

Acute to Chronic Pain Signatures (A2CPS)

Applicant Webinar

September 6, 2018



We will start @ 2:05 PM EST

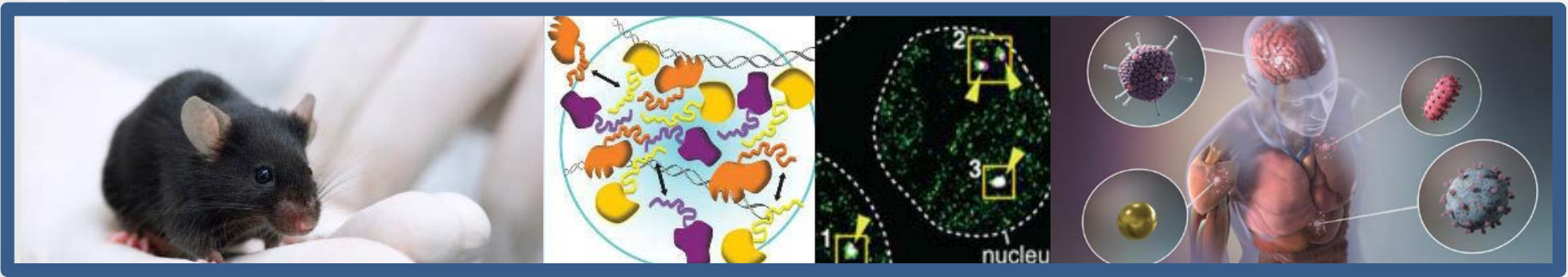
Webinar Logistics

WebEx

- Slides used in this webinar will be available on the Common Fund Website: <https://commonfund.nih.gov/pain>
- A list of commonly asked **FAQs** are posted and will be updated on the Common Fund Website: <https://commonfund.nih.gov/pain/faq>
- All attendees will be muted for the entire webinar. You will have the opportunity to ask questions during Q&A session at the end of webinar.
- Please ask your questions in Q&A box or via email to A2CPS@nih.gov.
- Email your question to the pertinent Program Officer after the webinar if you do not want to disclose project-specific details to other webinar participants.

Agenda

- **Introduction & WebEx overview** – 3 min; Nicolas Johnston, NIDA
- **Common Fund and A2CPS Program overview** – 5 min; Trish Labosky, Common Fund, OD/OSC
- **Funding announcement overviews** – 5 min per RFA; Linda Porter NINDS, John Satterlee, NIDA
- **Review procedure** – 5 min; Joseph Rudolph, CSR
- **Cooperative agreement overview & application deadlines** – 5 min; Trish Labosky, OD/OSC
- **Q&A session** – Until we run out of questions or 60 min, whichever comes first



Common Fund Overview

Trish Labosky, Ph.D.

Program Leader
Office of Strategic Coordination
Division of Program Coordination, Planning, and
Strategic Initiatives
Office of the Director, NIH



One Hundred Ninth Congress
of the
United States of America

AT THE SECOND SESSION

*Began and held at the City of Washington on Tuesday,
the third day of January, two thousand and six*

An Act

To amend title IV of the Public Health Service Act to revise and extend the authorities of the National Institutes of Health, and for other purposes.

*Be it enacted by the Senate and House of Representatives of
the United States of America in Congress assembled,*

SECTION 1. SHORT TITLE.

This Act may be cited as the "National Institutes of Health Reform Act of 2006".

TITLE I—NIH REFORM

Origins of the Common Fund

2004: NIH Roadmap is launched

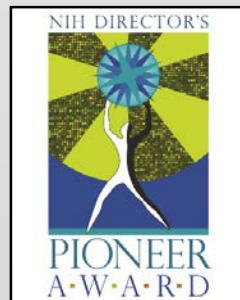
2006: Congress unanimously reauthorizes NIH



Establishes the **Division of Program Coordination, Planning, and Strategic Initiatives (DPCPSI)** within Office of the Director and the **NIH Common Fund** to provide a dedicated source of funding to enable *trans*-NIH research

Criteria for Common Fund Programs

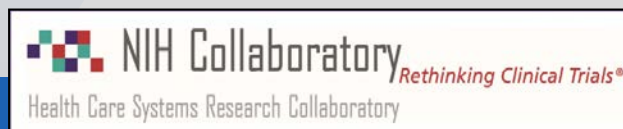
- **Transformative:** Must have high potential to dramatically affect biomedical and/or behavioral research over the next decade
- **Catalytic:** Must achieve a defined set of high impact goals within 5-10 years
- **Synergistic:** Outcomes must synergistically promote and advance individual missions of NIH Institutes and Centers to benefit health
- **Cross-cutting:** Program areas must cut across missions of multiple NIH Institutes and Centers, be relevant to multiple diseases or conditions, and be sufficiently complex to require a coordinated, trans-NIH approach
- **Unique:** Must be something no other entity is likely or able to do



exRNA
RESEARCH PORTAL



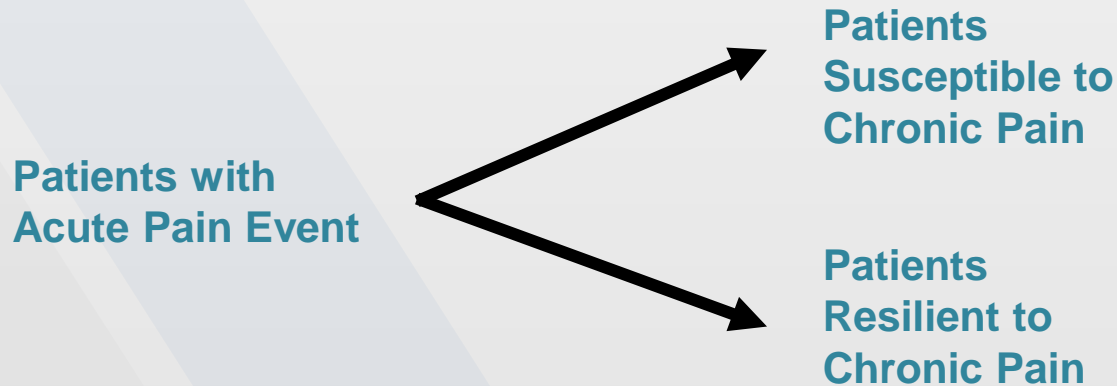
National Institutes of Health
Office of Strategic Coordination - The Common Fund



Acute to Chronic Pain Signatures (A2CPS)



Program Goal & Significance



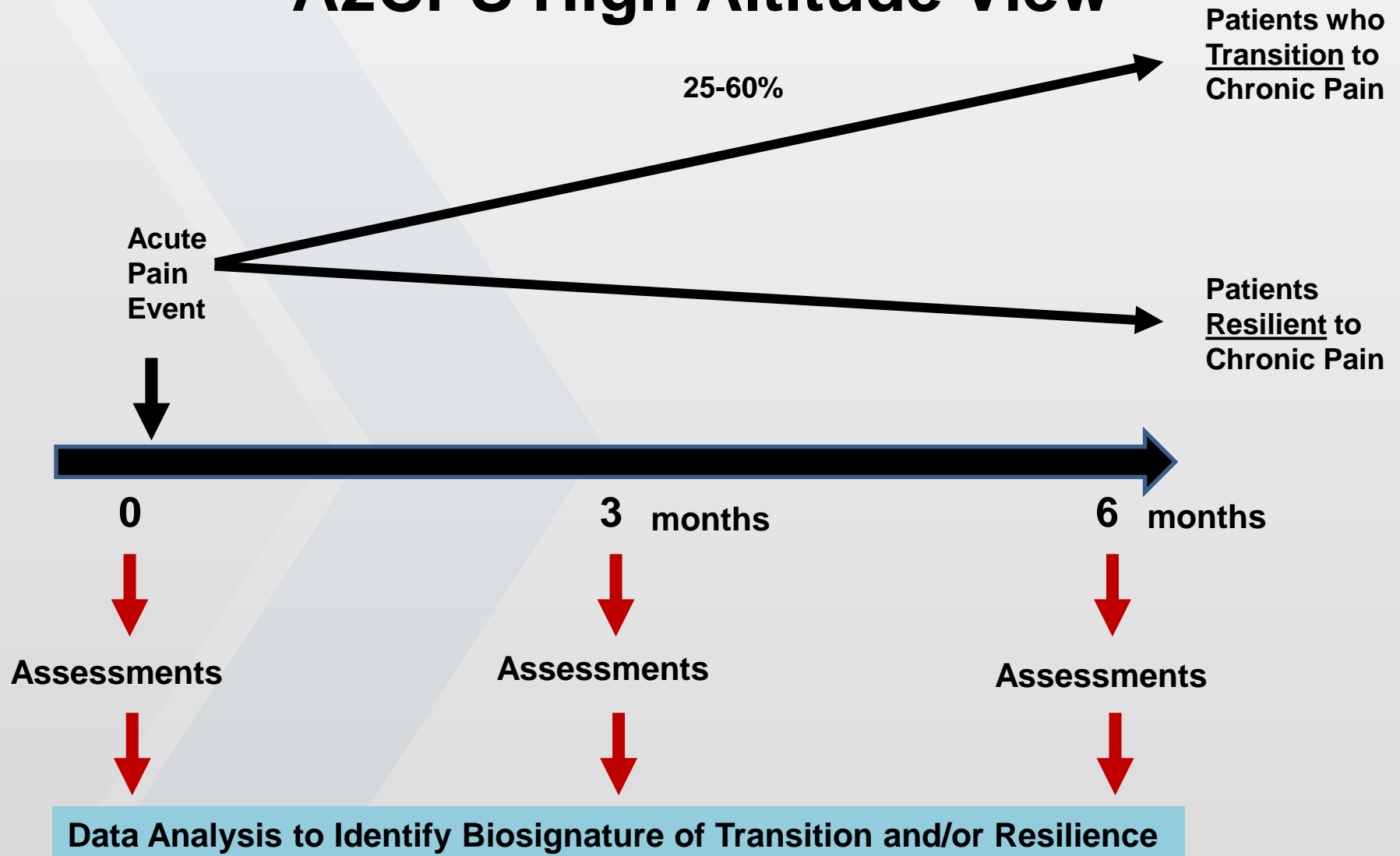
Goal: Identify *objective biosignatures* to predict

- which patients are likely to transition from acute to chronic pain, or
- which patients are resilient to the development of chronic pain

Significance:

- Personalized acute pain care to prevent chronic pain
- Reduced reliance on opioids
- Identification of therapeutic targets (brain circuits, genes, other)

A2CPS High Altitude View



Potential Biomarkers

Basic patient assessments:

- Vitals
- Demographics
- Care/meds received
- Actinography

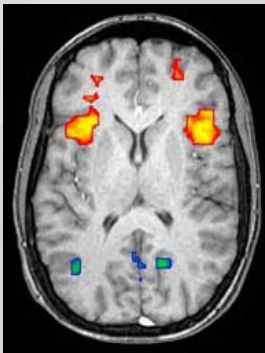
Patient reported outcomes (PROs):

- Pain severity
- Depression
- Prior trauma
- Co-occurring pain conditions



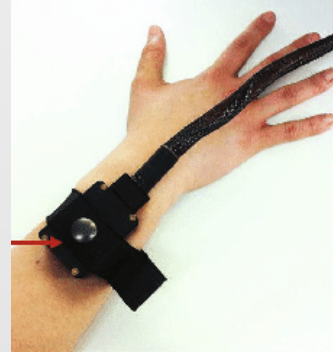
Brain imaging (one hour scan):

- fMRI
- RS-MRI with thermal stimulus
- Arterial spin labeling



Quantitative sensory tests:

- Thermal pain sensitivity
- Mechanical pain sensitivity
- Descending pain modulation

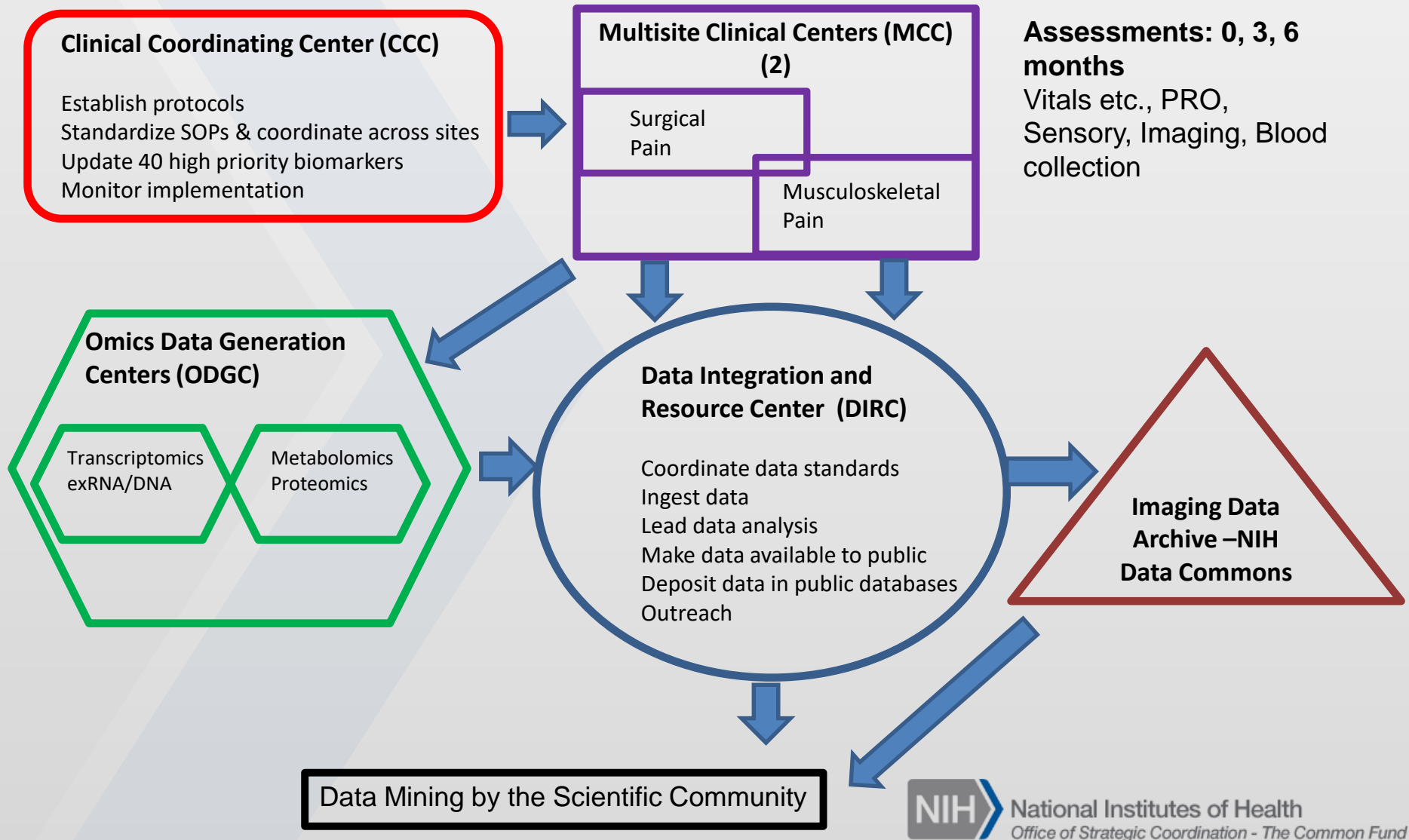


Bio-specimen analyses:

- Metabolomics (e.g. epiandrosterone sulfate)
- Proteomics (e.g. IL-1beta, VEGF)
- Extracellular RNA (e.g. miR-223, miR-199a, miR-122)
- Transcriptome of single cells (e.g. T cells/microglia)
- Microbiome?



Program Components



Anticipated A2CPS Timeline

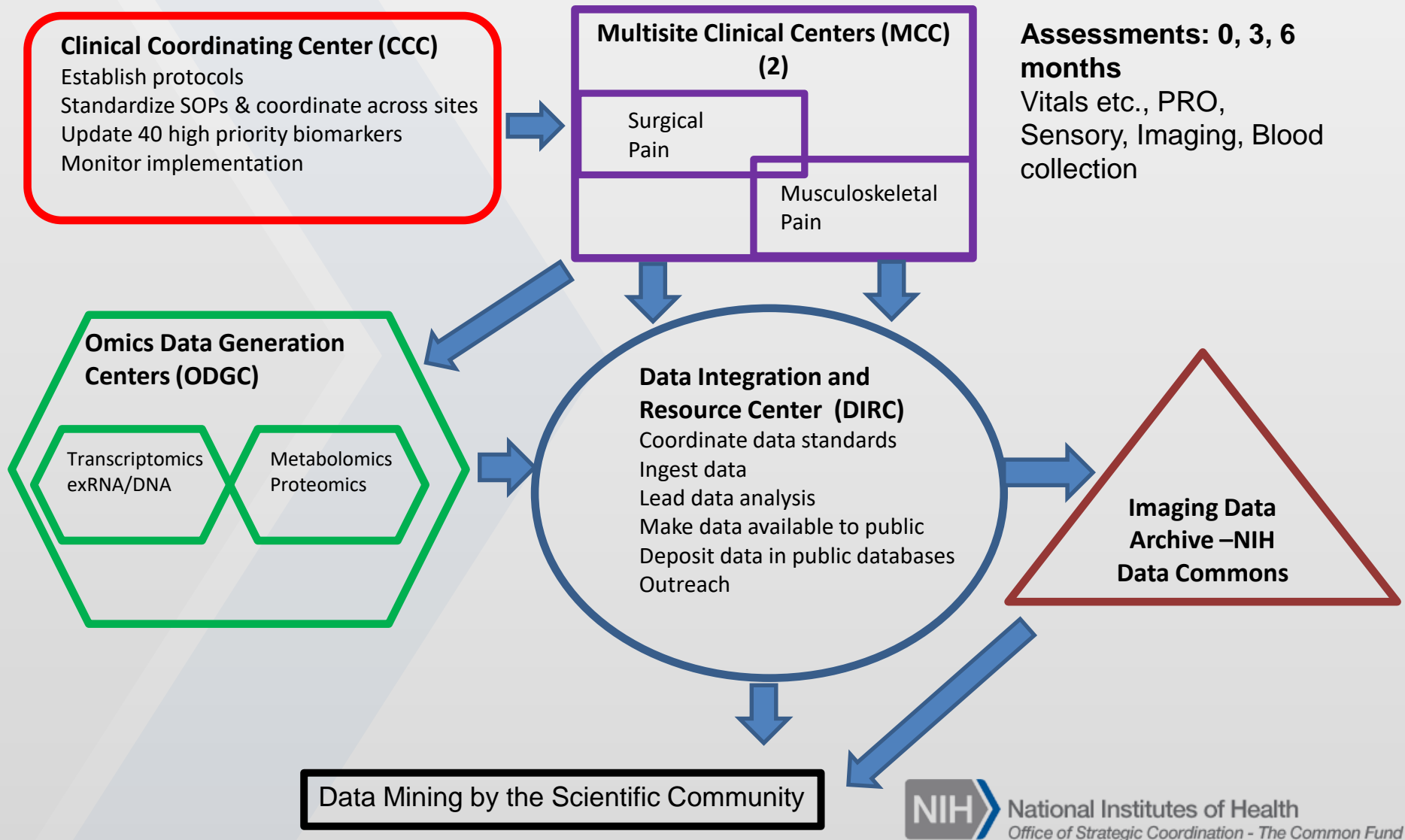
Receipt date	October 24, 2018
Award date	June 2019
Beginning of planning year	July 2019
Kick off Meeting	Sept 2019
End of planning year	July 2020
Beginning of recruitment	July 2020*
Futility analysis	July 2021
End of recruitment	July 2022
End of patient assessments	January 2023
Integrative publication	February 2024

* Budget scale up

Application Considerations for all FOAS

- **Read RFA carefully for suggestions on what to include in your application!!!**
- **Submit a couple days early, do not wait until the last minute!**
- Provide timeline and detailed quantitative annual milestones spanning funding period.
- Include information illustrating your past successes and how they relate to their planned A2CPS activities.
- Key personnel/consultants/team should demonstrate strong scientific expertise.
- Describe how you will manage the proposed project:
 - who will oversee the day-to-day activities (e.g., a project manager if not the PD(s)/PI(s))
 - how management structure supports achievement of proposed goals and milestones
 - Describe any experience coordinating large projects.
- Propose and justify at least ten potential candidate omics biomarkers (to be included as part of final set of approximately 40 primary outcomes to be tested) your team considers most compelling based on scientific literature or from your own preliminary data.
- Budget for PIs and essential team members to travel domestically for four face to face meetings program year one and for two annual meetings for the remainder of the funding period.

Program Components



Question: I am a pain researcher, but my project is not aligned with the A2CPS FOAs. Is NIH interested in my area of pain research?

Answer: A2CPS is focused on a specific scientific question in human patients. However, many NIH institutes support investigator-initiated projects in a wide array of topics in the area of pain research.

See:

https://painconsortium.nih.gov/Funding_Research/Funding_Opportunities or contact the pain consortium representative at appropriate institutes <https://painconsortium.nih.gov/About/Members>

Multisite Clinical Center Common Fund Acute to Chronic Pain Signatures Program: Acute Peri-operative Pain (UM1) (Clinical Trial Optional)

[RFA-RM-18-034](#)

Linda Porter

(porterl@ninds.nih.gov)

RM18-034 Funding Opportunity Purpose

To support a Multisite Clinical Center to implement enrollment and multimodal longitudinal assessment of a large cohort of **acute peri-operative pain** patients to identify a biosignature for resilience to and the transition from acute to chronic pain.

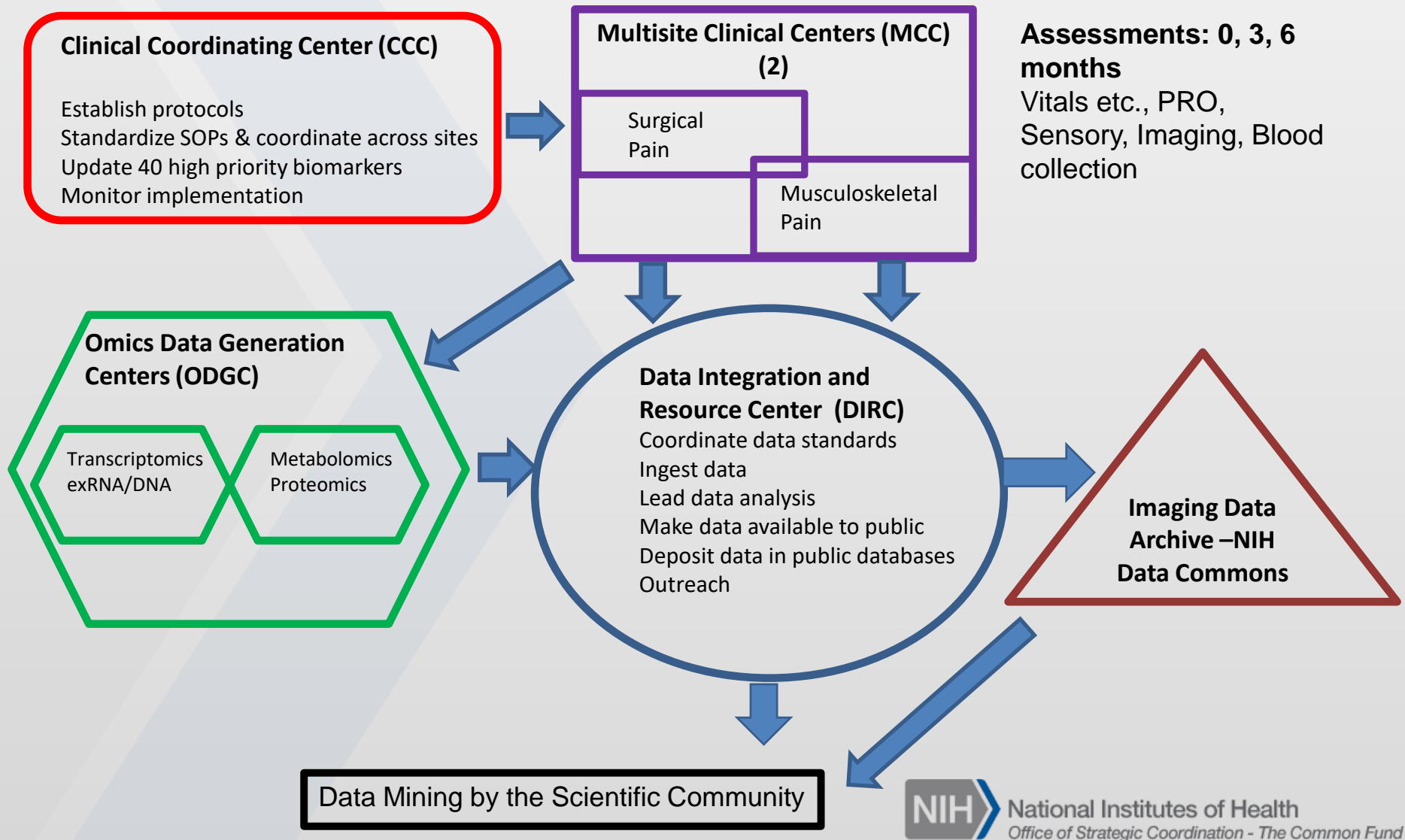
Key Activities of the MCC (peri-operative pain)

- Communicate effectively with other consortium members (CCC, DIRC, ODGC) and NIH staff to achieve overall goals of A2CPS. MCCs are expected to work as a consortium with the CCC, ODGCs, and DIRC.
- Work with consortium to assess and refine the power analysis for the consortium as a whole, to improve the likelihood of success.
- Recruit and enroll patients with selected acute pain event.
- Deliver, monitor, and record usual peri-operative care including pain care.
- Capture opioid use, including whether patient is dependent on opioids at 6 month assessment.
- Capture surgical details in electronic health records.
- Adapt electronic health records to align with A2CPS needs.
- Phenotype patients for study-determined characteristics.
- Perform study determined brain imaging and sensory tests at T=0, 3 months and 6 months.
- Collect bio-specimens for study determined assays at T = 0, 3 months and 6 months.
- Collect, store (on-site), and transfer biospecimens to ODGCs as needed.
- Deposit patient assessment data and all primary data at the DIRC.

Application Considerations:

- Develop study enrolling ~ 1800 patients over a two-year period from a SINGLE specific type of surgery (e.g. thoracotomy or other surgical procedure with expected 30%-60% transition rate from acute to chronic pain) and retain patients for assessments at time = 0, 3, and 6 months post-surgery.
- Justification for the selected surgical procedure with consideration of expected transition rate from acute to chronic pain based on the scientific literature and from own preliminary data, if available.
- Power analysis that will accommodate identification of multiple individual biomarkers to create predictive biosignatures.
- How will the MCC will collaborate with the cross-consortium efforts?
- Consider partnering with existing groups or leverage existing resources. This could include partnering with the National Center for Advancing Translational Sciences' Trial Innovation Network (www.trialinnovationnetwork.org) and/or Clinical and Translational Science Award (CTSA) awardees.
- Include steps to avoid unconscious experimenter bias with respect to diagnosis of transition chronic pain.

Program Components



Multisite Clinical Center Common Fund Acute to Chronic Pain Signatures Program: Acute Pain from Musculoskeletal Trauma (UM1) (Clinical Trial Optional)

[RFA-RM-18-033](#)

Linda Porter

(porterl@ninds.nih.gov)

Funding Opportunity Purpose

The purpose of this FOA is to support one Multisite Clinical Center (MCC) to implement the enrollment and multimodal longitudinal assessment of a large cohort of patients with acute pain from a **musculoskeletal trauma** to identify biosignatures for resilience to and/or the transition from acute to chronic pain.

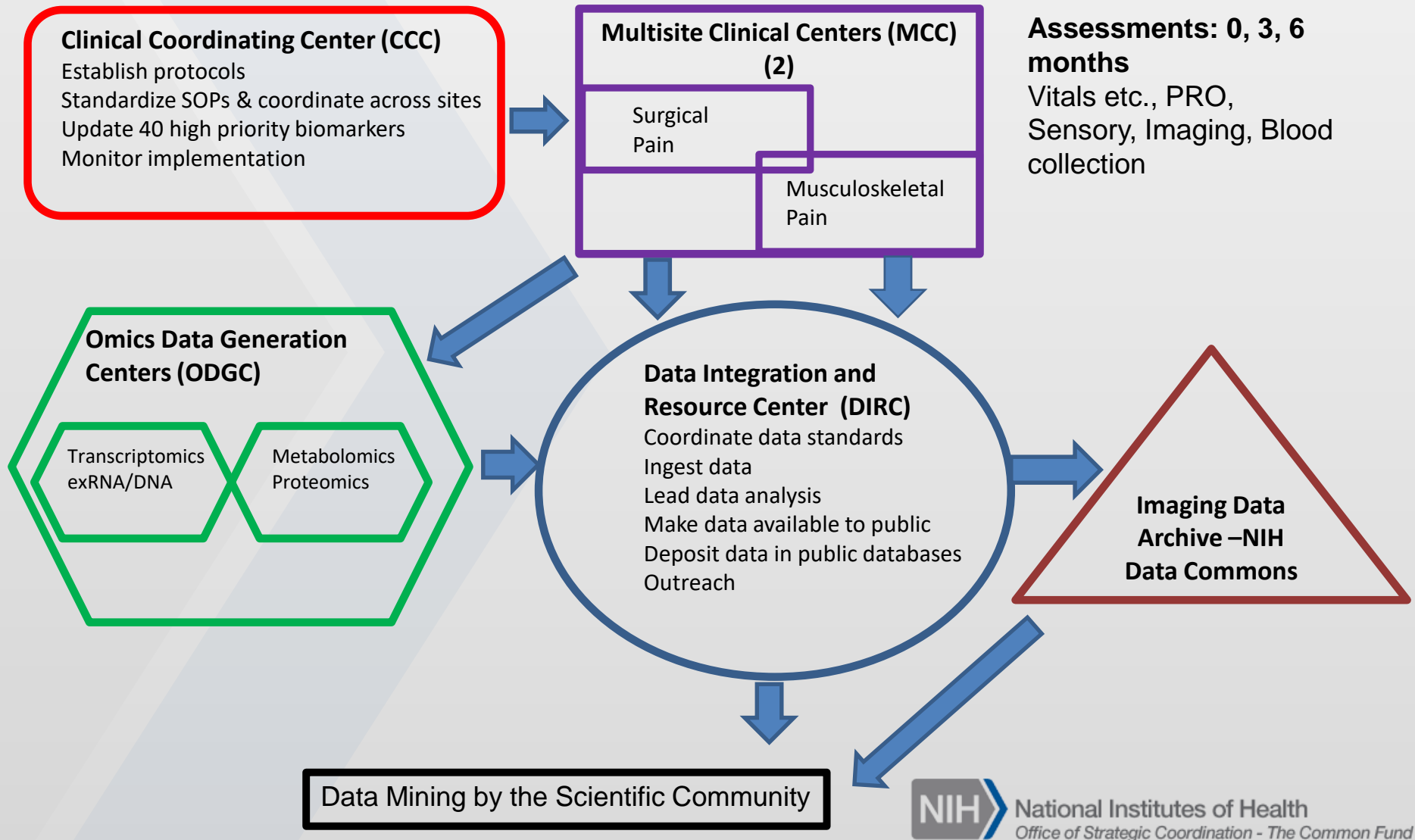
Key Activities of the MCC (musculoskeletal)

- Same as peri-operative pain RFA except:

- Applicants should plan to develop a study enrolling ~ 1800 patients over a two-year period from a SINGLE specific type of **musculoskeletal trauma** (e.g. bone fracture event with expected 30% to 60% rate of transition from acute to chronic pain), and retain these patients for assessments at time = 0, 3 months, and 6 months post-trauma.

- Applicants should plan to provide justification for the selected musculoskeletal trauma with consideration of expected transition rate from acute to chronic pain based on the scientific literature and from their own preliminary data, if available.

Program Components



Clinical Coordination Center for Common Fund Acute to Chronic Pain Signatures (A2CPS) Program (U24) (Clinical Trial Optional)

[RFA-RM-18-035](#)

Linda Porter

(porterl@ninds.nih.gov)

CCC (U24) Funding Opportunity Purpose

The purpose of this FOA is to identify and support a Clinical Coordination Center (CCC) for the Common Fund Acute to Chronic Pain Signatures (A2CPS) Program.

The Clinical Coordinating Center is expected to serve as the hub for the Multisite Clinical Centers (below) to support study design, efficiency, progress, and quality, and to coordinate and monitor study implementation across the clinical sites.

The Clinical Coordinating Center will lead the consortium in developing and implementing standardized protocols, safety standards, staff training protocols, electronic health record (EHR) data standards, patient phenotyping and testing, and regulatory processes.

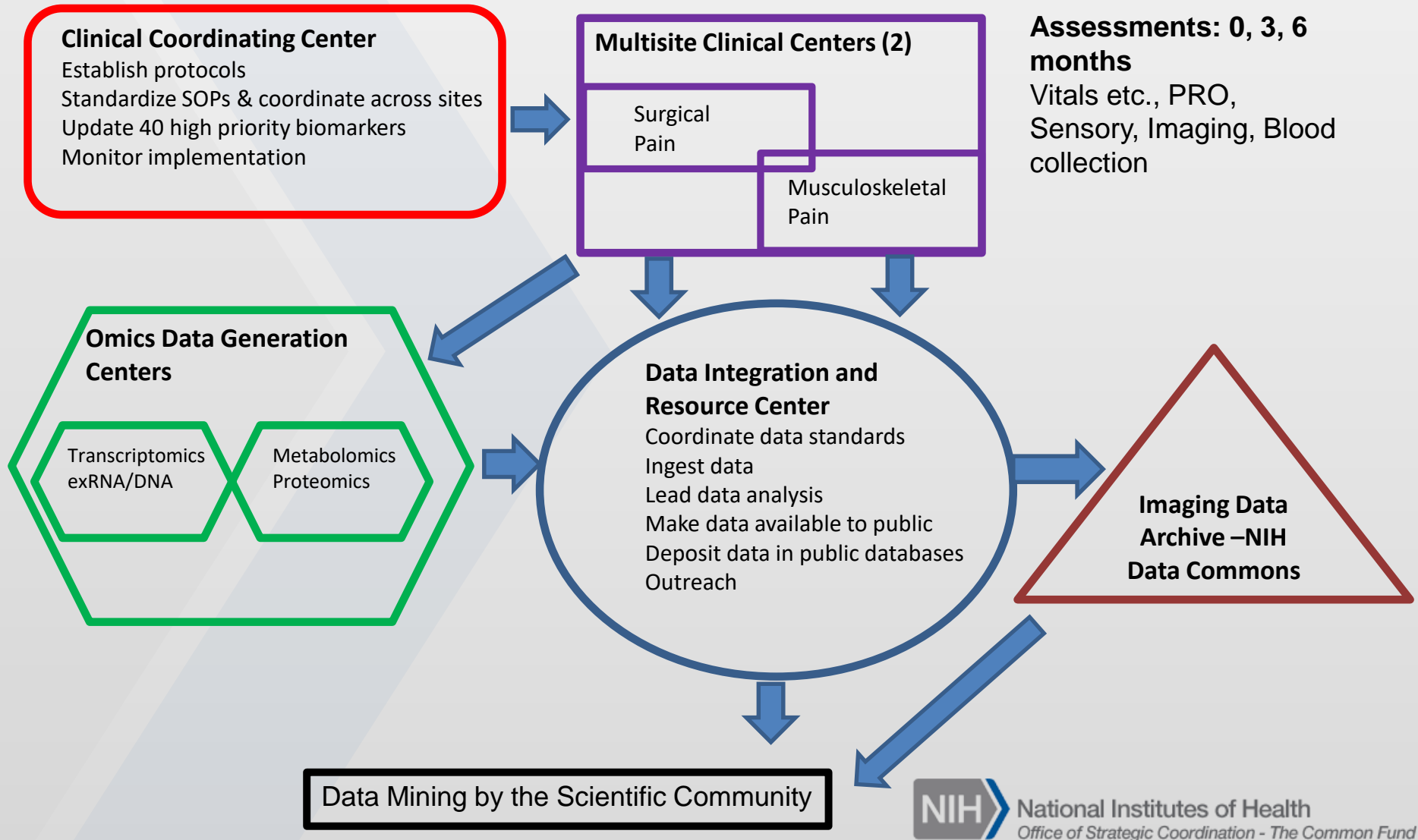
Key Activities of the CCC (U24)

- Interact extensively with the consortium members (MCCs, DIRC, ODGC) and NIH staff and provide oversight and management of collaborative activities across the consortium to define and achieve the overall goals of A2CPS.
- Lead the consortium PDs/PIs with input from NIH staff in assessing and refining study design to optimize likelihood of success.
- Establish regulatory processes, including an independent central Institutional Review Board.
- Establish clinical protocols and standard operating procedures.
(for patient reported outcomes, sensory testing, imaging, and other patient assessments). Develop staff training plans, recruitment and enrollment plans,
- Electronic health record standardization, safety standards, a Data Safety and Monitoring Board, and other regulatory processes.
- Work with the consortium to identify the biospecimen types and amounts to be collected and establish the specimen collection and storage protocols.
- Monitor implementation of recruitment, study assessments, and procedures.

CCC (U24) Application Considerations:

- Applicants should indicate their successful past experiences in this area and their plans to achieve the necessary functions of the CCC.
- Applicants must provide a timeline and detailed quantitative annual milestones throughout the funding period.
- Applicants should describe demonstrated scientific expertise of key CCC personnel/consultants in the areas of clinical research design, chronic pain, network coordination, administration of research consortia, management of clinical data, statistical analysis, and the development of harmonized protocols and procedures.
- Applicants should describe management of the proposed project, who will oversee the day-to-day activities (e.g., a project manager if not the PD(s)/PI(s)) and how the management structure will support achievement of the proposed goals and milestones. The effective management of the CCC requires a significant commitment by the PD(s)/PI(s) and the leaders of the individual CCC components.

Program Components



Omics Data Generation Centers (ODGCs) for Common Fund Acute to Chronic Pain Signatures Program (U54) (Clinical Trial Optional)

[RFA-RM-18-032](#)

John Satterlee
(satterleej@nida.nih.gov)

Purpose: Support the establishment of center(s) that will use cutting edge technologies to perform omics analyses (e.g. metabolomic, lipidomic, proteomic, extracellular RNA) of body fluids collected by the Acute to Chronic Pain Signatures (A2CPS) consortium. The omics data generated, in concert with other patient assessments, will be used to identify biosignatures predictive of susceptibility or resilience to the development of chronic pain.

ODGC U54 Components:

- **Components:** Metabolomics, Lipidomics, Proteomics, Extracellular RNA, and Other proposed Assays.
- **Cores:** Administrative, Genetic Variant

ODGC Scope:

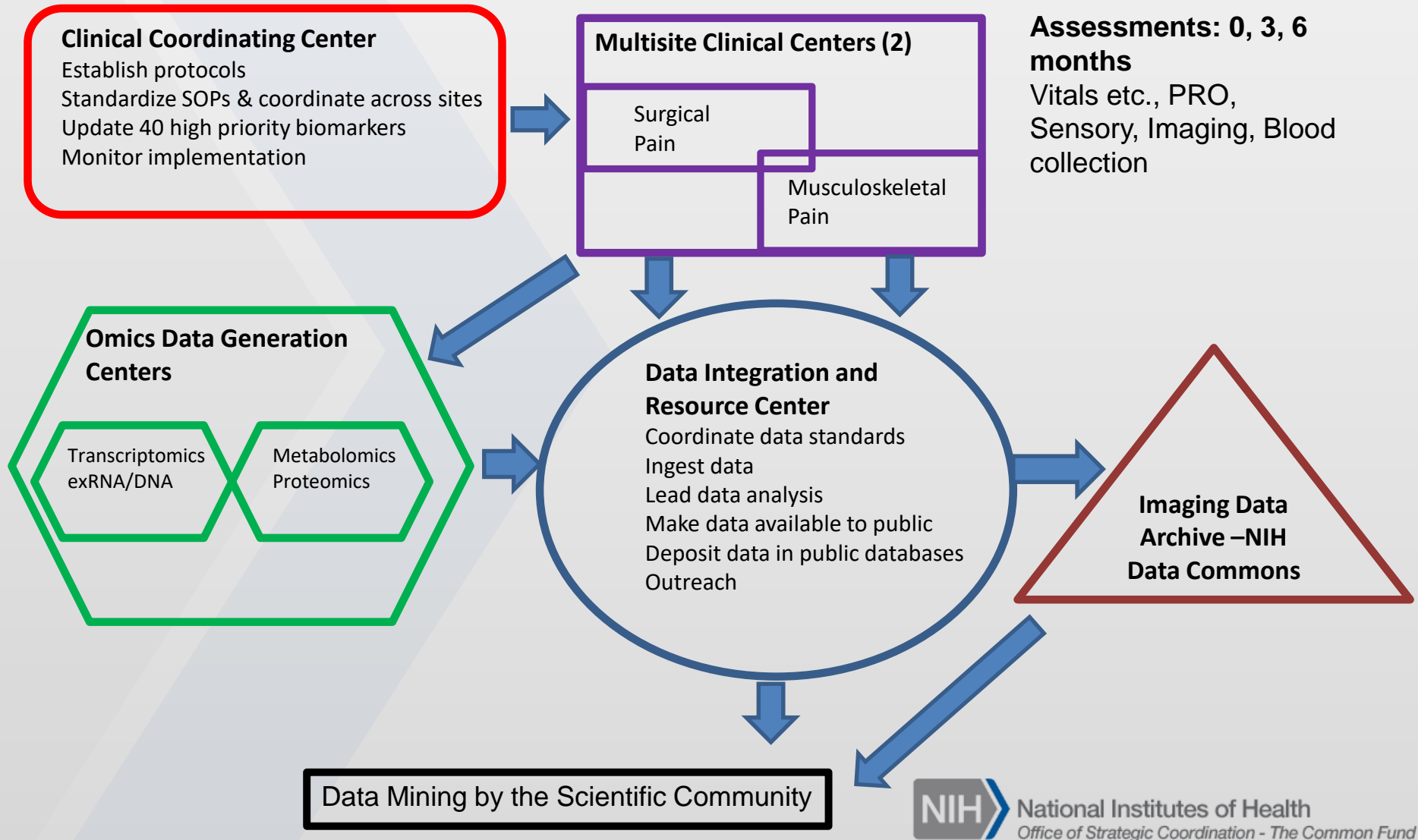
- It is anticipated that there will be two cohorts of ~ 1800 patients each (3600 patients total).
- Biospecimens, most likely blood, but possibly urine or other specimens, will be collected from these patients at the t=0, 3, and 6 month time points by the MCCs.
- Thus, there will be approximately 11,000 samples to be molecularly characterized, not counting any replicates that might be needed.
- These Centers will be expected to provide resources and expertise to perform high quality and reproducible assays on the consortium selected high value candidate biomarkers and additional secondary biomarkers.
- ODGCs will be required to set aside 20% of their budget in order to add any compelling additional omics assays identified by the consortium during the planning year.

ODGC Responsiveness Requirements:

- Include at least five components: proteomics, metabolomics, lipidomics, extracellular RNA, and “other proposed assays.”
- Include an administrative core and a genome variant core.
- Highlight your ability to perform reproducible analysis of blood for major types of assays: proteomics, metabolomics, lipidomics, and extracellular RNA.
- Perform human gene variant measurements using an array based format.
- Plan “other proposed assays” of potentially compelling molecular markers (e.g. cytokine levels, transcriptome/epigenome of purified cell types such as T cells or microglia from blood, microbiome, etc.).
- Detail the proposed omics assays and the total anticipated cost per assay for each sample.

NIH may support individual components from more than one U54 to ensure high quality data is generated for each category of omics assay.

Program Components



RFA-RM-18-031 Data Integration and Resource Center (DIRC) for Common Fund Acute to Chronic Pain Signatures Program (U54)

[RFA-RM-18-031](#)

John Satterlee

(satterleej@nida.nih.gov)

Purpose and Components of DIRC

Purpose: Integrate the efforts of all funded components of the A2CPS and serve as a community-wide nexus for protocols, data, assay and data standards, and other resources generated by the A2CPS Program.

U54 Components:

- Scientific Outreach Component (SOC)
- Data Coordination Component (DCC)
- Data Integration and Analysis Component (DIAC)
- Administrative Core

Key Activities of the DIRC:

- Develop website to serve as community-wide nexus for data and resources generated by A2CPS consortium (SOC).
- Develop workshops and implement a community outreach strategy to disseminate information about the community resources and data generated by the program (SOC).
- Facilitate data use by the scientific community (SOC)
- Ensure that all A2CPS-generated data and metadata have standardized formats and associated quality metrics (DCC).
- Ensure that all generated data and metadata have standardized formats and associated quality metrics (DCC).
- Archive raw and processed datasets generated by the A2CPS Consortium (DCC).
- Make the A2CPS data available to community using resources obtained through NIH Data Commons (<https://commonfund.nih.gov/commons>) to ensure the data will be FAIR (Findable, Accessible, Interoperable, and Reusable) and accessible via cloud based data storage and computing (DCC).
- Work closely with the A2CPS consortium PD(s)/PI(s) to analyze the data generated and share useful information and insights about these data with the broader biomedical research community (DIAC).
- Organize steering committee meetings, workgroup meetings, and other awardee meetings. (Admin Core)

DIRC Applicant Considerations:

- Applications that do not include a description of all three distinct stand-alone components (DCC, DIAC, and SOC) and an administrative core will be deemed by NIH staff to be **NON-RESPONSIVE** to this FOA and administratively withdrawn without review.
- Describe how the different components of the DIRC will interact with one another and how the different components of the DIRC will interact with other funded components of A2CPS.
- Applicants should describe how you will prioritize your activities to ensure that the main goal of the A2CPS, the identification of biosignatures for acute to chronic pain susceptibility or resilience, will be achieved.
- As the data storage, analysis, and dissemination needs of the A2CPS consortium change with time, components of the DIRC may be asked to implement modifications to their workflows as agreed upon by the A2CPS consortium. All components of the DIRC should indicate their willingness to be flexible in their implementation of data coordination, analysis, and outreach workflows.



Center for
Scientific Review

Overview of Scientific Review Process

Joseph Rudolph, Ph.D.

Acting Chief, Emerging Technologies and Training in
Neuroscience IRG

Center for Scientific Review, NIH

Review – who will review my application?

- Reviewed in Center for Scientific Review (CSR)
- Special Emphasis Panels (SEP) – no need to look up and request a standing study section. One-time panels held to review applications on special topics.
- Include only temporary members
- Meeting rosters will be posted online 30 days before the review meeting -
<https://public.csr.nih.gov/StudySections/SpecialEmphasis/>

Review Information

- Refer to Section V of the FOA – “Application Review Information”
- Read Criteria.
- **Pay special attention and address “Specific to this FOA” review questions.**

Overall Impact and Review Criteria

- **Overall Impact:** The reviewers will assess the likelihood for the project to exert a sustained, powerful influence on the research field(s) involved, in consideration of the following review criteria (as applicable for the project proposed).
- Five Scored Review criteria: Significance, Investigator(s), Innovation, Approach, Environment
- Additional Review Criteria: Protections for Human Subjects, Vertebrate Animals, Biohazards

Overview of Cooperative Agreements: U Mechanism

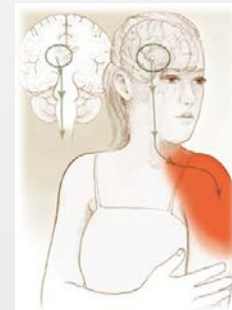
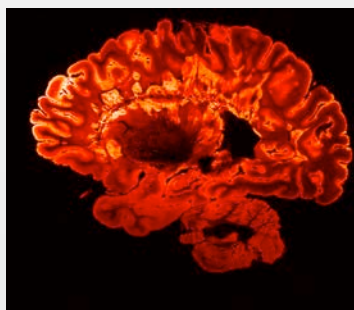
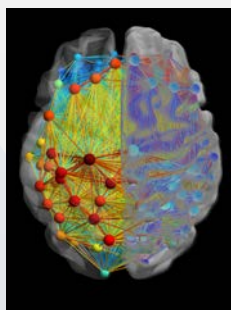
- Used when **substantial programmatic involvement is anticipated between the Federal agency and the recipient** during performance of the assisted activity.
- Supports and stimulates the recipients' activities by involvement in and working jointly with the award recipients in a **partnership role**; it is not to assume direction, prime responsibility, or a dominant role in the activities. **The dominant role and prime responsibility reside with the awardees** of the project as a whole.
- The Cooperative Agreement Terms and Conditions of Award in each FOA clearly outlines the roles and expectations of the PD/PI and NIH Program Staff.
- This information will also be in the Notice of Award (NoA)

Cooperative Agreements Terms and Conditions of Awards

- Acceptance of the Notice of Award (NoA) indicates recipients' willingness to work with NIH Program staff during the course of the award.
- To participate in semi-annual meetings and in regular conference calls with NIH program staff and other A2CPS grantees.
- To actively seek input from NIH regarding resource needs or expertise needs that may arise during the performance of the project.
- To work within a consortium agreement to meet the goals of the Program.

Resources

- NIH Grants Policy Statement:
<https://grants.nih.gov/grants/policy/nihgps/HTML5/introduction.htm>
- SF424 (R&R) General Instructions for NIH and other PHS Agencies:
<https://grants.nih.gov/grants/how-to-apply-application-guide/forms-d/general-forms-d.pdf>
- Funding Opportunity Announcements:
 - Data Integration and Resource Center (DIRC): [RFA-RM-18-031](#)
 - Omics Data Generation Centers (ODGCs): [RFA-RM-18-032](#)
 - Multisite Clinical Center: Acute Pain from Musculoskeletal Trauma: [RFA-RM-18-033](#)
 - Multisite Clinical Center: Acute Peri-operative Pain: [RFA-RM-18-034](#)
 - Clinical Coordination Center: [RFA-RM-18-035](#)



Important Contacts

Scientific/Research Contact(s)

RFA-RM-18-031 & -032

- John Satterlee, Ph.D.; NIDA
- Tel.: 301.435.1020
- Email: satterleej@nida.nih.gov

RFA-RM-18-033, -034, & -035

- Linda Porter, Ph.D., NINDS
- Tel: 301.451.4460
- Email: porterl@ninds.nih.gov

Peer Review Contact

- Joseph Rudolph, Ph.D.; CSR
- Tel: 301.408.9098
- Email: josephru@csr.nih.gov

Grants Management (RFA-RM-18-031 &-032)

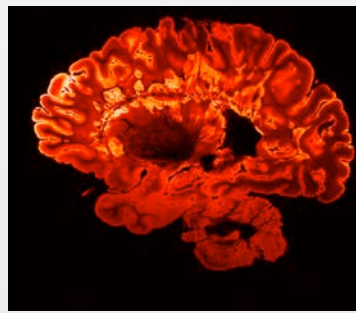
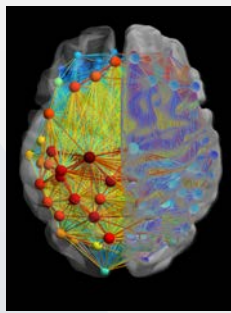
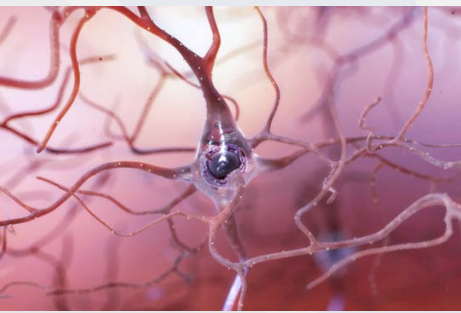
- Aida Vasquez; NIDA
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Grants Management (RFA-RM-18-033, -034, & -035)

- Yvonne Talley; NINDS
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- E-mail: yvonne.talley@nih.gov

Common Fund

- Trish Labosky, Ph.D., OD/OSC
- Tel: 301.594.4863
- E-mail: patricia.labosky@nih.gov



Questions?

Please submit using the **Q&A box**

All questions submitted to the A2CPS email address (A2CPS@nih.gov) during the webinar will be answered in the order they were received.