NIH Common Fund Metabolomics Program

August 28, 2017

Pre-application webinar for:

RFA-RM-17-011	National Metabolomics Data Repository
RFA-RM-17-012	Metabolomic Data Analysis and Interpretation Tools
RFA-RM-17-013	Compound Identification Development Cores
RFA-RM-17-014	Stakeholder Engagement and Program Coordination Center

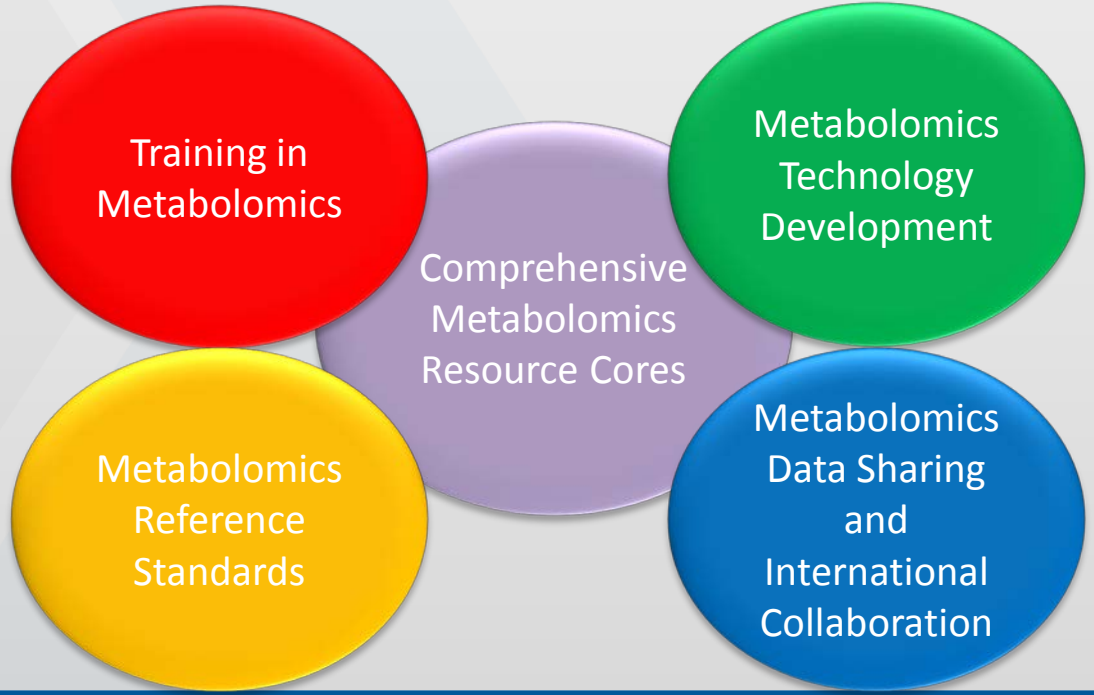
Questions

- Will be answered at the end of the webinar
- Can be submitted in advance to CFMetabolomics@mail.nih.gov

Slides are posted on the CF Metabolomics website:
https://commonfund.nih.gov/Metabolomics/webinars

Common Fund Metabolomics Program (Stage I)

The Common Fund Metabolomics Program was initiated in 2012 **to increase the national capacity in metabolomics** by developing:



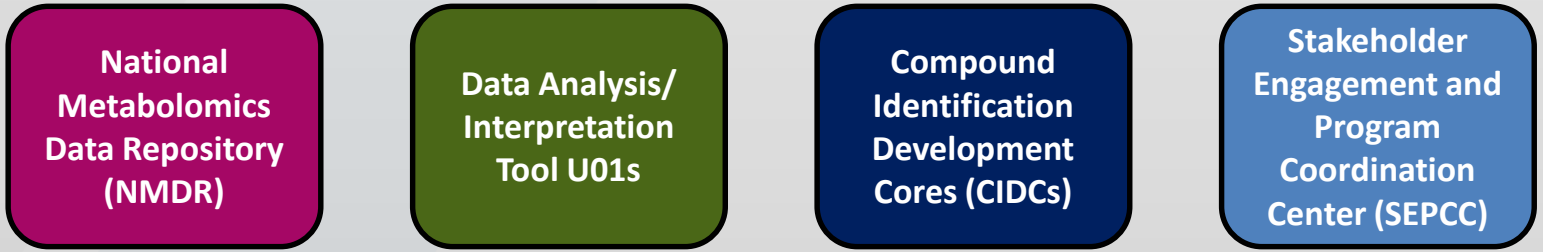
Challenges (Areas of Opportunity) Remain:

- Compound identification
- User friendly tools for data analysis and interpretation
- Questions of rigor/reproducibility
- Community consensus on protocols, data standards, best practices, etc.
- Storage and sharing of high quality metabolomics data and metadata available for reuse

Stage 2: Meeting these challenges in order to realize the potential of metabolomics in basic, clinical, and translational research

Goals for Phase 2:

- Transition the DRCC Data Repository into a National Repository for large basic and clinical metabolomics datasets
- Meet increasing demand for user-friendly, open-source, bioinformatics tools for data analysis and interpretation
- Develop novel approaches to facilitate compound identification
- Coordinate community-wide identification and adoption of best practices for rigor, reproducibility and data reuse



National Metabolomics Data Repository (NMDR)

RFA-RM-17-011
U2C Mechanism

Program Contact:
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Grants Management Contact:
Todd Le
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Data Analysis/ Interpretation Tool U01s

RFA-RM-17-012
U01 Mechanism

Program Contact:
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Compound Identification Development Cores (CIDCs)

RFA-RM-17-013
U2C Mechanism

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Stakeholder Engagement and Program Coordination Center (SEPCC)

RFA-RM-17-014
U2C Mechanism

Program Contact:
Arthur Castle
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castlea@niddk.nih.gov

Grants Management Contact:
Todd Le
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Scientific Review Officer: Mark Caprara, CSR capraramg@csr.nih.gov

Key Dates:

- Open Date (Earliest Submission Date): **September 20, 2017**
- Letter of Intent Due Date: **September 12, 2017**
- Application Due Date **October 20, 2017**

  (by 5:00 PM local time of applicant organization)

  We strongly suggest that applications be submitted a week in advance!
- Scientific Merit Review **March 2018**
- Advisory Council Review **May 2018**
- Earliest Start Date **July 2018**

Budget:

- The maximum budget allowed per grant is different for each RFA.
- Budget requests should reflect the actual needs of the proposed project.
- Project periods are limited to 4 years.

Administrative Details:

- Resource Sharing Plan will be considered by reviewers.
- Remember Rigor and Reproducibility Criteria, where applicable.
- Common Fund Programs are goal- and milestone-driven.
  - See specific FOAs for milestone guidance.
- Page limits:
  - U01 Research plan has a 12 page limit, not including Resource Sharing Plan.
  - U2C is a multicomponent mechanism.
    - 12 pages for Overall component.
    - 6 pages for most other Cores.
  - Do not use appendix to circumvent page limits.
- Read all directions carefully!

Cooperative Agreements:

- U01 and U2C are both cooperative agreement mechanisms.
- Grantees are expected to actively participate in a CF Metabolomics Consortium.
- PDs/PIs will serve on the Consortium Steering Committee (SC), the primary governing body of the Consortium, to discuss community issues, set policies, and plan and evaluate activities to meet Program goals.
- SC will meet regularly by teleconference, and Consortium members will meet in person twice a year.
- Read cooperative agreement terms carefully.

Scientific Review

- **These grants have additional review criteria (see RFAs)**
- Applications will receive an overall impact score. Individual components of U2C applications will be evaluated and will receive an overall adjectival rating.
- Recommended applications will receive a second level of review by the NIDDK, NCI, or NIEHS Advisory Councils.
- Appeals of initial peer review will not be accepted.
- Direct additional peer review questions to:

Mark Caprara, Ph.D.
Center for Scientific Review (CSR)
Email: capraramg@csr.nih.gov

Resource Sharing Instructions

- All data must be deposited into the appropriate publicly available data repositories.
- All grantees of the Metabolomics Program will be subject to sharing standards for data, software, and other resources adopted by the Metabolomics Steering Committee.
- Specific plans for sharing software are expected where applicable.
- See RFAs for more details.

Eligibility Criteria

- These FOAs are open to all eligible investigators.
  - Foreign institutions are not eligible, but components from foreign institutions are allowed.
- There is no limit on how many applications an institution or an investigator can submit, as long as each is unique.
- Similarly, applicants are free to apply to companion FOAs.
- However, when making funding decisions, NIH can consider the need for broad representation of the research community in the selection of awardees.

Information specific to individual FOAs

National Metabolomics Data Repository (NMDR)

RFA-RM-17-011
National Metabolomics Data Repository (NMDR)
U2C Mechanism

Program Contact:
Arthur Castle, Ph.D., NIDDK castlea@niddk.nih.gov

Grants Management Contact:
Todd Le, NIDDK let@extra.niddk.nih.gov

Goal: To establish a National Metabolomics Data Repository (NMDR), which is widely adopted by the national and international metabolomics community, supports facile data and metadata deposition and access for re-use, and provides a means for citing the data and its provenance.

Budget: The NIH Common Fund intends to commit approximately $3,000,000 total costs per year, but budgets must reflect the actual needs of the project. 1 award is anticipated.

Organizational structure:

- Administrative Core (required)
- Data Repository Core (required)
- Governance Core (required)
- Optional Cores

National Metabolomics Data Repository (NMDR)

NMDR Administrative Core

- Overall management of NMDR personnel and integration of sub-cores.
- Regular reporting to NIH on NMDR policies, progress, dataset upload and access, technical improvements.
- Identifying and securing access to important existing metabolomics datasets, including those from international partners.
- Implementing Governance Core recommendations.
- Succession Planning – models for enduring financial support, engaging invested communities.
- Promoting NMDR resources.
- Coordinating with the SEPCC in areas of joint responsibility.

Data Repository Core

- Transfer the data and technical capabilities of the current DRCC Data Repository
- Store, and make publicly available, raw and processed metabolomic data with associated metadata (including de-identified clinical data)
- Be in a cloud computing environment for searching and reanalysis by the biomedical research community
- Provide customer assistance for dataset upload and access
- Develop strategies to ensure that data formats and access meet evolving community needs and standards
- Implement technical improvements as directed by the Governance or SC.

Governance Core

- Goal - to initiate a representative and autonomous Governance structure for the NMDR that could extend beyond the term of this award.
- Structure
  - Board consisting of 6-8 external consultants from different disciplines relevant to NMDR management and metabolomics community needs
    - 3 or 4 committed members must be identified in the application.
  - NMDR staff to facilitate activities, e.g. meetings, analyses, surveys, reports, recommendation development.
- Activities
  - Develop recommendations, e.g., policy recommendations for data deposition, reuse, and sharing; technical improvements; how to secure community investment for the repository; how to increase use of the NMDR
  - Periodically evaluate performance of the NMDR

Specific RFA Review Criteria

- **Significance:** Does the proposed plan for the NMDR generate confidence that it will develop a resource of enduring value to the biomedical research community? Is this application likely to bring about community consensus and adoption of the data deposition and sharing policies and promote extensive use of the repository by the biomedical research community for both data deposition and re-analysis?
- **Investigator(s):** Does the PD/PI have experience with large multi-faceted consortia requiring policy development? Does the PD /PI have a history of productive interactions with the national and international metabolomics community? Have 3-4 external experts committed to serve on the Governing Board? Are they qualified to make the significant contributions described in their Letters of Commitment? Does their expertise cover a range of backgrounds needed to govern the NMDR activities? Are sufficient experienced personnel identified to meet community needs for assistance with data deposition, curation, and reuse?

Specific RFA Review Criteria (Cont.)

- **Approach**: Are appropriate plans proposed for transitioning the existing capabilities and data of the DRCC to the National Repository? Are all the requirements for the NMDR addressed in the research plan? Does the plan describe flexibility to adapt to changing community needs in metabolomics? Have appropriate issues related to deposition of, or access to, clinical data been addressed? Are adequate plans proposed for handling metabolomics data traditionally challenging to capture in databases (for instance stable isotope data and metabolite imaging), as well as the flexibility to adapt to the changing needs of the metabolomics community as the field matures? Have effective management and leadership plans been proposed to achieve the goals of the Governance Core? Have they described effective strategies for working with other components of the Consortium? Are plans and infrastructure in place to assure data back-up, integrity, and uninterrupted service to the data repository?
- **Environment:** Does the institution have managerial and technical infrastructure to implement the NMDR? Are their computing facilities sufficient to house the data and resources required?

Data Analysis/ Interpretation Tool U01s

RFA-RM-17-012
Metabolomic Data Analysis and Interpretation Tools
U01 Mechanism

Program Contact:
Krista Zanetti, Ph.D., NCI zanettik@mail.nih.gov

Grants Management Contact:
Dawn Mitchum, NCI dmitchum@mail.nih.gov

Goal: To develop novel tools and approaches to facilitate metabolomics data analysis and interpretation.

Budget: Budgets must reflect actual needs of the project, but cannot exceed $300K direct costs per year. 4-6 awards are expected.

Other details to note:

- A complete list of responsive topics is listed in the FOA.
  - Compound identification tools are **excluded** from this FOA.
- Development of open-source, generalizable, and scalable tools for scientists with limited expertise in bioinformatics is encouraged
- Plans to validate tools with real metabolomics data, compare tools with current approaches, and assess the usability of tools for their intended audience should be presented.

Data Analysis/ Interpretation Tool U01s

Specific RFA Review Criteria

- **Significance**: Will the project advance the field of metabolomics by overcoming current hurdles in data analysis and integration, and provide approaches easily adoptable by the biomedical research community?
- **Investigator(s)**: Has the investigator demonstrated awareness of the challenges of analyzing and interpreting metabolomics data? Does the investigator demonstrate a clear understanding of the biomedical questions that can be addressed through metabolomics? Does the investigative team have sufficient computational experience?
- **Innovation**: Will the proposed tool or algorithm simplify the analysis, interpretation, or integration of metabolomics data?
- **Approach**: Can the approaches be easily adapted or utilized by the broader metabolomics community? Is there a plan for testing the tool or algorithm on a data set distinct from the dataset used to develop the tool or algorithm? Are plans in place for testing the usability of the tool by the intended audience?
- **Environment**: Does the institution have appropriate computational core facilities?

Compound Identification Development Cores (CIDCs)

RFA-RM-17-013

Compound Identification Development Cores (CIDC)

U2C Mechanism

Program Contact:
David Balshaw, Ph.D., NIEHS ~~balshawd@mail.nih.gov~~
balshaw@niehs.nih.gov

Grants Management Contact:
James Williams, NIEHS williamsjr@niehs.nih.gov

Goal: To develop innovative approaches to enhance the ability to identify biomedically-significant unknown metabolites and consequently greatly increase the number of known metabolites. Proposed strategies can initiate from a computational approach or an experimental approach, but need to couple both disciplines to achieve validation and development of catalytic approaches.

Budget: Budgets must reflect the actual needs of the project, but cannot exceed $600K direct costs per year. 4-6 awards are expected.

Organizational structure:

- Administrative Core (required)
- Computational Core (required)
- Experimental Core (required)

Compound Identification Development Cores (CIDCs)

CIDC Required Cores

- Administrative Core
  - Overall management and interaction with other Program initiatives.
  - Manage outreach to, and opportunities for collaboration with, the biomedical research community.
- Computational Core
  - Build *in silico* models and informatics tools.
  - Test models/tools in conjunction with Experimental Core.
  - Deposit and share data in appropriate databases.
- Experimental Core*†
  - Validate outcomes of Computational Core.
  - Develop novel biochemical approaches to catalyze field of compound identification.

*The relative balance between these 2 activities of the experimental core will vary with the nature of the project.
†Research for biological understanding or biomarker discovery is **not** the purpose of this Core.

Specific RFA Review Criteria

- **Significance**: How likely is this application to significantly enhance the ability to quickly and inexpensively identify unknown compounds in HTP metabolomics experiments?
- **Investigator(s)**: Does the research team have complementary experience in biomedical research, metabolomics, chemistry, and computational science?
- **Innovation**: Have innovative approaches been proposed to catalyze the ability to identify unknown metabolites? Can these approaches be adapted to the identification of other compound classes?
- **Approach**: Are approaches relevant to a broad spectrum of metabolites? Is there a plan to validate computational approaches with metabolomics data? Will the tools and information developed be appropriately integrated into existing public metabolomics repositories and compound annotation resources? Can the approaches be easily adapted or utilized by the broader metabolomics community
- **Environment**: Does the institution have a base of funded research utilizing metabolomics? Does the institution have appropriate core facilities?

Stakeholder Engagement and Program Coordination Center (SEPCC)

RFA-RM-17-014
Stakeholder Engagement and Program Coordination Center (SEPCC)
U2C Mechanism

Program Contact:
Arthur Castle, Ph.D., NIDDK castlea@niddk.nih.gov

Grants Management Contact:
Todd Le, NIDDK let@extra.niddk.nih.gov

Goal: To coordinate the activities of the Metabolomics Consortium and to engage invested communities in developing and disseminating consensus best practices in metabolomics.

Budget: Budgets must reflect actual needs of the project, but the maximum budget is $300k direct costs per year. 1 award is expected. Additional funds may be available for specific projects but will be managed by the NIH.

Organizational structure:

- Administrative Core (required)
- Stakeholder Engagement and Program Promotion Core (required)
- Implementation Core (optional)
- Other Cores (optional)

Stakeholder Engagement and Program Coordination Center (SEPCC)

SEPCC Required Cores

- Administrative Core
  - Coordinate with the NMDR to facilitate transition of the DRCC to the NMDR.
  - Organize and manage consortium communications and meetings – secure web interface, monthly Steering Committee meetings, full consortium annual symposium, External Scientific Consultant meetings and reports.
  - Organize and manage Working Groups of the Steering Committee.
  - Create the Program web portal (or transition the current Metabolomics Workbench) and regularly update, evaluate, and enhance usability.

- Stakeholder Engagement and Program Promotion Core
  - Develop and implement plans to actively engage stakeholder communities in discussing issues to improve access to and use of metabolomics in biomedical research.
  - Develop plans to achieve community adoption of draft consensus positions.

SEPCC Optional Cores

- Implementation Core
  - If specific plans and approaches are anticipated to require dedicated staff and resources for implementation of activities to promote consortium collaborations or follow-up on recommendations ensuing from stakeholder engagement, a specific core may be included.
- Web Portal, Outreach, Other
  - If specific plans and approaches are anticipated to require dedicated staff and resources for maintaining the Web Portal or promoting consortium resources, a specific core may be included.

Specific RFA Review Criteria

- **Significance**: Does the proposed plan for the SEPCC generate confidence that it will engage relevant stakeholders in developing an enduring community to address how to best realize the potential of metabolomics in biomedical research?
- **Investigator(s)**: Does the PI have experience in managing large multi-faceted consortia requiring policy development as well as the technical infrastructure and experience in creating a user-friendly interface or portal and assessing usability? Does the PI have a history of productive interactions with the international metabolomics community?
- **Innovation**: Are the plans for stakeholder engagement innovative?
- **Approach**: Are specific plans proposed to engage national and international partners, scientific journal editors, and biomedical research end-users in solving issues impeding the use of metabolomics and the sharing of metabolomics datasets? Do plans include flexibility to adapt to changing community needs in metabolomics? Are plans proposed to evaluate usability of the resources of the Metabolomics Program?
- **Environment**: Does the institution have sufficient stature in the metabolomics community to effectively organize a metabolomics expert community?

Consortium Oversight

- Steering Committee
  - PIs of each funded grant, NIH representation
  - Monthly Steering Committee Teleconferences (1 face-to-face)
  - Annual Consortium Symposium
  - Annual specific workshops as needed
- Common Fund Metabolomics Working Group
  - Program Officers, Project Scientists, Common Fund Program Officers, NIH IC representatives
- External Scientific Consultants
  - 3-5 External experts in fields related the Metabolomics Program
- NMDR Governance Board
  - Regular meetings on issues affecting the NMDR; Interaction with SC and WG

Questions

Prior to August 24th, we encourage you to submit questions in writing to CFMetabolomics@mail.nih.gov. We will try to address these questions during the webinar.

There will be an additional opportunity to ask questions during the webinar.

We anticipate FAQs will be developed from these questions and posted on the Common Fund Metabolomics Program Website: https://commonfund.nih.gov/metabolomics