Metabolomics

Council of Councils Presentation May 20, 2016

Common Fund Metabolomics Working Group

Chairs:

NCI	Dinah S. Singer
NIDDK	Philip Smith

Coordinators:

NCI	Barbara Spalholz
NIDDK	Arthur L. Castle
OD	Leslie Derr

Project Team Leaders:

NCI	Keren Witkin (ME Program Director)
NHLBI	Pothur R. Srinivas (Reference Standards)
NIDDK	Padma Maruvada (RCMRCs, DRCC)
NIEHS	David M. Balshaw (Technologies)
NIGMS	Richard T. Okita (Training)

Working Group Members:

NCATS	Danilo Tagle
NCI	Mukesh Verma
NCI	Krista Zanetti
NHGRI	Lita M. Proctor
NHLBI	Simhan Danthi
NIA	Yih-Woei Fridell
NIAAA	Gary J. Murray
NIAID	Conrad Malia
NIAMS	Hung Tseng
NIDA	John Satterlee
NIDCR	Lillian Shum
NIDDK	Leeanna Arrowchis
NIEHS	Andy Maynard
NIEHS	Dan Shaughnessy
NIMH	Laurie S. Nadler
NINDS	Katrina Gwinn
OD	Aron Marquitz
OD	Nicole Lim

An Introduction to Metabolomics

Metabolomics: The study of all the small molecules (or metabolites) produced or consumed during the chemical reactions that sustain life.

Why it's important:

Metabolites are the functional read-out of biologic processes and as such can identify markers of health and disease and how processes are altered when perturbed.



Demand for Metabolomics Continues to Rise



And others . . . •

Common Fund Metabolomics Program

The Common Fund Metabolomics Program was initiated in 2012 with the goal of **increasing the national capacity in metabolomics** through:



Regional Comprehensive Metabolomics Resource Cores (RCMRCs)

- Six Regional Comprehensive Metabolomics Resource Cores (RCMRCs) have expanded access to affordable, high-quality metabolomics services by providing -
 - At cost metabolomics analyses on a variety of platforms and bioinformatics services
 - Technology development to improve methods
 - Collaborative opportunities for pilot studies

 0118 awards since 2013
 077% to outside institutions
- RCMRCs on target to be financially self-sufficient through expansion of fee-for-service customer base

Comprehensive Metabolomics Resource Cores Training in Metabolomics

Metabolomics Training

- Development of Courses and Workshops (R25)
 - 82 Scientists have trained at UAB Hands-on Workshop covering all aspects of metabolomics since 2014
 - Online learning offered in vignettes with integrated comprehension assessments launched in 2015

- Mentored Development in Metabolomics (K01)
 - 10 awards 6 have moved on to metabolomics-focused careers
- Collaborative Supplements to promote metabolomics research
 - o 71 awards to researchers beyond the consortium members
 - **o** 44% of these introduce metabolomics into clinical research
 - Collaborations have already resulted in 17 publications

Metabolomics Technology Development

Project	PI		Technology		Publications	Total Cita	tions
R01ES022181	Patti	Unt	argeted Workflo	W	21	405	
		Me	tabolite Extractio	on			
R01ES022186	Patterson	S [.] C	frontiers in GENETICS			METHODS ARTICLE published: 28 July 2014 doi: 10.3389/fgene.2014.00237	
R01ES022191	Fan	С	Development and <i>i</i> metabolite identific	evaluation of larget ethods using fur	ge-scale nctional grou	р	
R01ES022190	Baker	U S	detection for metal Joshua M. Mitchell, Teresa WM. Department of Molecular and Cellular Biochemistry,	Fan, Andrew I Markey Cancer Cente	S N. Lane and Hunter N. B. Mos ar, University of Kentucky, Lexington, KY, USA	seley * 4	
NATURE METHODS BRIEF C	OMMUNICATION		< ₽		7	0	
LinidBlast in silico tandem mass spectrometry				C	10		

iubiasi in silico lanuent mass specifomelly database for lipid identification

Tobias Kind, Kwang-Hyeon Liu, Do Yup Lee, Brian DeFelice, John K Meissen & Oliver Fiehn

Affiliations | Contributions | Corresponding authors

7	0
3	12
62	570

Program has improved the extraction, separation, detection and identification of metabolites

Metabolomics Technology Development

Metabolite Standards Synthesis

- Synthesized and characterized high purity standards of novel or not readily available metabolites
- Freely available to research community including synthetic procedures, analytical methods, spectroscopic, chemical, and physical properties of these metabolites

SRI International

- Capacity to synthesize 35-40 standards (less if isotopic labeling is requested)
 - > 18 standards have been synthesized
 - > 26 standards undergoing synthesis

Metabolomics Reference Standards

Data Repository and Coordinating Center

- Developed data repository for raw and processed metabolomics data
 - o 438 registered users
 - o 320 datasets deposited
 - o 64 downloads

Metabolomics Data Sharing and International Collaboration

- Developed minimal metadata standards
- Created a reference directory of metabolite names (RefMet)
- Coordinated an inter-lab reproducibility exercise
- Created a directory of public data sets with international partners
 Metabolome change
- Developed a web portal for consortium activities that provides access to datasets, analytical tools and training

METABOLOMICS

Moving Forward

How to realize the value of metabolomics in basic, clinical, and translational research

Substantial Technical Challenges Remain

Untargeted Metabolomics Workflow:

Compound Identification of Spectral Features

- Workshop held November 2015 Beyond the Known Metabolome: Discovery and Identification of Biologically Relevant Small Molecules
- Only a fraction of known biomedically relevant metabolites are found in current reference databases for structural identification
- ~50% of metabolite peaks associating with a biomedical phenotype are unknowns
- New algorithms and approaches are needed to expedite identifications
- A coordinated effort to populate reference databases with specific MS/MS and MSⁿ fragmentation data will exponentially facilitate discovery of unknowns of interest

Goals for a Continuing Metabolomics Program

- Coordinate community-wide identification and adoption of best practices for rigor, reproducibility and data reuse
- Expand support of metabolomics capacity building to meet increasing demand for data analysis and interpretation
- Develop more efficient methods or processes for compound identification

Thank you!

To learn more:

NIH Metabolomics Consortium 2016 Annual Program Meeting September 27-29, 2016 Natcher Conference Center, NIH

Or visit:

http://www.metabolomicsworkbench.org