiome beyond sequenced-based analyses will yield important new insights in understanding human health and disease.[3]

## Goals

### Phase I

The overall goal of the HMP was to enable deep characterization of human microbiota and studies of the relationship of changes (e.g., from disease, host genotype, age, environment) at one or more sites to health and disease status. It also aimed to demonstrate the feasibility of this new approach and generate resources and fundamental knowledge for the scientific community to use in research leading to new strategies for diagnosis, prevention, and treatment of human diseases. In Phase I, the program consisted of the eight initiatives listed below with their milestones:

Milestones[4]

Initiative 1: Reference genomes and metagenomic survey

- Accrue samples
- Complete 200 genomes per year in three years
- Complete metagenomic sequencing within three years
- Sequence non-prokaryotic flora in years three-five

Initiative 2: Demonstration projects to determine relationship between disease and changes in the human microbiome

- Accrue samples from cases and controls
- Select most promising projects by end of year one based on assessment of survey data
- Determine whether a relationship between the microbiome and health state exists for those projects that are selected

Initiative 3: Development of new technologies needed for studying the human microbiome

- Introduce novel technology within five year pilot project
- Develop novel technology concepts for implementation in subsequent microbiome projects

Initiative 4: Development of new tools for computational analysis of HMP data

- Projects will demonstrate application to data analysis problem using HMP data within five year grant period

Initiative 5: Support for housing of HMP sequence data at National Center for Biotechnology Information (NCBI) Trace Archive

- On-going service to the research community through storage and display of different types of sequence trace data

Initiative 6: Establishing a Data and Analysis Coordinating Center (DACC)

- Establish robust data tracking, storing and dissemination system by end of year one
- Provide on-going service to community via display and dissemination of data
- Provide on-going service through storage and display of different types of sequence trace data

Initiative 7: Resource repository

- Establish system to receive, renew, and provide samples to user community by end of year one
- Provide on-going service to community through dissemination of samples

Initiative 8: Ethical, legal, and social implications (ELSI) of HMP research

- Milestones for this initiative will be set based on individual grants/projects

In addition to these funding initiatives, the HMP Working Group helped to establish The International Human Microbiome Consortium, which fostered data sharing and the establishment of international standards for microbiome data. This international partnership has extended the impact of the program and has accelerated the analysis and comparison of large data sets.

**Phase II**

The goal is to generate exploratory datasets from microbiomes of well-phenotyped subjects in order to create a combined dataset of microbiome and host properties as a community resource. The long term objective of this activity is for the community to be able to utilize this combined dataset to explore whether study of the human microbiome beyond sequenced-based analyses will yield important new insights in understanding human health and disease. In Phase II, the program consists of the single initiative listed below with its milestones:

Milestones[4]

Initiative 9: Evaluation of multi-'omic data in understanding the microbiome's role in health and disease

- Sample collection and distribution- collect clinical specimens from a well-phenotyped cohort(s) of a specific health or disease state(s)
- Data production- generate various microbiome data types from these clinical specimens
- Data integration and testing- combine the microbiome and host phenotype data into an integrated dataset and test the usability of this dataset through a proof-of-principle test
- Data deposition- deposit all data into public databases and appropriate web-based databases
- Data analysis- as time allows, attempt an analysis of the integrated dataset

**Management**

The first phase of the HMP was managed by a large trans-NIH Working Group, co-chaired by four Institute and Center (IC) Directors and comprised of program staff from nearly every IC.[1] The HMP coordinator was responsible for overall programmatic oversight and coordination including organization and activities of the HMP research network consortium, which included hundreds of researchers, some of whom were not supported by the HMP. The HMP Coordinator also played a key role in the organization and coordination of the International Human Microbiome Consortium. The HMP scientific co-chairs and the HMP Working Group advised and approved major programmatic decisions about HMP as well as funding recommendations for the program. From the beginning of the program, Office of Strategic Coordination (OSC) staff were involved in overseeing progress and helping to ensure success of the program.

A steering committee consisting of the NIH HMP Working Group members and both intramural and extramural HMP-funded principle investigators discussed issues affecting project progress, meeting milestones, and otherwise completing the work set out in the project. For Phase I, there was a panel made up of seven scientific consultants known as the External Scientific Consultants (ESC). The ESC, comprised of prominent scientists in the field who were neither HMP grantees nor consortium members, attended annual HMP network consortium meetings and provided advice to the NIH Working Group on a frequent basis. They also reviewed progress of the grantees and participated in the midcourse review of the program.[5]

For the second phase of HMP, a similar management structure is in place. A smaller ESC of three members has been formed with one member from the previous ESC included for continuity.

**Panel Review and/or Formal Evaluation Conducted**

A panel review of the Demonstration Projects was conducted in 2010 and a midcourse review of the entire program was held in February 2012.

In 2010, a panel comprised of the ESC and other experts met to review the progress of the 15 Demonstration Projects. The panel found that unexpectedly good progress had been made on 13 of the 15 projects. They also recommended that any continuing projects strengthen their bioinformatics approaches. Three ICs expressed interest in contributing funds to continue Demonstration Projects of relevance to their missions. The Common Fund also contributed extra funds such that all of the Demonstration Projects continued, either with increased funding into the seond phase (nine projects) or with bridge funds to close out the project (five projects). In response to the panel's recommendations, the Demonstration Project teams collaborated with some of the HMP Computational Tools investigators to improve their analytical approaches to their data. In addition, some of the HMP sequencing centers collaborated with some of the Demonstration Projects to improve their sequencing outputs and to assist in data analysis. Also in 2010, the ESC made recommendations on the pace of progress at the sequencing centers, particularly in data analysis and publishing. In response, the centers subsequently picked up the pace of their deliberations on quality control and set deadlines for data freezes and publications on the healthy microbiome.[7] As a result, in 2012, the HMP research network collaborated to publish two seminal papers in Nature and a series of companion papers in the PLoS family of journals.[8, 9, 10]

In February 2012, the ESC, along with some additional outside experts, assessed progress and provided guidance on the need for a second phase of the HMP. The panel agreed that the HMP had met its original goals, catalyzed the nascent field of human microbiome research, and brought together a diverse community of scientists. The panel concluded that a major success of the program was organizing and maintaining a data analysis Working Group of over 100 people, some of whom were not funded by the HMP. Together, the members of this group analyzed the healthy cohort data such that it could be presented to the rest of the world.[11] The panel also agreed that the trans-NIH Common Fund mechanism used to support the HMP was important to the successes of the program. They found that other scientists were leveraging the datasets, tools, and standard operating procedures created by the HMP in their own research. Regarding a second phase, the panel advised that understanding the key functional properties of a normal host-microbiome system was the next step needed to establish the foundation for understanding the role of the microbiome in health and in disease. The panel recommended building capacity for large-scale, high throughout functional assays for the microbiome and host tissue and immune system properties in human and in animal model systems. Panel members also suggested strengthening the bioinformatics infrastructure for systems-level analyses of DNA, RNA, proteins and small molecules. Finally, they noted that, "*The goals of a Microbiome 2 Program are too extensive to be supported by one NIH institute. The program is an ideal fit for the Common Fund criteria. NIH should also consider the possibility of the formation of a Microbiome Institute*."[5]

**History and Evolution**

The NIH began planning the HMP as a natural extension from the Human Genome Project, to decipher the associated microorganisms that help extend our genetic diversity. The program was launched in a phased approach with the sequencing centers funded first to sample healthy people and to generate the reference microbial genome sequences. In 2009, the Demonstration Projects were funded through a new grant mechanism (the UH2/UH3) that allowed NIH to stop projects that were not meeting their milestones. The HMP Working Group developed this new funding mechanism because it anticipated that many projects would not have the technical sophistication needed to reach the demanding milestones. Several solicitations were made for projects to develop both analytical tools and laboratory methods for culturing and/or sequencing microbes. Because the HMP was designed as a community resource, the sequence data were made available prior to publication. The NCBI at the National Library of Medicine stored the raw data and an extramural HMP DACC tracked, stored, analyzed, and distributed the primary data and derived datasets. In addition, a repository was set up to receive HMP microbial strains and distribute them to the community.[6]

In May 2012, NIH decided to continue support of the HMP for a focused three-year program to explore whether study of the human microbiome beyond sequenced-based analyses will yield important new insights in understanding human health and disease.[11,12] The second phase of the HMP consists of a single initiative to create a community resource that can be used to decipher the role of the microbiome in human health through: (1) acquiring multi 'omic types of data from a well-phenotyped human cohort studies, (2) defining practices for sample collection that support multi-omic analyses, (3) making these data available to the broad community through appropriate databases, and (4) improving upon all of these methods and protocols. Two IC and

two DPCPSI program offices were interested in expanding the number of projects that could be supported, so they contributed funds. In addition, the Common Fund provided extra funding in FY 2013 and FY 2014. At the end of 2013, there is no progress to report since the projects were funded at the end of FY 2013, and the first steering committee meeting is planned for January 2014.

## Notable Challenges

### Managerial

The HMP research activities are coordinated through a research network consortium. During the first phase, there were challenging interactions between the sequencing center Principal Investigators (PIs) and the DACC PI that led to delays in the overall progress of the HMP. In addition, there was friction between the four sequencing centers because one of them received a far larger award than the others but did not appear to be taking on a leadership role in the network consortium, as was expected. Further, the consortium members were unclear as to the roles and authorities of the steering committee members, which caused strife amongst the consortium members. Finally, one steering committee member published on embargoed data without requesting explicit permission of the other consortium members. The HMP coordinator brought these issues to the NIH Ombudsman Office, which provided advice leading to a more equitable, transparent, and sensible distribution of roles and responsibilities in the consortium. Further, steps are being taken to avoid these problems in the new research consortium for Phase II by clearly outlining the roles and responsibilities of the steering committee and the members in the inaugural meeting of the HMP2 consortium.[7, 5]

The UH2/UH3 mechanism that was employed for the Demonstration Projects posed significant challenges to these projects and was counterproductive to the collaboration that investigators desired. The quarterly reports and tight timelines for achieving milestones that were required as part of this mechanism were incompatible with the actual pace of clinical research and hypothesis-driven science. Also, the budgets of the projects were not uniform as a result of this mechanism. Coordinated communication and group objectives for these Demonstration Projects grantees were lacking. While there was much communication at the start, strategic planning, defined objectives, and follow-up were never clearly articulated in the planning calls.[11]

### Scientific

In the first phase of the HMP, four sequencing centers were funded to sequence the samples from the healthy cohort study. In order to ensure the methods were comparable, each was provided a sample of a mix of bacteria of known composition. None of the centers identified the correct number of microbes in the mixture, leading the HMP network to decide to invest in developing careful sampling, purification, and analytical procedures that eventually enabled the HMP centers to combine their data.

## Selected Outputs Through 2013

Initiative 1: Reference genomes and metagenomic survey

Accrue samples

- The recruitment goals of the study were achieved within approximately 24 months, with 49.1 percent of the subjects being male and 19.3 percent being either racial or ethnic minorities. Of the 300 subjects recruited, 279 returned for a second sampling within 12

months of the first sampling and 100 returned for a third sampling within six months of the second sampling.[7]

Complete 200 genomes per year in three years

- By late 2010, about 500 reference microbial genomes had been sequenced, and, because of reductions in sequencing costs, the HMP goal of sequencing 600 bacterial strains was increased to 3,000 strains.[7] By late 2013, over 2,000 microbial reference genomes had been either finished or nearly finished, and the sequencing centers had committed to completing the 3,000 during their no cost extension period.[4]

Complete metagenomic sequencing within three years

- By October 2012, all 11,000 samples from the healthy cohort had been sequenced for the 16S rRNA gene and the raw sequences deposited in NCBI. Ten percent of these primary samples had been sequenced by whole genome shotgun (WGS) metagenomic sequencing and with supplemental funds in FY 2012, the HMP sequencing centers committed to sequencing an additional 1,500 samples by WGS metagenomic sequencing.[5]

Sequence non-prokaryotic flora in years three through five

- In the 2012 Nature paper, the HMP reported that a typical healthy United States adult was host to approximately 1,000 species of bacteria that contributed a total of approximately 2,000,000 unique microbial genes to its host.
- Further, in the same paper, the HMP reported that there was a global pool of approximately 10,000 bacterial species that could be found across the population of healthy United States adults, highlighting the extensive genetic capacity of the human microbiome.
- By the end of 2013, the genomes of over 100 viruses as well as numerous microbial eukaryotic genomes were completed or in the pipeline.[4]

Initiative 2: Demonstration projects to determine relationship between disease and changes in the human microbiome

Accrue samples from cases and controls

- Each Demonstration Project succeeded in accruing sufficient samples to make progress.

Select most promising projects by end of year 1 based on assessment of survey data

- A review of progress in 2010 led to the identification of the most promising projects for expanded funding in the UH3 phase.[7]
- By 2012, the HMP Demonstration Projects began reporting that they could identify disease-specific microbiomes across a wide range of complex diseases including cancer, which differed from the microbiomes of healthy control populations.
- By the end of 2013, this HMP initiative of 15 clinical projects had published 121 papers.[4]
- As an indication of the quality of these projects, at least one of the projects that was terminated early was leveraged into R01 funding independent of the HMP.[13]

Initiative 3: Development of new technologies needed for studying the human microbiome

Introduce novel technology within five year pilot project

- Several new techniques were developed for isolating and sequencing new microbes.[7]

Develop novel technology concepts for implementation in subsequent microbiome projects

- One HMP project developed techniques for culturing microbes that were subsequently used by another HMP investigator to study ulcerative colitis.[4]
- Other novel technologies have been used to fill gaps in the reference genome collection.[7]

Initiative 4: Development of new tools for computational analysis of HMP data

Projects will demonstrate application to data analysis problem using HMP data within five year grant period

- By fall 2010, the HMP analytical tool projects had contributed a suite of computational tools and approaches to analysis of HMP data including data organizing/processing pipelines, metagenomic sequence assembly tools, and tools to measure microbial diversity.[7]

Initiative 5: Support for housing of HMP sequence data at NCBI Trace Archive

On-going service to the research community through storage and display of different types of sequence trace data

- All raw sequence, genome assemblies, genome annotations and clinical phenotype data generated from the various HMP projects is stored in appropriate archives at NCBI.[7]

Initiative 6: Establishing a DACC

Establish robust data tracking, storing and dissemination system by end of year one

- The DACC facilitated and coordinated data formats, metadata content and data transfer and release from the multiple sequencing centers participating in the HMP to NCBI.[7]

Provide on-going service to community via display and dissemination of data

- The DACC has been developing documentation that describes the various sub-projects that are part of the HMP, the scientific hypothesis of these projects and the type and location of data.
- The DACC has been heavily involved with the HMP data analysis Working Groups where it provides analysis and general informatics expertise for the HMP.
- The DACC developed and proto-typed a number of analysis pipelines that have been utilized by groups within the HMP.

Provide on-going service through storage and display of different types of sequence trace data

- The DACC has been involved with facilitating and supporting transfer of clinical phenotype data to dbGaP. It has provided extensive support to investigators in the various HMP initiatives projects.
- The DACC has been actively involved in designing a clinical phenotype ontology that can be used by all participants in the HMP and the International Human Microbiome Consortium (IHMC).

Initiative 7: Resource repository

Establish system to receive, renew and provide samples to user community by end of year one

- The HMP took advantage of existing infrastructure by establishing the HMP repository at the Biodefense and Emerging Infections Research Resources Repository (BEI), funded by the National Institutes of Allergy and Infectious Disease.[7]

Provide on-going service to community through dissemination of samples

- The HMP repository at BEI provides and distributes microorganisms that have undergone extensive quality control and monitoring to the scientific community.

Initiative 8: ELSI of HMP research

Milestones for this initiative will be set based on individual grants/projects

- HMP supported ELSI work led to the first book on ELSI issues related to the microbiome.
- A Working Group led by an HMP ELSI grantee authored a white paper on the federal regulation of probiotics. [14]
- HMP ELSI investigators published several papers on patients' perceptions of probiotics.[5]

**Notable Reported Outcomes**:

In 2008, the HMP Working Group worked with members of the European Commission to develop the IHMC.

In 2010, a group of European scientists utilized publically available HMP sequence data to assemble a gene catalog for the human gut.[15]

By 2011, the new grant mechanism developed by the HMP (UH2/UH3) was in use by other NIH programs.

In 2012, inspired by the HMP Demonstration Projects, the Foundation for the NIH formed a partnership with industry partners to support HMP research.

In 2013, a scientist used public HMP sequence data to show that human gene variation appears to affect the composition of the microbiome.[16]

In 2013, Amazon Cloud Services provided five terabytes of HMP data free of charge to the public.[17]

In 2013, a group of non-HMP scientists began working with the DACC to analyze HMP data along with other publically available human microbiome datasets. This analysis includes the development of new methods for constructing a representative set of reference genomes in order to automate the analysis pipeline and to enable high speed comparison of sequences against the reference set.[4]

**Transition Out of the Common Fund**

Although phase II continues, several measures have been put in place to transition the HMP out of the Common Fund. These include:

- The creation of a trans-NIH Microbiome Working Group (TMWG): The number of ICs supporting microbiome research has expanded greatly since the HMP program began. A TMWG was formed to provide a forum for NIH extramural staff to discuss their interest in microbiome program development, announce upcoming FOAs, seek co-funding for existing RFAs or foster the development of joint program announcements. The HMP coordinator serves as the chair and the TMWG has been meeting monthly since 2012.
- The organization of a 3-day meeting to highlight the state of the science for the human microbiome field at NIH: The "NIH Human Microbiome Science: Vision for the Future" meeting was held July 24-26, 2013. Two meeting reports are being prepared for public consumption.
- The inclusion of protocols for microbiome sampling in the National Children's Study (NCS): The main objectives of NCS are to collect biological specimens and extensive metadata from 100,000 children from ethnically and racially diverse families and to create a biobank of samples for researchers to use to address scientific and biomedical questions of relevance to the NCS mission. The original plan for NCS did not include the microbiome but the NCS has decided to include the microbiome in a pilot study of 5,000 children to evaluate protocols and methodologies.[4]

**References**


1. HMP Proposal 2007
2. Common Fund HMP Overview Website: http://commonfund.nih.gov/hmp/overview.aspx
3. Common Fund HMP Initiatives Website: http://commonfund.nih.gov/hmp/initiatives
4. HMP Annual Progress Report FY 2013-2014

5. HMP Annual Progress Report FY 2012-2013
6. NIH Builds Substantial HMP; Appendix in HMP Annual Progress Report FY 2010-2011
7. HMP Annual Progress Report FY 2010-2011
8. The Human Microbiome Project Consortium. 2012. Structure, function and diversity of the healthy human microbiome. *Nature,* 207-214, Volume 486 [June].
9. The Human Microbiome Project Consortium. 2012. A framework for human microbiome research. *Nature,* 215-221, Volume 486 [June].
10. Companion Papers in PLoS Journal: http://www.genome.gov/27549115
11. Executive Summary of External Panel Report
12. Proposal for Human Microbiome Project Transition Program
13. Personal Communication, Mary Perry, OSC Program Leader for HMP
14. Hoffman et al. 2012. Federal regulation of probiotics: an analysis of the regulatory framework and recommendations for alternative frameworks. White Paper, November 15.
15. Qin et al. 2010. A human gut microbial gene catalogue established by metagenomic sequencing. *Nature,* 59-65, Volume 464 [March].
16. The Scientist Website: http://www.the-scientist.com/?articles.view/articleNo/37982/title/It-s-in-the-Genes/
17. Human Microbiome Project Data Set Website: http://aws.amazon.com/datasets/1903160021374413

## Appendix 21: Epigenomics Program Summary

### Why This Program was Selected for Review

The Epigenomics Program provides an example of a program that has succeeded due to the clear articulation of goals, advice from an external panel of scientific experts, active international partnerships, and adaptation of program goals in response to the emerging needs and opportunities. This document provides details for context, but the primary purpose is to illustrate how the Working Group reached agreement on specific goals for the program, developed milestones, coordinated internationally to extend the impact of the program, worked with an external panel to ensure success of the program, and adjusted to changing scientific opportunities. It also provides a sense of the effort involved to manage a program of this size. Highlighted text is intended to focus the reader's attention on these management issues. The Selected Output section at the end of the document is intended to provide enough information for the reader to determine whether the management processes have been successful.

### Common Fund Support

FY 2007 Actual: $3,000,000
FY 2008 Actual: $20,181,476
FY 2009 Actual: $24,876,785
FY 2010 Actual: $25,810,127
FY 2011 Actual: $23,768,602
FY 2012 Actual: $22,042,953
FY 2013 Actual: $14,035,798
FY 2014 Budgeted: $10,500,000
FY 2015 Budgeted: $7,000,000
FY 2016 Budgeted: $4,000,000
FY 2017 Budgeted: $4,000,000

### Common Fund Criteria

Epigenomics met the criteria for Common Fund because the NIH felt that new knowledge of epigenomes would have widespread and profound implications for human health and disease.[1] The program was designed to enable epigenomic research, and therefore to transform understanding of the origins of disease and identify new therapeutic targets and/or biomarkers. All ICs were seen as the beneficiaries of the program, since epigenetic mechanisms were considered to be likely contributors to many diseases affecting all organ systems. NIH Roadmap/Common Fund investment in the program was intended to catalyze NIH-wide analyses of epigenetic contribution to human health and disease through its provision of core data sets, tools, and demonstration projects.[2]

### Program Description

The Epigenomics program includes a series of complementary initiatives aimed at generating new research tools, technologies, datasets, and infrastructure to accelerate epigenomic analyses. Five original initiatives included: 1) development of reference human epigenomes; 2) identification of novel epigenetic marks; 3) development of new technologies for epigenomic assays and imaging; 4) investigations into epigenomic processes in a variety of diseases; and 5) development of monoclonal antibody tools for epigenomic research.[3]

A sixth initiative was developed in FY13 in response to challenges that arose during the tenure of the program concerning epigenetic manipulation. This initiative was developed to address the fact that manipulation of the genome largely relied on pharmacological or genetic manipulation of epigenetic regulatory proteins and that more precise temporal, spatial, or locus-specific manipulation of the epigenome remained problematic. To overcome this scientific barrier, the

initiative sought to develop novel tools and technologies to enable: 1) tissue or cell-specific manipulation of epigenetic modifications or their effector molecules; 2) temporal manipulation of the epigenome; 3) locus-specific manipulation of the epigenome; and/or 4) novel approaches that enable any combination of the previous three goals.[4]

In addition to the funding initiatives above, the Epigenomics Program has included a concerted effort to coordinate internationally to develop recommended standards for epigenomic assays and data sharing. This has increased the impact of the program and has facilitated sharing and comparison of data between labs worldwide.

**Goals and Milestones** [4, 5]

Milestones were established to guide the management of the program. Progress has been made on all milestones. Refer to the "Selected Outputs Through 2013" section for more information.

Initiative 1: Reference Epigenome Mapping Centers (REMCs) – To develop reference epigenomic maps from normal/healthy human cells and tissues and to generate antibodies for epigenomics research.

- FY 2008: Protocols for cell/tissue processing and epigenomic mapping developed and shared among REMCs and with community; data and metadata standards developed, agreed upon, and shared; first draft of epigenome: maps of 3-4 human ES cell lines, differentiating/differentiated cells, selected cell lines or tissues; new high quality antibodies for epigenomic analyses available; data transferred to EDACC and high quality data made available to public through NCBI
- FY 2010: 12 comprehensive epigenome maps as public resource
- FY 2012: 24 comprehensive epigenome maps as public resource
- FY 2013: Issue a Request for Application (RFA) to support integrative computational analyses that take advantage of the data generated through the Reference Epigenome Mapping Centers [6]

Initiative 2: Human Health and Disease – To determine if epigenomic changes happen in multiple diseases and conditions and to strengthen Institute and Center (IC) support for research into the epigenetic basis of disease

- FY 2009: Epigenomics and disease grants funded; IC co-funding secured for Common Fund awards (Note: initiative only released once for FY 2009 funding)
- FY 2010: Sample collection/patient recruiting well underway; identification of best epigenomic assay for the biological question at hand
- FY 2011: Epigenomic maps of diseased vs. normal cell types begin to be generated; IC funding for RM-affiliated disease initiative secured
- FY 2012: Epigenomic differences between disease and normal cell types presented at meetings and indicated in progress reports; publications showing these differences begin to come out
- FY 2013: Data transferred to EDACC and made publicly available through NCBI. (Note: Sharing data is primarily through publications with data sets deposited in NCBI as appropriate.)
- FY 2014: The scientific community uses the discoveries made by the disease researchers as indicated by citations of the above publications

Initiative 3: EDACC and NCBI Public Interface – To identify types of data and develop standard data formats, to provide bioinformatics support for data analysis and integration, and to disseminate and store data via the NCBI public interface

- FY 2008: Application funded/Interagency Agreement implemented; data pipeline and infrastructure established and analysis tools developed for epigenomics data and metadata; relevant REMC data imported
- FY 2009: EDACC takes in data during quarterly data freezes; ensures data has appropriate metadata, assigns each data set data quality metrics; data transferred to NCBI
- FY 2010: Enhanced analysis tools developed by EDACC and NCBI
- FY 2011: Public accesses NCBI data as measured by web hits, data downloads, and by publications citing use of the datasets; improve and expand communication efforts in concert with other components of the program to ensure scientific community is aware of the data and what can be done with it
- FY 2012: Enhancements to enable data users of different types (power users, genomics experts, disease researchers, naïve users) to use the data effectively

Initiative 4: Technology Development in Epigenetics – To develop new revolutionary epigenetic technologies including remote imaging of epigenetic activity in cells/tissues and whole animals

- FY 2008: New revolutionary technology development applications funded
- FY 2009: Revolutionary technologies are developed to enable *in vivo* imaging or analysis of epigenetic changes[7]
- FY 2010: One or more new technologies developed, as measured by publications and/or patents on the new technology
- FY 2011: New technologies shared with community, as measured by citations of the publications describing the technology
- FY 2012: One or more new technologies applied to a biological question or disease, as measured by publications using the new technology to address a specific biological question or disease
- FY 2013: Applications of the new technology shared with the community, as measured by citations of the publications describing the application of the technology

Initiative 5: Discovery of Novel Epigenetic Marks in Mammalian Cells – To identify new/novel epigenetic marks

- FY 2008: New/novel marks applications funded
- FY 2010: Novel marks identified to date as measured by publications on these novel marks
- FY 2011: Information on novel marks shared with the scientific community as indicated by citations of the papers describing these novel marks

Initiative 6: Functional Epigenetics – To develop technologies and research tools to enable functional cell-type, temporal, or locus-specific epigenomic manipulation and potentially provide a foundation for developing new epigenome-based therapeutics

- FY 2013: Fund five to eight R01 applications responsive to Funding Opportunity Announcement (FOA)
- FY 2014: Projects will have achieved their individual year 1 quantitative milestones; each project will exhibit qualitative progress towards their ability to manipulate the epigenome (Note: another part of the original milestone was for PIs to attend a meeting in Bethesda and

share progress; however, the Working Group has indicated that it is unclear at this point if there will be another Epigenomics program meeting.)
- FY 2015: PIs will have achieved their individual year 2quantitative milestones
- FY 2016: PIs will have achieved their individual year 3 quantitative milestones; two projects from the overall functional epigenomics initiative show proof of concept that they can achieve cell-specific, locus-specific, or temporal epigenome manipulation
- FY 2017: PIs will have achieved their individual year 4 quantitative milestones; publication of at least one original research article by 80 percent of participants (Note: another part of the original milestone was for PIs to attend a meeting in Bethesda and share progress; however, the Working Group has indicated that it is unclear at this point if there will be another Epigenomics program meeting)
- FY 2018: Publication of at least two papers from the overall functional epigenomics initiative describing new tools or technologies to manipulate the epigenome; PIs will have achieved their year 5 quantitative milestones
- Post- FY 2018: See if any researchers have applied any of the developed tools or technologies to investigate a specific biological or disease process, as measured by monitoring publications/citations

**Management**

The Epigenomics Working Group (EWG) was established with leadership from the National Institute of Environmental Health Sciences (NIEHS) and the National Institute on Drug Abuse (NIDA). The Director of the National Institute on Deafness and Communicative Disorders (NIDCD) joined later as a third Co-Chair. The EWG consists of representatives from 19 ICs. The EWG is responsible for review, modification, and recommendation of changes to the original Epigenomics project plan. The program leadership is informed by the activities of the International Human Epigenome Consortium (IHEC). Two program staff members from NIDA and NIEHS serve as representatives to the IHEC Executive and Scientific Committees.[8, 9]

- Initiative 1, REMCs, is led by NIEHS. A REMC Consortium was established to develop maps for use by the larger scientific community, and a Steering Committee (SC) was established for this consortium consisting of Principal Investigators (PIs) and NIH staff Working Group members. The SC meets bimonthly by conference call and twice a year face-to-face with PIs, NIH program staff, and external advisors to assess progress relative to stated milestones. An External Scientific Panel (ESP) was also established to provide recommendations to the consortium and input on goals the consortium should pursue. In 2013, a FOA was released to support integrative computational analyses that take advantage of the data generated by the REMCs. The FOA will be administered by the NIEHS on behalf of the NIH.[10]

- Initiative 2, Human Health and Disease, is coordinated by the NIEHS. The first set of awards from this initiative was co-funded by the Common Fund and the most relevant IC for each award. A subsequent round of awards was paid solely by the ICs, illustrating the considerable interest in this area of research by many ICs. Lead ICs for specific awards work through the

Epigenomics Project Teams and the EWG to establish funding initiatives and funding plans, and provide programmatic input into the program.

- Initiative 3, the EDACC, is administered by program staff at NIDA. NIDA staff coordinate with project staff at the lead ICs for the other initiatives, and participate in the SC for Mapping Centers.

- Initiative 4, Technology Development in Epigenomics, is administered by program staff at NIDA and NIEHS. Each application has a program officer from NIDA and a Science Officer from a different IC.[8]

- Initiative 5, Discovery of Novel Epigenetics Marks, was led by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK).[11] One round of awards was made; these awards ended in FY13.

- Initiative 6, Functional Epigenomics Tools and Technologies, was added in 2013. It is administered by NIDA.

**Panel Review and/or Formal Evaluation Conducted**

An ESP met periodically to advise the Mapping Consortium on areas of focus and various scientific issues. The ESP has consistently focused on addressing problems with public access to the data, completing the available protocols, publicizing the program, and encouraging completion of gaps in the epigenomic data sets.[12, 13]

In May 2010, the ESP met with the SC and recommended, among other things, to develop data quality metrics, address problems the public has had with the browser to access the epigenome data sets, better coordination with the Encyclopedia of DNA Elements (ENCODE) program, and additional interaction with Roadmap Centers and Roadmap Disease Projects, as well as the IHEC. Regarding the recommendation on data quality metrics, the program team responded that the Data Quality Working Group developed four metrics for Level 2 data which have now been applied to all data released by the program and the group is continuing to work towards establishing metrics for Level 1 data.[14, 15]

In 2011, a process evaluation was conducted to address broad study questions for the overall program, and more detailed questions specific to the program components. Information was to be collected from program documents, a survey of Program PIs, a follow-up interview with selected PIs, and from user testing of the NCBI data interface by epigenomics researchers external to the program. The overall study questions were:

- Are the components of the program being conducted as planned?
- What unanticipated needs were identified and how were they dealt with?
- What/how did the American Recovery and Reinvestment Act (ARRA) supplements and additional projects contribute to the program/improve the program?
- Do output and outcomes from process demonstrate that the program is moving in the right direction for achieving its goals?

- What are key features to show how the SC, EDACC, and REMCs worked together for the expedient development and function of the data pipeline, and for the coordinating of function and product development at the REMCs? What outcomes from this process demonstrate its success?
- What changes and improvements to the design of the data interface were made on recommendations obtained from the user feedback?

The findings and recommendations from the evaluation included the following:[16, 11]

- Plan for a possible outcome evaluation before the end of the program in two years, include data on indicators of "potentially transformative" future outcomes as well as on outcomes that have already been realized and whose impact can be assessed
- Develop a short list of key informational elements needed from PIs on a semi-annual basis
- Provide better mining and search tools, and secure future funding
- Develop indicators of progress, set targets, and then measure progress
- Require an expanded set of information needs for Roadmap Programs

The ESP met in May 2012 and made 11 recommendations to the Epigenomics project team, summarized below. The Working Group indicated that the team was working on addressing all recommendations except the recommendation to conduct additional outreach such as training grants, noting that no additional resources were available to support such activities.[5]

The ESP made the following specific recommendations:

1. The consortium should immediately begin work on a high-profile manuscript describing the first 50 epigenomes, to be submitted in Fall 2012.
2. Issues about how genotype-epigenome relationships will be determined and presented must be resolved.
3. The consortium members should work with NIH Roadmap staff and their local IRBs to ensure that the maximum amount of useful sequence/genotype data is utilized and released.
4. It was recommended that 10 genomes be sequenced for hydroxymethyl C. A list of the exact samples to be used should be circulated for approval before commencing.
5. The consortium should develop, as soon as possible, a detailed long-term plan for the storage and availability of all data created by the project.
6. The NIH or consortium members should explore exporting the hands-on data-access workshops model to the community through other meetings, perhaps meetings that disease-focused investigators attend.
7. NIH should investigate mechanisms to inform other program officers about the datasets available, to prevent redundancy in funding.
8. The consortium should make public its plans for what tissues will be analyzed, perhaps by using differently colored squares in the data grid.
9. It was recommended that a major symposium be organized at the end of this project to publicize the datasets and highlight the impact of the project.
10. The NIH and PIs need to consider other forms of outreach to make community aware of datasets.
11. A 100 epigenome effort would be fantastic, and a clear marker of success for the project.

## Notable Challenges

### Managerial

Before RFAs for the original five initiatives were issued, the Working Group experienced some disagreement concerning the scope and specific goals of the program. Discussion centered on five issues: 1) Must embryonic stem cells be analyzed by the Reference Epigenome Mapping Centers (REMCs) as reference cells, or should the group of PIs, in consultation with an external panel select the most useful set of cells for analysis? 2) Must the REMCs restrict their analysis to human cells, or should the scope include animal cells? 3) Must the REMCs restrict their analysis to normal/healthy cells, or should they be allowed to include diseased/treated/aged cells in their analysis? 4) Must the RFA that was to focus on healthy cell/diseased cell comparisons be restricted to human cells, or should animal models be included? 5) Should the technology and tool development RFA include computational tools at the program's outset, or should that be a later emphasis, once epigenomic data began to be generated?

These issues were resolved in part through discussion with the OD, in consultation with a small group of IC Directors, and in part through a democratic voting process within the Working Group. Discussion with the OD and IC Directors led to a focus on human cells for the entire program and to a focus on normal/healthy cells for the Mapping Centers. It also led to the agreement to allow the Mapping Center Steering Committee (made of PIs and NIH staff), in consultation with an external panel, to determine the most appropriate cells for analysis. A vote within the Working Group led to a decision to defer a focus on computational tool development to 2010.

The Working Group noted that establishing an engaged group of individuals for the ESP was critical. This required some adjustment to original panel membership. The group also noted some challenges with PI lack of flexibility and cooperativity. As PIs enter large community resource-producing consortia, it may take time for the collective goals to be recognized as a top priority. Early emphasis on these goals may be helpful.

### Scientific

The Working Group indicated two current pressing roadblocks: 1) Poor ability to functionally manipulate the epigenome; and 2) challenges developing ways for novel mining of Roadmap Epigenomics program data.[4] The first roadblock has been addressed with the Functional Epigenomics Initiative (Initiative 6 above). The second has been addressed with a recent funding announcement designed to assist investigators in proposing computational analysis to take advantage of the reference epigenomes that are published.[10]

## Selected Outputs Through 2013

Initiative 1: To develop reference epigenomic maps in human cells and tissues, including human embryonic stem cells, and to generate antibodies for epigenomics research

- Year 1 and 3 milestones met, with 70 Class 1, 2, or 3 Epigenomes completed to date
- 64 publications since program inception
- A package of more than 20 papers including a high profile integrative manuscript describing at least 70 epigenomes is being submitted to *Nature*. It is anticipated the papers will be published in Nature or the Nature family journals.

Initiative 2: To determine if epigenomic changes happen in multiple diseases and conditions and to strengthen IC support for research into the epigenetic basis of disease

- 22 applications were awarded under the "Epigenomics in Health and Disease" RFA[17]
- 89 publications since program inception

Initiative 3: To identify types of data and develop standard data formats, to provide bioinformatic support for data analysis and integration, and to disseminate and store data via the NCBI public interface

- The Genboree Workbench as well as all of its associated tools and software have now been installed at IHEC's data centers in Tokyo and Vancouver
- The GEO database staff has processed 682 new experiment records from the Roadmap project
- An article describing new features and recent updates in the NCBI Epigenomics Resource was published in *Nucleic Acids Research* and was included in the most recent database issue
- Increased usage of the Epigenomics Resource dramatically, with web analytics and log analysis showing an increase of roughly 60 percent in site usage in 2013 compared to the previous year
- 16 publications since program inception

Initiative 4: To develop new revolutionary epigenetic technologies including remote imaging of epigenetic activity in cells/tissues and whole animals

- Five R21s and four R01s were funded in 2008
- 60 publications have been produced citing the funded R21 or R01 grants. 13 of the publications from the R21 grants have been cited at least 10 times, with one cited 118 times

Initiative 5: To identify new/novel epigenetic marks

- Approximately 70 new histone PTMs have been identified in human cells, increasing the current number of known histone marks by about 70 percent
- 58 publications since program inception

Initiative 6: To develop technologies and research tools to enable functional cell-type, temporal, or locus-specific epigenomic manipulation and potentially provide a foundation for developing new epigenome-based therapeutics. Ten R01s were funded in 2013.

- Initiative too recent to have reported outputs

**Notable Reported Outcomes**

A landmark paper in *Science* was published showing that the majority of disease associated single- nucleotide polymorphisms (SNPs) reside in or near regions of open chromatin in regulatory regions of DNA, indicating that these SNPs are actively regulating genes.[18]

Advances in technology development such as real time selection and analysis of methylated DNA by fluorescence-activated single molecule sorting in a nanofluidic channel.[5]

As a part of the Roadmap Epigenomics program Mapping Consortium, researchers in the Ecker lab adapted their MethylC-Seq assay and applied it to two different human cell types, generating the first genome-wide single base resolution maps for any human cell type. [19] Since that time, the

use of this and related assays for interrogating DNA methylation state have become widespread. As of August 31, 2013, this paper has been cited 865 times.[3]

As part of the IHEC Metadata and Data Standards Working Group, EDACC has produced a metadata standards document that has now been adopted as an IHEC standard, and is presented as such on the IHEC website.[20] It is expected that all projects that are part of IHEC, and any project that would like to submit data to the Consortium, will use these standards.[4]

**Transition Out of the Common Fund**

The Epigenomics program requested funding for eight years. Five initiatives were proposed initially and a sixth was added (i.e., Functional Epigenomics) in 2013. The initiatives were on different funding cycles. The Working Group noted that if all 2012 funds were not expended, some of the Mapping Centers would go into no cost extensions, and that future funding might come through the work with the ENCODE program. A Memorandum of Understanding (MOU) developed in 2011 also established the responsibilities for the NCBI to serve as the long term data archive for the epigenomics data. The EDACC is being supported until July 2014 to ensure any data generated by the Mapping Centers is appropriately deposited in NCBI. The project team published a FOA using FY 2014 and 2015 funding re-budgeted from the EDACC and NCBI, RFA-RM-14-001 Computational Analyses Exploiting Reference Epigenomic Maps (R01).[10, 5]

**References:**


1. IHEC Goals, Structure, Policies & Guidelines, December 1, 2011
2. Roadmap Retreat 2007 Summary, Epigenetic Excerpt
3. Book Chapter. "Technologies and Community Resources Developed through the NIH Roadmap Epigenomics Program" by Dr. John S. Satterlee et al.
4. Common Fund FY 2013-2014 Annual Progress Report
5. Common Fund FY 2012-2013 Annual Progress Report
6. Epigenomics FOA Website: http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-12-026.html
7. Epigenomics FOA Website: http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-09-016.html
8. Epigenomics Detailed Plans 08-13-2007
9. Email from Dr. Betsy Wilder to EWG Dated January 27, 2011
10. Epigenomics FOA Website: http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-14-001.html
11. Process Evaluation of the NIH Roadmap Epigenomics Program, December 16, 2011
12. ESP Recommendations from November 2010 SC Meeting
13. ESP Recommendations from May 2011 SC Meeting
14. Roadmap Epigenomics Website: http://www.roadmapepigenomics.org/data
15. Response to ESP Recommendations from May 2010 SC Meeting
16. Common Fund FY 2010-2011 Annual Progress Report
17. Epigenomics FOA Website: http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-08-017.html
18. Common Fund FY 2011-2012 Annual Progress Report
19. Lister et al. 2009. Human DNA methylomes at base resolution show widespread epigenomic differences. *Nature*, 315-322, Volume 462 [November].

20. IHEC Recommendations for Epigenomic Analysis Website: http://ihec-epigenomes.net/research/operating-procedures/

## Appendix 22: Description of Common Fund Evaluative Processes

This document pertains to Management/Oversight Question II, "Are evaluative processes sufficient to provide critical assessment throughout the program's lifespan?" It describes the processes that the Office of Strategic Coordination (OSC) uses to monitor the progress of Common Fund (CF) programs and provides information for Working Groups on how to measure program effectiveness.

Sections A & B describe standard ways that each Common Fund program is regularly assessed. Section C contains guidance that OSC provides to each Working Group to help them understand the importance of and plan for additional evaluative activities.

### A: Annual Progress Report

The Office of Strategic Coordination (OSC) asks each Common Fund Working Group (WG) to complete an annual progress report at the start of each fiscal year. The purpose of the report is to track the progress of the program, explain any issues that WGs encountered, and propose plans for the upcoming fiscal year. The template for the progress report is sent to WGs in early October. WGs have approximately four weeks to prepare and submit the report.

The annual progress report provides WGs an opportunity to:

- Review their goals and milestones and discuss the program with their OSC Program Director (PD)
- Describe progress and challenges in meeting goals and milestones in the past year
- Articulate plans for the coming year
- Describe any issues encountered in the management of the program (including those encountered by the principal investigators)
- Report on emerging issues in the field that their program supports and whether the program should be modified to respond to those emerging issues
- Communicate new tools or publications produced through their program
- Update WG membership or leadership
- Describe any new requests for additional funds or supplements

Annual progress reports are submitted in conjunction with the annual operating budget requests. Therefore, any major requests to modify or add funds within the program's operating budget are described in the annual progress report.

The annual progress report is developed through conversation with the OSC PD, who reviews the document first and may ask the WG to clarify certain sections. The reports are then reviewed by the OSC Director and the Director of the Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI), who may approve the WG's proposed plans as submitted or may approve with modifications. If concerns are raised or if substantial changes are proposed, OSC/DPCPSI generally meets with the WG leaders prior to finalization of the annual budget. If all additional information is submitted as requested, WGs should expect to receive approval for their plans in December.

### B: Site Visits

Common Fund Working Groups may conduct site visits to better understand the context in which the program is being implemented. Questions that are addressed by site visits typically require assessment of the adequacy of the physical environment and/or access to resources and equipment. They typically also assess local collaborative interactions and institutional commitment to the project. For some programs, advance site visits are done prior to award.

## C: Measuring the Effectiveness of Common Fund Programs

### C1: Why is Measuring Effectiveness Important?

Every CF WG should be concerned with the effectiveness of its program. Understanding the program's effectiveness helps to answer the following questions:

- Is the program on track to meet its goals?
- Should NIH move funding from one group of grantees to another group of grantees or from one initiative to another?
- Should NIH change how it structures the scientific review or funding terms for future Funding Opportunity Announcements (FOAs)?
- Is the initiative focused on the most pressing scientific needs?
- How much has the field grown since the program started?
- Do the right people know about the tools that have been developed and are they using them?
- Are the outputs of the program (e.g., knowledge generated, services, products of research) being disseminated?
- To what extent have the capacity building efforts been successful (e.g., trained researchers, infrastructure development, and expansion into new fields and integration into existing ones)?

WGs that are actively thinking about these issues are able to adapt to change, track their progress, and demonstrate their success. Not only are these actions fundamental to program management, they also position the program to receive continued support from the Common Fund or other sources.

### C2: What Are the Ways to Measure Effectiveness?

There is no one-size-fits-all approach to measuring effectiveness. Different programs need different approaches at different points in their lifecycle. Typically, conducting a very simple evaluative activity (survey, panel, etc.) may be all that is needed.

Examples of evaluative activities include:

- User feedback survey, request for information, questionnaire, social media discussion
- Interview, focus group, external panel, workshop, meeting
- Literature review, portfolio analysis, bibliometric analysis

Occasionally, a WG may need to conduct an evaluation of an entire program or some of its components. A program evaluation is a systematic study conducted periodically or on an ad hoc basis to assess how well a program is performing. It involves the collection of information about the activities, characteristics, and results of a program. It is often conducted by experts external to the program as well as by program managers.

Common types of evaluations are as follows:

- ***Assessment of Needs, Gaps, and Opportunities****:* In the planning or early implementation stage of a program, the purpose of this evaluation is to assess the magnitude of the need and identify gaps in knowledge, services, products of research (e.g., tools, technologies, etc.), training, and resources. Later during program implementation, the purpose is to determine if there is a need to extend the program beyond its originally funded period, to update the baseline in response to changes in external influences, and to determine if the community is satisfied with the services and outputs of the program.
- ***Process Evaluation:*** This form of evaluation assesses the extent to which a program is operating as it was intended. It typically assesses program activities' conformance to statutory and regulatory requirements, program design, and professional standards or customer expectations. Programs that are trying a new funding mechanism will typically conduct a process evaluation.
- ***Outcome Evaluation*****:** This form of evaluation assesses the extent to which a program achieves its outcome-oriented objectives. It focuses on outputs and outcomes (including unintended effects) to judge program effectiveness but may also assess program process to understand how outcomes are produced.
- ***Impact Evaluation:*** Impact evaluation is a form of outcome evaluation that assesses the net effect of a program by comparing program outcomes with an estimate of what would have happened in the absence of the program.

The OSC PD works with the WG to determine the evaluative activities a program should undertake. Being proactive in planning for evaluations helps to ensure that baseline data are collected early so that the impact can be assessed more effectively. It also helps to ensure that measurable goals are established.

**C3: When Should an Evaluation Activity Be Conducted?**

***During Strategic Planning***

Evaluation planning should be done in tandem with the initial strategic planning to create the program. WGs can begin by conducting an activity to determine the baseline data for the program. The baseline indicates the state of the field of research is at the start of the program. WGs can use this data to set goals for the program and its initiatives. Next, WGs can develop milestones which will describe the steps to take to reach the programmatic goals. While doing this, WGs should consider the questions that will need to be answered at each step throughout the program lifecycle and determine the appropriate evaluative activities needed to inform those answers.

The program initiatives need to connect to the goals in some logical way. Each RPG, contract, or training award needs to support an overarching goal either at the initiative or program level. The goals of the program/initiative must be clear to potential grantees from reading the FOAs, or RFPs. The funding announcements should also state both the expected milestones and reporting requirements for grantees.

***When the Program "Continues" or "Ends"***

If the WG is planning to request a continuation of funding beyond the initial funding period, they must complete the continuation template and status report. As the program comes to an end (typically after five or ten years), the WG must complete a program close-out report. To complete these packages, OSC anticipates the WG will conduct evaluative activities and/or

compile data that has been gathered during the program. The WG works closely with their OSC Program Director to get feedback on which questions should be addressed as part of this process. For more information on the continuation process or program ends process, see the "Requesting Continuation of a Common Fund program" or "Program Ending" sections, respectively.

***When it Supports the Goals of the Program***

Most evaluative activities for a program are planned at the discretion of the WG. They should be planned to occur whenever the WG feels the activity will support its goals. Most frequently, this takes the form of informal evaluation through external scientific panels that provide input as the program is implemented.

***When Required by OSC***

Only occasionally will OSC *require* that an evaluation be conducted for a program. Each year OSC considers how each program is affected by factors such as Presidential/Congressional interest, NIH Director's priority, visibility, budget size, plans for scale-up, performance, design/structure, need, and awareness. If a program is affected by any of these factors, OSC will let the WG know that an evaluation will be expected. For example, if there is a highly visible program with a large budget that is planning to scale-up and is a priority for Congress and the NIH Director, an evaluation may be required to discern any issues and plan a path forward. As always, the form this evaluation may take would vary based on the questions that need to be addressed and the data that are already available.

**C4: Logistically, How is an Evaluation Activity Conducted?**

As mentioned earlier, planning is essential. A WG must have an idea of the questions that need to be addressed, when they should be addressed, and the type of evaluative activity that will help answer those questions.

Based on the depth of the review/assessment necessary, the use of existing data vs. collecting new data, the sample size for surveys or interviews, and the type of data analysis, some activities may be conducted in house by NIH staff and some may be contracted out. Activities that are more detailed, that need more time, that require substantial collection of new data, and that require a deeper (often statistical) analysis are usually conducted by a contractor with specialized evaluation expertise.

## Appendix 23: Examples of Program Changes in Scientific Landscape

This document pertains to Management/Oversight and addresses Question IV: "Are management processes flexible and adaptive to changing scientific landscapes?" Five programs are discussed in this document. The changes took the form of additional funding for new initiatives or continue funding for Phase II to address changes in the field, allow data to be accessed more easily, or validate earlier results.

***Epigenomics***

The program originally had five initiatives. A new initiative was added in FY13 to address challenges that arose during the tenure of the program concerning epigenetic manipulation. The initiative sought to develop novel tools and technologies to enable: 1) tissue or cell-specific manipulation of epigenetic modifications or their effector molecules; 2) temporal manipulation of the epigenome; 3) locus-specific manipulation of the epigenome; and/or 4) novel approaches that enable any combination of the previous three goals. This sixth initiative was developed to address the fact that manipulation of the genome largely relied on pharmacological or genetic manipulation of epigenetic regulatory proteins and that more precise temporal, spatial, or locus-specific manipulation of the epigenome remained problematic.

***Human Microbiome* Project**

At the end of Phase I, NIH leadership decided to build upon the opportunities the first phase results had provided by supporting the program for three more years with a more focused initiative. A new initiative was added for phase two of the program. This initiative was to create a community resource that can be used to decipher the role of the microbiome in human health through: (1) acquiring multi 'omic types of data from a well-phenotyped human cohort studies, (2) defining practices for sample collection that support multi-omic analyses, (3) making these data available to the broad community through appropriate databases, and (4) improving upon all of these methods and protocols.

***PROMIS***

In Phase II of the program, and in response to the conclusions of an expert review panel, the PROMIS Working Group requested applications for clinical validation studies. These studies were necessary to demonstrate the utility of PROMIS in the clinic to before clinical researchers adopted PROMIS.

***Molecular Libraries***

In 2013, six of the MLPCN centers launched the new BioAssay Research Database (BARD) to enable scientists without specialized training to effectively utilize data to answer complex cross-cutting target and cross-compounding questions. BARD allows mining of data on more than 35 million compounds, 4,000 assays and over 300 probe projects. This allowed scientists to efficiently develop and test hypotheses on the influence of different chemical probes on biological functions.

***Single Cell Analysis***

Single Cell Analysis released an FOA in 2012 to support high innovation–high impact efforts in single cell analysis technology development, which was a shift from the clinical emphasis

originally planned. Upon further consideration by the Working Group, the original plan to have a clinical emphasis was considered premature.

---

*Programmatic adjustments are possible each year because the overall budget envelope for each program is considered flexible.

## Appendix 24: Intramural Research Program – Management

This document pertains to Management/Oversight Question V, "What should the process be for management of intramural-only programs?"

Most Common Fund (CF) award solicitations are open to applicants from all organizations, including the NIH Intramural Research Program (IRP), with the goal of supporting the best science regardless of where the research is conducted. In these programs, IRP projects are subject to the same planning, application, review, and oversight processes that are used for extramural awardees.

In certain cases, funds have been allocated to intramural investigators without competition. This document provides context for these initiatives and summarizes management strategies. As with all CF program management, communication of goals, expectations, and progress is critical. The specific challenge for IRP-only projects involves establishing clear communication channels in the absence of standard processes that typify extramural program management. This communication challenge has been addressed in varying ways, as described below.

**Gulf Long Term Follow-up (GuLF) Study:**
The GuLF study was initiated in response to the oil spill from the Deepwater Horizon explosion in 2010. The goal of the study was articulated by the NIH Director and demanded rapid implementation and coordination with many federal agencies and other entities.[1] The coordination of this effort with many related activities at the NIH and elsewhere involved frequent meetings between OD staff, NIEHS leadership, other federal agencies, and the NIEHS IRP leader of the GuLF study. A Working Group of the NIEHS Board of Scientific Counselors was established to provide ongoing oversight, and the DPCPSI Director was directly involved in monthly meetings. This communication strategy ensured that the goals and expectations of internal leadership and external advisors to the study were well aligned, and that all parties were kept apprised of challenges and progress. This facilitated budget management from year to year, since OSC/DPCPSI was well aware of the causes of delays and the capacity to advance in subsequent years.[2,3]

**PubChem (2004):**
PubChem originated as the Molecular Libraries (ML) program's publicly available, central repository for organic molecule chemical structures as well as those acquired by the ML Small Molecule Repository initiative and probes generated by optimization of hits in assays screened by the ML centers. Discussions between Dr. Elias Zerhouni and NIH IC Directors prior to the ML launch identified the National Center for Biotechnology Information (NCBI) at the National Library of Medicine (NLM) as being uniquely positioned to design and manage a central database of chemical structure and biological assay activity information as a key component of

the ML CF program and to "link out" to numerous internal (e.g., NCBI's PubMed and ChemID) and external databases. The Molecular Libraries and Imaging Implementation Group (MLIIG) outlined these PubChem initiative goals in its 2003 Implementation Plan.[4] NLM's Dr. Steve Bryant served as the principal investigator for PubChem. Dr. Bryant interacted with other ML initiatives in various ways, such as attending regular meetings of the ML Working Group, monthly meetings of the ML Steering Committee, and periodic meetings of the PubChem Working Group. The ML Steering Committee and PubChem Working Group meetings included external experts who provided feedback on issues of importance for implementing PubChem as a resource for the chemical biology research community. While the ML Working Group did not have direct oversight, these meetings served as a valuable opportunity for Dr. Bryant to discuss acquisition, curation, and categorization of biological data as well as issues related to mining the chemical biology data, all of which were key components of the PubChem initiative. Feedback was also garnered through a 2006 Mid-Course review conducted by an expert panel and a 2009 ML "Needs Assessment" that incorporated customer satisfaction surveys.[5,6]

As an IRP investigator, Dr. Bryant was also subject to the review of NCBI's Board of Scientific Counselors. PubChem was very successful, with >60,000 daily users of the chemical structure and growing inventory of biology data, and uses and goals reaching well beyond the initial goals established through the ML Program. The BSC review of PubChem was separate from the ML program oversight, with the eventual result that plans for PubChem diverged from the ML-established goals. NCBI ultimately committed to future support and management of PubChem, while the ML program established a separate database for a biology-friendly user interface – the BioAssay Research Database (BARD.)

**Imaging Probe Development Center (IPDC, 2004):**

A second ML component, IPDC, was established as an NIH intramural core facility that would provide imaging probes not available through a commercial supplier, generate novel imaging probes (e.g., optical, PET, SPECT, and MRI) and serve as counterpoint to extramural initiatives (P20 RFA; R21 RFA) focused on improving probe detection sensitivity 10x – 1000x. In addition, the IPDC planned to expand its probe services to the ERP following a successful IRP pilot phase.[4]

The ML Implementation WG recommended hiring a senior synthetic chemist to serve as IPDC Director who, in turn, would serve on a governing Steering Committee populated with representatives from participating ICs. The center director, Dr. Gary Griffiths, was not hired until late 2005 and the facility was not finished until the Fall of 2006. This hiring process was overseen by members of the Working Group who had developed the initial vision for the IPDC; they left the NIH and/or the Working Group by 2007. Dr. Griffiths served on an IPDC Steering Committee that also included 14 IC representatives whose ICs utilized the IDPC. In addition to the monthly Steering Committee meetings, Dr. Griffiths attended the ML Working Group

meetings which served as his opportunity to understand the goals of the larger program and to interact with leaders of the program.

In preparation for the 2009 CF Mid-Course review, the OSC and the ML Working Group began to assess the IPDC's progress. It became clear that goals for the IPDC had not been clearly communicated to Dr. Griffiths.[9] This seemed to be the result of an exit of the individuals who had developed the vision for the IPDC and the transfer of oversight to individuals who were disconnected from the overarching objectives of the ML program. The review panel recommended major managerial and organizational changes within the IPDC.[9] Several of these modified objectives were at odds with the IPDC Steering Committee and Dr. Griffith's Board of Scientific Counselors. Support for the IPDC was not renewed, and transition from the CF to intramural funding occurred in FY2011.[10]

**Re-Engineering the Clinical Research Enterprise (CR) – Clinical Research Training Program (CRTP):**

The Roadmap Re-engineering the Clinical Research Enterprise program began as a series of eight complementary initiatives that were intended to transform clinical research. The program had a significant emphasis on training physician scientists for clinical research.[11]

The training component of this program initially included multiple extramural training and career initiatives. It also included support for the CRTP – an extant training program within the IRP that supported 15 medical or dental students for a one year clinical or basic research fellowship at the NIH. In 2004, the CRTP was expanded by Roadmap/CF funding to double the number of trainees each year from 15 to 30.[12] The NIH Clinical Center and NIH Office of Intramural Research continued to oversee and manage the CRTP as established prior to CF involvement.[13] In addition, a Board of Tutors composed of NIH physicians reviewed applications, interviewed applicants, ultimately placed the selected CRTP fellows in clinical and/or translational research teams, and provided career and academic advisement during the fellows' 12-month term.[14]

In 2010, the OSC began to interact with the CRTP through the CF annual progress report process. A CRTP transition plan became an increasing concern as the end of CF support approached.[14,15] In FY2012, the CRTP was re-branded as the Medical Research Scholars Program (MRSP) as it merged with a related program that had formerly been supported by the Howard Hughes Medical Institute.[16] Oversight of the new program expanded to include an Executive Advisory Committee, composed of 18 Board of Tutors members, tasked with reviewing program objectives and progress, and providing final approval of selected applicants. An evaluation of the CRTP/MRSP conducted by the program's leader shows that over 40% of trainees remain in research career paths. The CF supported the new MRSP by committing funds until FY2015 to enable partnerships with external funding sources to be established.

**Epigenomics – Data Management (2007):**

The CF Epigenomics Data Management Center (DMC) was created specifically to provide public access to the data generated by the Epigenomics Program and epigenomic data generated by other sources.[17,18] NCBI was asked to develop and implement this publicly accessible, long-term data repository in support of the international epigenetics research community. The DMC worked closely with the Epigenomics Data Analysis and Coordinating Center (EDACC) to address user needs, issues and requests through tool development, creation of data standards, extensive modifications to the website user-interface (e.g., YouTube tutorials, integration with the ENCODE database), and quarterly progress reports to track data usage by the scientific community. Epigenomics Working Group members served on a sub-Working Group managing this initiative with additional guidance provided by a Steering Committee.[17] In addition an External Scientific Panel (ESP) reviewed NCBI's progress annually.[19, 20, 21]

The ESP and the Working Group identified the creation of a user-friendly Epigenomics Interface as a key need, but an oversight mechanism was not in place to ensure that this new goal was met by the DMC. Ultimately, two administrative supplements were issued to create data mirror sites at UCSF and UW in FY2010.[22] Funding levels for the DMC were subsequently reduced.[23] To improve communication and establish firmer expectations about shared goals, an MOU between NCBI, the National Institute of Environmental Health Sciences (NIEHS), the National Institute for Drug Abuse, and the OSC was implemented in 2012.[24] The MOU shifted governance of the NCBI Data Management Center to the Epigenomics Working Group through FY2013 (or subsequent annual renewals) and redefined NCBI's role within the Epigenomics program.

**NIH Center for Regenerative Medicine (NIH CRM, 2010):**

As part of Dr. Collins' vision for translational medicine and in response to the opportunities provided by induced pluripotent stem cells (iPSCs), the CRM was established within the IRP to identify and overcome the translational challenges for iPSC therapies.[25] The CRM was designed to support and fund iPSC research and collaborations between NIH ICs and the extramural community. In addition, the NIH CRM Director was expected to address procedural and policy issues associated with stem cell therapy development, working closely with the FDA to facilitate regulatory clearances.[25] Recruitment of a Director was led by two IC Scientific Directors, with input from the DPCPSI Director. Pilot projects were begun to establish a critical mass of stem cell investigators within the IRP, and an NIH Stem Cell Interest Group was formed. An Oversight Committee, consisting of the DPCPSI Director, the Director of the NIH IRP, and the Directors of NIAMS and NINDS, was established to provide broad guidance to the CRM.

A Director for the CRM was appointed in 2011. He developed plans and presented them to the Oversight Committee and requested monthly meetings with this group. He also established an external panel to provide general input about CRM activities. Goals were fluid and encompassed broad stimulation of IRP stem cell research as well as supporting research that aimed at clinical applications of iPSCs.[26,27]

OSC convened an external scientific panel in 2012 to review the plans for CRM and help establish priorities.[28] Using this input, the Oversight Committee and the CRM Director agreed that the majority of CRM funds would be used to support IRP Translational Challenge Projects. The expectation was that the CF would launch these projects, but the relevant IC would be required to commit to future year support for clinical studies. OSC organized an external peer-review process for these applications. One was selected for support.[29,30]

As the CRM moves into a new phase, the Translational Challenge awardee will report annually to OSC on progress toward stated aims. He will have the flexibility to follow the science within a framework of defined translational milestones that must be met for future support. OSC is also working with NCATS and extramural program officers to prioritize recommendations from external groups concerning translational barriers to iPSC therapies and developing a strategy to address these.

## References


1. Gulf Annual Progress Report FY 2010-2011
2. Gulf Annual Progress Report FY 2011-2012
3. Gulf Annual Progress Report FY 2013-2014
4. Roadmap Molecular Libraries and Imaging Implementation Group (MLIIG) – Implementation Plans (9/2003)
5. The Molecular Libraries and Molecular Imaging Program – A Component of the NIH Roadmap for Medical Research(7/2008)
6. Needs Assessment of the Roadmap Molecular Libraries Program – Executive Summary (2009)
7. Common Fund Program FYs 2012-2013 Annual Progress Report (11/2013)
8. DHHS Memorandum of Understanding – NCBI, NLM, NIMH, NHGRI, DPCPSI (7/2011)
9. NIH Imaging Probes Development Center – Mid-Course Review Report (4/2009)
10. Common Fund Program FYs 2010-2011 Annual Progress Report (11/2010)
11. Common Fund Fiscal Year 2012 Congressional Justification
12. Re-Engineering the Clinical Research Enterprise – 909: Enhance CR Training via the National Multi-disciplinary Clinical Research Career Development Program, and CRTP and MSTP Expansions (2004)
13. Submission of New Roadmap Programs – NIH Clinical Research Training Program for Medical and Dental Students (2/2008)
14. Common Fund Program FY 2010-2011 Annual Progress Report (11/2010)
15. Common Fund Program FY 2010-2011 Annual Progress Report and Operating Budget Summary (11/2010)
16. Common Fund Program FY 2011-2012 Annual Progress Report (11/2011)

17. Epigenomics Program – Epigenomics Working Group Program as a Whole (7/2007)
18. RM Epigenomics Program – Epigenomics Working Group Program as a Whole (8/2007)
19. Executive Summary, Roadmap Epigenomics Program, NIH – External Science Panel (ESP) Recommendations for the Roadmap Epigenomics Mapping Centers (REMC), Epigenomics Data Analysis Coordinating Center (EDACC) and the National Center for Biotechnology Information (NCBI) (11/2009)
20. ESP Recommendation for NIH Reference Epigenomics Centers (5/2010)
21. ESP Recommendations - Epigenomics (5/2011)
22. Response to ESP Recommendations from May, 2010 Steering Committee Meeting (2010)
23. Annual Progress Report and Operating Budget Summary – Epigenomics (11/2010)
24. DHHS Memorandum of Understanding – NCBI, NLM, NIEHS, NIDA, and OSC/DPCPSI (1/2012)
25. NIH iPS Cell Center FY2010 Funding Plan (2010)
26. Common Fund Program FY 2011-2012 Annual Progress Report – NIH Center for Regenerative Medicine (11/2011)
27. Common Fund Program FY 2012-2013 Annual Progress Report – NIH Center for Regenerative Medicine (11/2012)
28. Common Fund External Consultants for NIH Center for Regenerative Medicine Meeting (9/2012)
29. NCRM-NOT-RM-12-008 RFI
30. The NIH Common fund and Center for Regenerative Medicine (NIH CRM) Therapeutic Challenge Program (3/2013)