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

- Infrastructure Expansion
- Workforce Development
- Technology Enhancements
- Reference Standard Synthesis
- Data Repository
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
    - 118 awards since 2013
    - 77% to outside institutions

- RCMRCs on target to be financially self-sufficient through expansion of fee-for-service customer base
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**
  - 71 awards to researchers beyond the consortium members
  - 44% of these introduce metabolomics into clinical research
  - Collaborations have already resulted in 17 publications
# Metabolomics Technology Development

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Total: 62 publications, 570 total citations

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

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**References**

1. Development and *in silico* evaluation of large-scale metabolite identification methods using functional group detection for metabolomics
   - Joshua M. Mitchell, Teresa W.-M. Fan, Andrew N. Lane and Hunter N. B. Moseley
   - Department of Molecular and Cellular Biochemistry, Markey Cancer Center, University of Kentucky, Lexington, KY, USA

2. LipidBlast *in silico* tandem mass spectrometry database for lipid identification
   - Tobias Kind, Kwang-Hyeon Liu, Do Yup Lee, Brian DeFelice, John K Meissen & Oliver Flehn
   - Affiliations | Contributions | Corresponding authors

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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

• Capacity to synthesize 35-40 standards (less if isotopic labeling is requested)
  
  ➢ 18 standards have been synthesized
  ➢ 26 standards undergoing synthesis
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
• 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
• Developed a web portal for consortium activities that provides access to datasets, analytical tools and training
Moving Forward

... How to realize the value of metabolomics in basic, clinical, and translational research
Substantial Technical Challenges Remain

Untargeted Metabolomics Workflow:

Challenges
• Rigor and reproducibility
• Data analysis and interpretation
• Compound Identification

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 MS^n 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