

The NIH Bench-to-Bedside Program: A Second Review, 2006-2009

Charles R. Sherman, Ph.D.
Program Evaluation Consultant
December 2010

Abstract

Since 1999, the NIH Clinical Center has worked to promote health by encouraging meaningful research collaborations between bench scientists and clinical investigators. The Bench to Bedside Program award competition provides incentives for such collaborations. Initially, the awards were made only to NIH intramural staff. In 2006 the program extended to allow collaborations between intramural and extramural investigators. This report summarizes the findings of a voluntary survey of intramural lead investigators on 48 projects that were awarded funds between 2006 and 2009. Enthusiasm for the B2B Program is strong, but the timing and timeliness of fund transfers are persistent problems for some projects. Principal Investigators report that research productivity has been improved because of the basic-clinical collaborations, but more so for the clinical investigators. There are numerous benefits of intramural-extramural partnerships, but the difficulty of human protocol clearance may be multiplied.

Background

Program and goals

Since 1999, the NIH Clinical Center has worked to promote health by encouraging meaningful research collaborations between bench scientists and clinical investigators. The Bench to Bedside Program award competition provides incentive for such collaborations. Initially, the awards were made only to NIH intramural staff.

Changing emphasis

In 2005 the program extended its offering to allow some collaborations between intramural and extramural investigators. There was an enthusiastic reaction, reported in the first program evaluation.¹ The intramural-extramural component of the program has been expanded. From 2006-2009, approximately ninety percent of funded projects involved an extramural partner.

¹ Sherman, C.R., "A Quantitative Assessment of the NIH Bench-to-Bedside Program: Accomplishments of the First 100 Projects" available on-line at http://www.cc.nih.gov/ccc/btb/pdfs/2008_quantitative_assessment.pdf

Projects per year

In the first twelve years of the B2B program, 176 projects have been supported. Table 1 displays the number and cumulative number of supported projects per year. The number of projects with extramural collaborators each year is also displayed.

Table 1. Number of Bench-to-Bedside projects supported			
Year	New Projects	Cumulative Projects	Projects with Extramural Partners
1999	8	8	0
2000	9	17	0
2001	9	26	0
2002	6	32	0
2003	13	45	0
2004	19	64	0
2005	17	81	1
2006	19	100	15
2007	19	119	16
2008	16	135	13
2009	17	152	16
2010	24	176	22

Method of current review

Survey design, returns from October 2009 to July 2010

In October 2009, a very brief survey was e-mailed to the lead intramural Principal Investigator (PI) of all 71 projects that were awarded in the years from 2006 through 2009. A copy of the survey instrument is provided in Appendix A. Of the 71 projects, 60 were intramural-extramural collaborations

Response rate

Responses were received from 48 (67.6 percent) of the 71 projects. All lead Institutes and Centers (ICs) reported at least 50 percent of their projects. Of the 60 intramural-extramural collaborative projects, 39 (65 percent) responded.

Limitations

The survey provided information about only the lead intramural investigator and the lead extramural investigator (if there was one). Researchers from other ICs and additional extramural hospitals and research centers were involved in many of the projects, but their views are not enumerated here.

Majority of projects not yet finished

It should be noted that over three fourths of the projects reporting indicated that they are “not yet completed”. Many are at various stages of planning, IRB review, patient recruitment, data analysis, publication or following new directions. Therefore it is difficult to gauge the outcomes that will be eventually attained.

B2B Program by the numbers, 2006 to 2009

Funding

The amount of funds solicited from sponsors and awarded by the B2B Program is not a topic of this (or the previous) evaluation study. The numbers of applications and awards and the competition success rates are available from the Bench to Bedside Program Office in the Office of the Director, NIH Clinical Center (BenchtoBedside@cc.nih.gov).

Institutes and Centers and Extramural Institutions

Thirteen ICs provided lead intramural PIs for the 71 B2B projects from 2006 through 2009. Table 2 presents the numbers of PIs in each IC.

Table 2. Number of B2B project lead investigators from each participating IC

NHLBI	17
NIAID	13
NCI	12
NIDDK	7
NICHD	7
NINDS	4
NIDCR	3
NIDCD	2
NHGRI	2
NIDA	1
NINR	1
NIMH	1
CC	1
TOTAL	71

Researchers at the following extramural institutions collaborated on B2B projects as co-principal investigators (number of projects also shown):

Abuth, Zaria Nigeria	Inova Fairfax Hospital (2)	University of Maryland (2)
Boston University	Johns Hopkins University (2)	University of Michigan
Case Western Reserve	M.D. Anderson Cancer Center	University of Minnesota
Children's National Medical Center	Medical University of South Carolina	University of Pennsylvania
Cincinnati Children's Hospital Medical Center	Memorial Sloan-Kettering Cancer Center	University of Pittsburgh (2)
Food & Drug Administration	Uniformed Services University of the Health Sciences	University of South Carolina School of Medicine
Fred Hutchinson Cancer Research Center (2)	Oregon State University	University of Toronto (2)
Hackensack University Cancer Center	Sackler School of Medicine, Israel	University of Virginia
Harvard School of Public Health	San Francisco General Hospital, UCSF	University of Washington
Imperial College, London	St. Michaels Hospital, NJ	University of Wisconsin
	SUNY Downstate Medical Center	Washington Hospital Center (2)
	Tufts University	

As noted above, other investigators from these and other ICs and extramural institutions participated in the 71 B2B projects funded during the four-year study review period.

Lead Investigators and partners

Degrees

The B2B program encourages collaboration between clinical investigators and bench scientists, typically someone with a clinical degree (e.g., M.D) and a science degree (e.g., Ph.D.). The previous evaluation found that the degree distinction was not closely correlated with the research role played by the investigator. But the simple pairing of intramural and extramural co-PIs may be of interest to some. Twenty-one of the 48 projects paired co-PIs with clinical and science degrees. Seventeen paired two with only clinical degrees, two pairs had only science degrees, and one project had intramural and extramural collaborators both holding doctorates in pharmacology.

Research Categories

Bench-to-Bedside projects are categorized by the NIH administrative units that provide funding in support of their research missions. The NIH Office of Rare Diseases, Office of Research on Women's Health, Office of AIDS Research and Office of Minority Health and Health Disparities have provided the most funds. There is also a "General" category indicating funding from ICs or other sources. Some projects are co-funded by several administrative units. The number of projects supported whole or in part in each category are shown in Table 3.

**Table 3. Research Categories, Frequency of 71 B2B Projects ²
2006-2009**

Rare Diseases	30
AIDS	16
Minority Health	14
General	7
Women's Health	4
Pharmacogenomics	2
Behavioral and Social Sciences	1

Clinical-Basic Collaborations

All B2B lead-PIs were asked to rate several qualities that might vary between projects.³

Satisfaction

There was fairly uniform satisfaction with the collaboration between clinicians and basic scientists, although there was greater satisfaction among the PIs with MD degrees; they were likely to rate their collaborations "excellent." Those with MD-PhDs or PhDs were much more likely to rate their qualities of collaboration as just "satisfactory", but "excellent" was the modal rating of the following attributes:

² Three projects were counted in two separate categories.

³ The attributes of collaboration satisfaction and impact were adapted from Masse, L., Moser, R., et al., "Measuring Collaboration and Transdisciplinary Integration in Team Science", *Am J Prev Med*; 2008; 35 (2S): 151-160.

- Acceptance of new ideas (75% “excellent”)
- Communication among collaborators (73% “excellent”)
- Ability to capitalize on the strengths of different researchers (73% “excellent”)
- Organization of structure of collaborative teams (69% “excellent”)
- Resolution of conflicts among collaborators (73% “excellent” & 5% reported “no conflict”)
- Ability to accommodate different working styles of collaborators (77% “excellent”)
- Involvement of collaborators from outside the center (73% “excellent”)
- Involvement of collaborators from diverse disciplines (72% “excellent”)

Several commented that there “were no conflicts” to resolve. Some confused basic-clinical collaboration with intramural-extramural collaboration.

Impact

The attributes of collaboration impact that were assessed are:

- Productivity of collaboration meetings
- Productivity in developing new products (e.g., papers proposals, courses)
- Overall productivity of collaboration
- In general, collaboration has improved your research productivity
- In general, collaboration has improved the quality of your research
- Collaboration has posed a significant time burden in your research

While the formatting and wording of the questions and response alternatives were not always clear, the meaning was probably clear, and the benefit of collaboration was generally perceived by all 48 B2B investigators reporting.

However, the experience of basic scientists may be different from their clinical colleagues. The response pattern across all of the above questions indicates that productivity of *clinical investigators* was improved more by the B2B collaborations than was the productivity of *basic scientists*.

Intramural-Extramural Partnerships

Source of research idea

Of the 39 PIs with extramural collaborators who responded to the survey, only one said the idea for the research topic came from the extramural partner. Twenty reported that the idea arose intramurally. Eighteen gave credit to both intramural and extramural partners.

Finding collaborators

Only one of 39 intramural PIs reported any difficulty identifying an extramural partner. In only two cases did the extramural partner initiate the collaboration.

Continuation of working relationship

Some respondents added comments about their pride in having fostered productive partnerships. Eighty-four percent indicated their teams had continued on to other

projects, as well. Long-term relationships were solidified or started by the B2B program. Some are seeking funding opportunities to take their projects “to the next level.”

Visitations

Collaborating intramural and extramural investigators visited each other, sometimes frequently, sometimes less frequently or at appropriate national meetings. A few projects (18 percent) exchanged fellows between intramural and extramural laboratories as a result of the collaboration. For others, such an exchange had simply not yet happened. The projects stimulated sabbaticals infrequently (less than 10 percent); some institutions do not support having sabbaticals.

Student participation

A large minority (42 percent) reported that medical students participated in the B2B research.

Patient exchange

The collaborative B2B projects led to a little exchange of patients. It was slightly more likely (in less than 20 percent of projects) that extramural patients came to the NIH Clinical Center than the reverse (in less than 10 percent). It was also reported that patient samples were sometimes processed at extramural facilities. For several studies, it is too early for the exchange of patients to take place, but it is anticipated.

Difficulties

Receiving clearance from an Institutional Review Board (IRB) for approval to use human subjects can be difficult. Intramural-extramural collaborations sometimes led to the necessity of dealing with *two* IRBs.

Recruitment

Only one reporting project indicated attempted recruitment of personnel from intramural to extramural or from extramural to NIH.

Communication within team facilitated

Ninety-five percent of the PIs reported that communication with their extramural partners was facilitated by the B2B award. Getting information out of eRA Commons baffled investigators in both sites.

Awareness of NIH facilities

A large majority of PIs (86 percent) agreed that the B2B program promotes awareness of NIH and the Clinical Center’s resources.

Qualitative

The Progress Reports received from 48 intramural B2B Project PIs included many long narratives, attached papers, new protocols, and other comments and supporting materials. These are difficult to summarize, but they give a flavor of the enthusiasm with which the Program has been received and some difficulties that have been encountered and addressed. An assortment of these comments are provided, for brevity here, in Appendix B, but here is one example:

- “As a result of this B2B, a fellow has performed an entirely new analysis of immune responses in patients suppressed on antiretroviral therapy. As a result of this award, we have also completed an entirely new analysis of genetic variation upon addition of antiretroviral therapy”

Intermediate outcomes and accomplishments

It is difficult to quantify the impact of research, but numbers and quality of published articles and patents are more tangible, certain and easier to count than numbers of lives saved.

Number of new projects

Most B2B projects produced just the one B2B project, but nearly a third reported one or two additional projects stemming from the collaboration. A smaller proportion reported new research protocols emerging after the initial project. A PI from NCI signed a CRADA with Lentigen to develop lentiviral-based suicide gene therapy clinical protocols. No one reported new licensed drugs or devices or new indications for previously licensed drugs.

Publications

Forty-two projects reported a total of 48 publications, but several others have publications at various stages of preparation and review.

Invention reports, Patents, Licensing

Seven PIs (15 percent) reported filing one or more invention reports. Five have patents pending. Two have claimed patents, one for use of mTOR inhibitors in HNSCCv, and one for Lentiviral Vectors Expressing Mutated TMP.

New grants and additional funding

One-fourth of the B2B awards have led to requests for and receipt of additional funds, frequently as extramural grants.

Summary of Intermediate Accomplishments

Table 4 provides a summary of the intermediate accomplishments of 48 projects reporting by the year in which the Award was made:

Table 4: Sum of intermediate outcomes by year of award				
	2006	2007	2008	2009
# awards	19	19	16	17
# projects reporting	15	12	9	12
# new protocols	10	16	6	9
# publications	14	17	11	6
# inventions	3	3	2	1
# patents pending	2	1	2	2
# patents awarded	1	0	0	1
# new licensed drugs	0	0	0	0
# new grants & additional funding	2	4	4	4

Program Management

Call for Proposals

PIs overwhelmingly indicated that the call for proposals was clear. The time allowed was deemed “adequate” by all but one who wanted more lead time to contact the Scientific Director of the Institute.

Funding adequacy

Eighty-eight percent of the responding PIs indicated that the funding was adequate, a slightly higher proportion than in the 2006 Survey. One refrained from answering because of uncertainties stemming from an incomplete protocol review. One PI had underestimated the number of postdoctoral fellows he needed because of new genomic and stem cell technologies. In another case, the funds needed were underestimated because of the extended time needed to do a clinical trial. Another reported he relied on supplemental departmental support.

Advice to management

Open-ended suggestions

Asked for suggestions to improve the management of the B2B Program, three-fourths of the PIs offered none, and indeed several wrote praises: “Everything was smooth,” “excellent program,” etc. The other suggestions and comments are provided here:

- Expedite the IRB review process.
- Provide funds at the beginning of the fiscal year, rather than middle or end, as they must be spent before the end. There were several such comments. Because of such a delay in funds reaching the extramural collaborator, one B2B project was never initiated.
- Clinical protocols have significant delays due to regulatory issues that are not easily foreseen or controlled by PIs; consider longer award periods or other funding flexibility.
- The same investigators seem to get B2B funding year after year. Is the review fair?
- Changing employment of some PIs can cause delays.
- Delays and reviews can strengthen a project: “This program has provided a unique opportunity to develop an intramural-extramural team effort in head and neck cancer research. It involves three ICs (NIDCR/NCI/NIDCD) and MUSC in our extramural community. The development of the clinical protocol was relatively fast, though we encountered numerous issues during the IRB review process. As a result, the protocol is now much stronger than anyone of us had anticipated. We look forward to working together on a project that we expect will have a direct benefit for the head and neck cancer patients.”
- “It would be terrific to have the BTB money allocated with a distinct CAN to facilitate 1) project expenditure accounting and 2) timely allocation of extramural funds. The funds for this project were allocated over 2 years (extramural partners) and over a single year (intramural FY2010). Despite this minor drawback, this is an outstanding opportunity for young investigators at NIH!”

Conclusion

Enthusiasm for the B2B Program remains strong, but the timing and timeliness of fund transfers are persistent problems for some projects. PIs report that research productivity improved because of the basic-clinical collaborations, but more so for the clinical investigators. There are numerous benefits of intramural-extramural partnerships, but the difficulty of human protocol clearance is greater with *two* Institutional Review Boards. There was strong agreement that the B2B Program promotes an awareness of the NIH and its resources to others in the wide community of medical researchers.

Appendices

- A. Questionnaire, "Progress Report for Bench-to-Bedside (B2B) Project"
- B. Comments from Project Reports
- C. Bench-to-Bedside projects, 2006-2009

PROGRESS REPORT FOR BENCH-TO-BEDSIDE (B2B) PROJECT

Project Title	
Years of Award	

Principal Investigators:

Name	Degree	IC or Institution
Lead Intramural PI		
Lead Extramural PI		

Summary of Accomplishments To-Date:

Activity	Number	Comment
# new projects		
# new protocols		
Start date		
Demographics of subjects		
# of new patients admitted via protocol(s)		
# publications		
# invention reports		
# patents pending		
# patents awarded		
# new licensed drugs/devices or new indications for previously licensed drugs		
# new grants and additional funding to support project long term		

B2B Program Assessment:

Activity	Yes	No	Comment
Was the call for proposals clear?			
Was the timeline for submission of proposals adequate?			
Were resources adequate to have questions answered?			
Any suggestions to improve program management?			

B2B Collaborations (both intramural and extramural)***Satisfaction with collaboration:**

	1 Inadequate	2 Poor	3 Satisfactory	4 Good	5 Excellent
Acceptance of new ideas					
Communication among collaborators					
Ability to capitalize on the strengths of different researchers					
Organization or structure of collaborative teams					
Resolution of conflicts among collaborators					
Ability to accommodate different working styles of collaborators					
Involvement of collaborators from outside the center					
Involvement of collaborators from diverse disciplines					

Impact of collaboration:

	1 Inadequate	2 Poor	3 Satisfactory	4 Good	5 Excellent
Productivity of collaboration meetings					
Productivity in developing new products (e.g., papers, proposals, courses)					
Overall productivity of collaboration					
In general, collaboration has improved your research productivity					
In general, collaboration has improved the quality of your research					
Collaboration did not pose a significant time burden in your research					

*ratings adapted from L. Masse, R. Moser, et.al. 2008. *Am J Prev Med*; 35 (2S): 151-160.

Extramural Partnerships: (if applicable)

Activity	Choose one		Comment
Was the idea for your project initiated by the intramural, extramural, or both investigators	Intramural Extramural Both		
Was it difficult for you (as intramural PI) to identify extramural collaborators for this project?	Yes No		
Were you contacted by an extramural investigator to serve as the Intramural PI?	Yes No		
Have members of the team continued to work together on other projects?	Yes No		
Did bench-to-bedside collaborations lead to long-term relationships?	Yes No		
Was there an exchange of fellows between intramural and extramural labs as a result of the collaboration?	Yes No		
Was it difficult to form collaborative partnerships for this project?	Yes No		
Did intramural and extramural investigators visit each other during the project?	Yes No		
Did the project stimulate new sabbaticals for either intramural or extramural investigators?	Yes No		
Did intramural patients go to extramural sites? If so, for what purpose?	Yes No		
Did extramural patients come to the NIH Clinical Center? If so, for what purpose?	Yes No		
Did project result in intramural investigators being recruited to extramural institutions/positions or vice versa?	Yes No		
Were communications with extramural partners facilitated by this award?	Yes No		
Did this award promote awareness of NIH and CC resources for your extramural partners?	Yes No		
Did medical students participate in the project?	Yes No		
Did the Bench-to-Bedside award result in a long term project that continued (will continue) after Bench-to-Bedside funding?	Yes No		

Funds Distribution:

Activity	Yes	No	Explain
Did you receive funding in a timely manner to conduct your project as planned?			
Were you able to use funds as anticipated in your proposal?			
Were funds adequate to complete your project and meet objectives?			
If you needed to re-allocate funding during the project, were you successful?			

Project Completion:

Activity	Yes	No (Please provide targeted completion date)
In your opinion, is the project completed?		

Additional Comments: We welcome any suggestions you would like to offer to improve the program.

If you have supporting materials to accompany this progress report (e.g., protocol information, publications, etc.), you are encouraged to submit these documents along with your report.

Thank you for taking the time to provide this information. We will contact you again next year with a request for updates.

Comments from Project Reports

- This is an ongoing project that is now being supported through a CRADA. We still have the goal of bringing this new form of cell therapy to clinical trial.
- As the basic science portion of the project matured, it became clear that the clinical aspect would require some modification, but in general the [funding] distribution was accurate. We have learned enough to get into the details of genetic characteristics of HIV during suppressive therapy.
- As a result of this B2B, a fellow has performed an entirely new analysis of immune responses in patients suppressed on antiretroviral therapy. As a result of this award, we have also completed an entirely new analysis of genetic variation upon addition of antiretroviral therapy”
- I loved this program and that I was able to do the work we did. We followed it up with a set of subsequent studies involving Miriam Udler, a medical student (M.D., Ph.D.) who you can see is first author on two of the papers. A great program.
- Protocol approval was time consuming and unnecessarily difficult.
- Based on some of this work, a promising test was developed for serological diagnosis of HHV8/KSHV. A patent application was submitted entitled “Serological screening for HHV8 infection using antigen mixtures.” Moreover, there has already been commercial interest in potentially licensing this HHV8 diagnostic test.
- In addition to these current milestones, the advances made with this BTB funding have also catalyzed other new collaboration projects including HIV-related malignancy in children (Univ. of Washington), rapid and comprehensive HIV-HCV-HVB serological testing (NIAID, NIH) and other point of care tests (NIBIB).
- All of the work described here would not have been possible without BTB funding which was needed to hire personnel and to purchase the reagents required for these HIV-related studies.
- We were not able to initiate this project for two reasons. //The first problem was difficulty in having the funds reach the extramural collaborator for this project (this project involved only extramural funding with no B2B funds requested for the intramural NHLBI investigator). Funds were to be attached to an extramural NIAID grant that was held by University of Maryland and provided funding to the extramural collaborator at Johns Hopkins University as a sub-investigator. The funds were delayed at two points; (i) release from extramural NIAID and (ii) approval and routing by the grants offices at the U. of Maryland and Johns Hopkins University. //The second problem was that by the time the extramural collaborator received the funding, there was less than 4 months remaining on the extramural NIAID grant, which was expiring and her status as a sub-investigator

was not renewed by the project PI at the University of Maryland. Consequently, the project was never initiated due to the short time period that remained to complete the project. As far as I am aware, none of the B2B funds were utilized. //We have a clinical protocol that remains active to support this collaboration and will be utilized if the extramural collaborator can allocate funds/research effort to support this project.

- This bench to bedside award has led to a major collaboration between me and Dr. Frank M. Sacks, Harvard School of Public Health. We have three published abstracts. The third abstract was chosen for an oral presentation at the 2010 American Diabetes Association Meeting in Orlando, Florida. Our plan is to now work on a paper and submit in February 2011 an R01 application that will be an intramural-extramural collaboration.
- The project has been markedly delayed because of legal-IP issues related to the use of inhaled CSA to treat BOS. After nearly 2 years of negotiating, we finally have a clinical trial agreement in place with the APT Company, the NHLBI and the University of Maryland. This CTA will allow us to pursue the original proposed clinical trial between both institutions. An IND for the use of inhaled CSA to treat BOS after allogeneic stem cell transplant has just been submitted to the FDA. The clinical trial is written and will be presented to the NHLBI IRB in 6 weeks. We anticipate accruing patients in about 2 months.
- [The Project is not yet complete,] but it has led to many related projects between our labs.
- Yes, this is a very productive partnership. It instigated the application of the successful training awards for young Ugandan researchers.... This is an excellent program that provided our laboratory with the opportunity to expand our collaborations and research into the area of HIV and liver disease in an international setting.
- Progress has been slow because of prolonged manufacturing time and regulatory issues. The clinical grade peptides have only recently been delivered by the manufacturer and confirmatory testing prior to the clinical trial is underway. The clinical protocol will then be written and will be submitted for IRB approval together with an application to FDA for an IND for the use of the peptides. At the rate of one patient per month, the clinical trial is expected to last two years. Throughout the entire funding period, basic research to find new and better antigens and to further characterize T cell responses to leukemia have continued and results of these studies were published (Blood 2009). Dr. Gerritt Weber at the NIH is leading the studies for the discovery of new class I and class II epitopes to broaden the repertoire of candidate vaccine peptides. This project has formed a platform for future clinical trials as detailed above.
- The clinical protocol is approved by the NIAID IRB and has a CC protocol number. The protocol is under an IDE and we just received approval from the FDA. The regulatory approval process lasted more than a year. The protocol has just completed review and was approved at Yale. The protocol underwent continuing review and approval of the amendments to harmonize with the CC protocol at Tufts. The sites are now getting ready for a site initiation visit.

- The delays in this project resulted from a combination of having to take alternative scientific approaches based upon initial results. Would have benefited from funding flexibility in the ability to delay or spread out the funds further to accommodate these delays. A major problem was the uncertainty as to whether funds would be available or not at the beginning of the project, and the lack of sufficient infrastructure at the NIH (stem cell initiative was not in place, nor were next generation sequencing facilities) ready to be used for this project.
- This program has provided a unique opportunity to develop an intramural-extramural team effort in head and neck cancer research. It involves three ICs (NIDCR/NCI/NIDCD) and MUSC in our extramural community. The development of the clinical protocol was relatively fast, though we encountered numerous issues during the IRB review process. As a result, the protocol is now much stronger than anyone of us had anticipated. We look forward to working together on a project that we expect will have a direct benefit for the head and neck cancer patients.
- Our overarching hypothesis is that hemolysis in SCD leads to elevated TSP1 levels which inhibit NO and alter vascular hemostasis, predisposing patients to increased hemostatic activation and vascular disease. One of the hallmark manifestations of vascular disease in SCD is pulmonary hypertension. Preliminary results show that blockade of the TSP-1-CD47 signaling axis has a critical role in preventing pulmonary hypertension in response to hypoxemia in animal models. We therefore hypothesized that the TSP1-CD47 axis also plays an important role in the development of PH in SCD. Dr. Novelli and his mentoring team have received funding through a Hemophilia and Thrombosis Research Society Mentored Award and an American Society of Hematology Scholar Award to further elucidate the role of TSP1 in PH in vitro and in vivo using the BERK murine model of SCD. Dr. Novelli will evaluate whether myeloablated CD47KO recipients transplanted with BERK BM will be protected from pulmonary hypertension. Another line of experiments will test the vascular responses of the BERK arterial network to endothelial-dependent vasodilators. These studies are unique and complement the aims of the bench-to-bedside award in characterizing TSP1-driven vascular disease and NO dysregulation in SCD.
- It would be terrific to have the BTB money allocated with a distinct CAN to facilitate 1) project expenditure accounting and 2) timely allocation of extramural funds. The funds for this project were allocated over 2 years (extramural partners) and over a single year (intramural FY2010). Despite this minor drawback, this is an outstanding opportunity for young investigators at NIH!

Appendix C

NIH Bench-to-Bedside Projects, 2006-2009

Year	Project title	IC	Category
2006	Role of Cyclin D1 in Myelodysplasia	NHLBI	Rare Diseases
2006	Exploring the Anti-Tumor Effects of in vitro Expanded Natural Killer (NK) Cells Against Renal Cell Carcinoma Sensitized to NK-TRAIL Cytotoxicity with Bortezomib	NHLBI	Rare Diseases
2006	A New Global Function for a Rare Disease Gene: Clinical Significance of the Regulation of Mitochondrial Respiration by Tumor Suppressor p53 in Li-Fraumeni Syndrome	NHLBI	Rare Diseases
2006	Therapeutic Approaches for Cancer Stem Cells in Small Cell Neuroendocrine Carcinomas	NCI	Rare Diseases
2006	High Density Genotyping in Diffuse Large B-cell Lymphoma (DLBCL) and Follicular Lymphoma – Translating Etiologic Clues into Prognostic Relevance Within the NCI-SEER NHL Case Control Study	NCI	Rare Diseases
2006	Novel Suicide Gene-Modified Donor Th2 Cells for GVHD Prevention	NCI	Rare Diseases
2006	A Nutrigenomics Intervention for the Study of the Role of Dietary Sitosterol on Lipid, Glucose and Energy Metabolism	NIDDK	Rare Diseases
2006	Pilot Trial of Intravenous Nitrite for Sickle Cell Vaso-Occlusive Pain Crisis	NHLBI	Rare Diseases
2006	The effect of HIV-1 Infection on Endogenous miRNA Expression in vivo	NIAID	AIDS
2006	Genetic Characteristics of HIV-1 During Suppressive Antiretroviral Therapy	NCI	AIDS
2006	Evaluation of Molecular Methods for the non-invasive Diagnosis of Pneumocystis and Tuberculosis and Molecular Evaluation of Non-subtype B HIV Quasispecies in the Lung	CC	AIDS
2006	Microalbuminuria and Podocyturia in Patients with HIV disease: Detection, Characterization, and Therapy	NIDDK	AIDS
2006	Hemolysis, HIV/AIDS and Parasitic Infections Associated Secondary Pulmonary Arterial Hypertension in Sickle Cell Diseases	NHLBI	Minority Health
2006	Novel Bench-to-Bedside Research Methods for Drug Addiction: Development, Validation and Application	NIDA	Minority Health

2006	Breast Cancer among African American Women: The role of Missense Changes in the BRCA1 and BRCA2 Breast Cancer Susceptibility Genes Using a Population-Based Approach	NHGRI	Minority Health
2006	Melanocortin 3 receptor Mutations as an Etiology for Obesity in African American and Caucasian children	NICHD	Minority Health
2006	Vitamin E Pharmacokinetics and Oxidative Biomarkers in Normal and Obese Women	NIDDK	Women's Health
2006	Immunosuppression Minimization by Biological Response Monitoring	NIDDK	Co-funded (IC and NCRR)
2006	A Preliminary Assessment of the use of Ocular Coherence Tomography and Magnetic Resonance Imaging as Outcome Measures for Studying the Optic Nerve in Studies of Neuroprotection in Multiple Sclerosis	NINDS	Co-funded (IC and NCRR)
2007	Antiproliferative Therapy for Severe Pulmonary Arterial Hypertension	NHLBI	Rare Diseases
2007	Dynamic Measurement and modeling of Immune Homeostasis and Reconstitution in Pre-clinical and Clinical Studies of Cytokine Therapy and Allogeneic Hematopoietic Stem Cell Transplantation (AHSCT).	NCI	General
2007	Intensification of Antiretroviral Therapy Using HIV Integrase Inhibitor (MK-0518) to Assess Decay of Viral Reservoirs in Peripheral Blood and Gut-Associated Lymphoid Tissue of Chronically Infected Patients	NIAID	AIDS
2007	Humoral Response Profiling of Viral and Cellular Tumor Antigens for Predicting, Diagnosing, and Monitoring HIV Malignancies	NIDCR	AIDS
2007	¹ H Magnetic Resonance Spectroscopy for Quantification of Hepatic Triglyceride Content: Validation and Application in HIV-infected Patients	NIAID	AIDS
2007	Development of Immunotoxins against Kaposi's Sarcoma Associated Herpesvirus for Treatment of Multicentric Castleman's Disease (MCD)	NIAID	AIDS
2007	Effects of Beta Cell Rest in Young Individuals with Type 2 Diabetes and in Relevant Animal Model	NIDDK	Minority Health
2007	Identification of Predictive Biomarkers of Asthma Exacerbations in Exhaled Breath Condensates from High Risk Patients	NHLBI	Minority Health

2007	Ethnic Differences in Triglyceride Levels and Vascular Disease: A Study of Premenopausal African American and Caucasian Women	NIDDK	Minority Health
2007	Contribution of Stromal Free Hemoglobin, Red Cell Membranes, and Red Cell Lysate on Nitric Oxide Inactivation in the Chronic Hemolytic State	NHLBI	Minority Health
2007	Targeting HPV E2 as a vaccine against HPV mediated CIN1 and CIN2	NCI	Women's Health
2007	Characterization of Glycosphingolipid Accumulation in Smith-Lemli-Opitz Syndrome and Treatment with N-butylidoxynojirimycin	NICHD	Rare Diseases
2007	Life-Threatening Pulmonary Complications of Organ Transplantation: An Investigation of the Pathogenesis of Bronchiolitis Obliterans and Its Novel Treatment with Aerosolized Liposomal Cyclosporine A	NHLBI	Rare Diseases
2007	Role of Pathogen-specific IgE and histamine release in the hyper-IgE syndrome	NIAID	Rare Diseases
2007	WAGR Syndrome: Clinical Characterization and Correlation with Geneotype	NICHD	Rare Diseases
2007	Sensitivity and resistance to Rituximab therapy in SLL/CLL: the role of antigenic modulation, immune effector mechanisms and direct pro-apoptotic signaling	NHLBI	Rare Diseases
2007	Quantification of urinary oxidized lipids, 8-hydroxyguanine, and 8-hydroxy-2'-deoxyguanosine in Friedreich ataxia patients undergoing idebenone treatment in a phase II double-blind placebo-controlled study	NINDS	Rare Diseases
2007	Translational Studies of Hereditary Spastic Paraplegias types SPG4 and SPG20	NINDS	Rare Diseases
2007	Genetics of inherited paragangliomas and gastric stromal tumors associated with adrenal and other tumors	NICHD	Rare Diseases
2008	Targeting cancer-testis gene expression for lung cancer therapy	NIAID	General
2008	Molecular mechanisms of glial cell modulation of chemotherapy-induced painful peripheral neuropathy	NINR	General
2008	New strategies to decrease and eradicate HIV-1 reservoirs	NCI	AIDS
2008	HIV-1 suppression by Acyclovir in patients coinfectd with human herpesviruses from basic mechanism to clinical application	NICHD	AIDS

2008	Non-invasive cardiac 3T MRI for evaluation of premature coronary artery disease and myocardial dysfunction in adolescents and young adults with HIV acquired in infancy and childhood	NIAID	AIDS
2008	Hepatitis B and HIV co-infection in Uganda	NIAID	AIDS/Minority Health
2008	Development and evaluation of a nanoparticle-based HIV-1 p24 antigen assay for monitoring therapy in resource limited settings	NCI	AIDS/Minority Health
2008	Towards molecular marker based management of diabetic nephropathy in Pima Indians	NIDDK	Minority Health/Health Disparities
2008	Predicting the response to treatment using gene mutation profiling in metastatic melanoma patients	NHGRI	Rare Diseases
2008	Graft-Versus-Host Disease: novel cellular therapy using selective thawing of umbilical cord blood to obtain an aliquot for ex-vivo natural killer cell expansion and infusion following allogeneic hematopoietic stem cell transplantation	NHLBI	Rare Diseases
2008	Evaluation of the platelet transcriptome expression profile in pulmonary arterial hypertension	NHLBI	Rare Diseases
2008	Characterization of Jak/Stat activation in patients with monosomy 7 and the development of targeted therapy for patients using a Jak2 inhibitor	NIAID	Rare Diseases
2008	Development of immunotherapeutic strategies to overcome tolerance in leukemia	NHLBI	Rare Diseases
2008	Immunologic studies of IL-7 therapy in the treatment of idiopathic CD4 lymphopenia.	NIAID	Rare Diseases
2008	Immunogenicity of quadrivalent human papilloma virus vaccine (HPV Types 6, 11, 16, 18) in recipients of reduced intensity hematologic stem cell transplantation (HSCT)	NICHD	Women's Health
2008	Histaminergic pathways and energy intake in obese women	NICHD	Women's Health
2009	Searching for persistence of infection in Lyme disease	NIAID	General
2009	GABAB Receptor Antagonist SGS-742 treatment in SSADH Deficiency	NINDS	Rare Diseases
2009	Aneurysm formation in patients with mutations in STAT3	NHLBI	Rare Diseases

2009	FTO and Eating in Absence of Hunger	NICHD	Behavioral & Soc.
2009	MYH9 genetic variation in kidney disease among African-Americans	NIDDK	AIDS
2009	Genomic and Stem Cell Approaches to Hemophagocytic Lymphohistiocytosis	NIAID	Rare Diseases
2009	Development of a Diagnostic Test for Latent Tuberculosis Infection	NIDCR	AIDS
2009	Leukotriene inhibition for the amelioration of bronchiolitis obliterans	NCI	Rare Diseases
2009	Repositioning metformin as an anti-cancer agent in Li-Fraumeni syndrome	NCI	Rare Diseases
2009	Targeting mTOR as a novel mechanism-based therapy for head and neck cancer	NIDCR	Minority Health
2009	Connectivity Analysis for Investigation of Auditory Impairment in Epilepsy	NIDCD	General
2009	Frequency and TCR diversity of FOXP3+ regulatory T cells in chronic GVHD	NIAID	Rare Diseases
2009	Cardiometabolic Assessment in HIV	NIAID	AIDS
2009	Hemolysis-Associated Hemostatic Activation in Sickle Cell Disease	NHLBI	Minority Health
2009	Gene Expression Profiling to Predict Sickle Cell Anemia Sub-Phenotypes	NHLBI	Minority Health/Rare Diseases
2009	Genetic markers of CNS adverse events during interferon treatment	NIMH	Pharmacogenomics
2009	Clopidogrel Pharmacogenetics: Practical Application	NCI	Pharmacogenomics