

Acute to Chronic Pain Signatures (A2CPS)

Applicant Webinar

September 19, 2019



We will start @ 11:05 AM EST

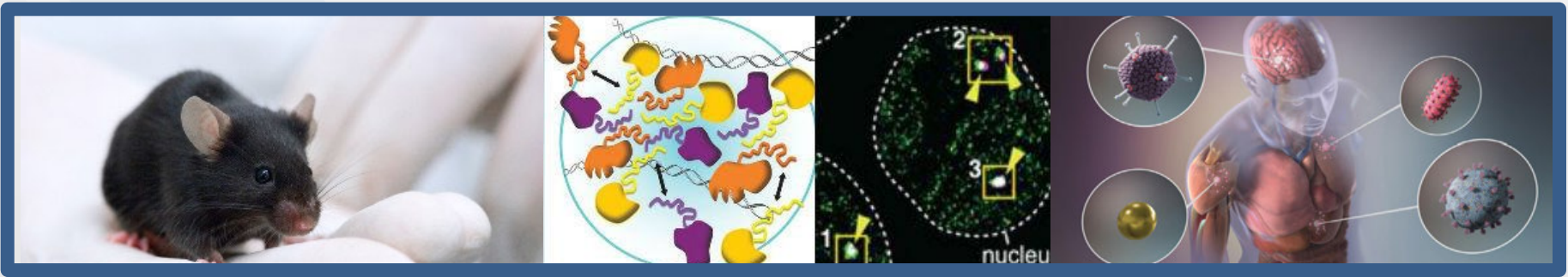
Webinar Logistics

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 Linda Porter (porterl@ninds.nih.gov) 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** – 10 min; Trish Labosky, Common Fund, OD/OSC
- **Funding announcement overviews** – 10 min; Linda Porter, NINDS
- **Review procedure** – 5 min; Jasenka Borzan, CSR
- **Cooperative agreement overview & application deadlines** – 5 min; Linda Porter, NINDS
- **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



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

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,*

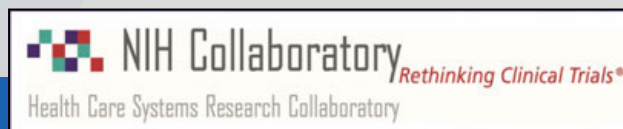
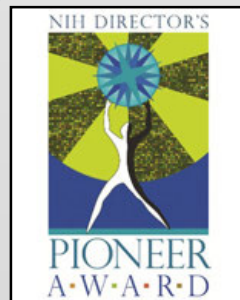
SECTION 1. SHORT TITLE.

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

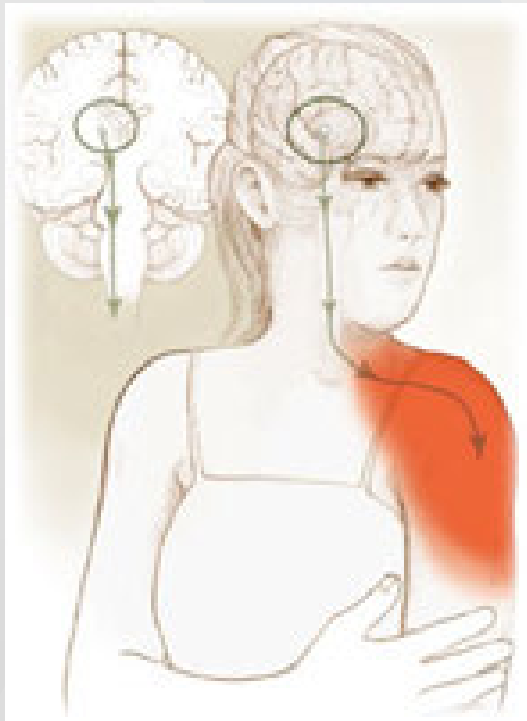
TITLE I—NIH REFORM

Criteria for Common Fund Programs

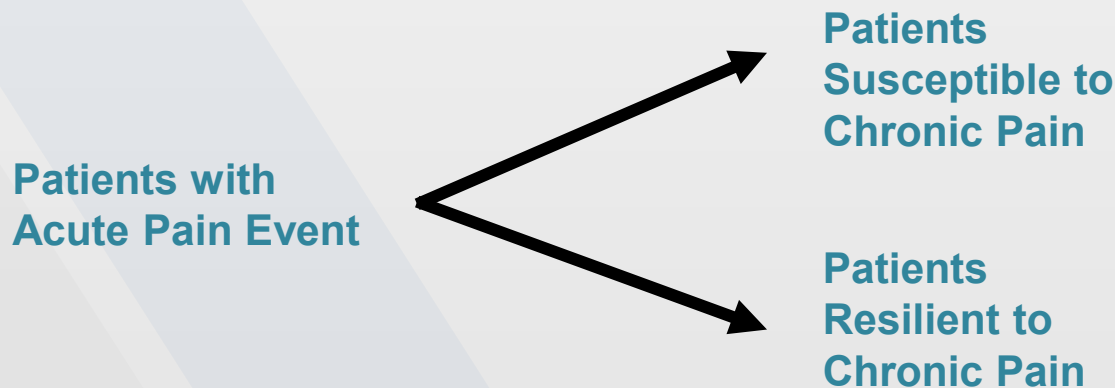
- **Transformative:** Must have high potential to dramatically affect biomedical and/or behavioral research over the next decade
- **Catalytic:** Must achieve a defined set of high impact goals within 5-10 years
- **Synergistic:** Outcomes must synergistically promote and advance individual missions 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



Acute to Chronic Pain Signatures (A2CPS)



Program Goal & Significance



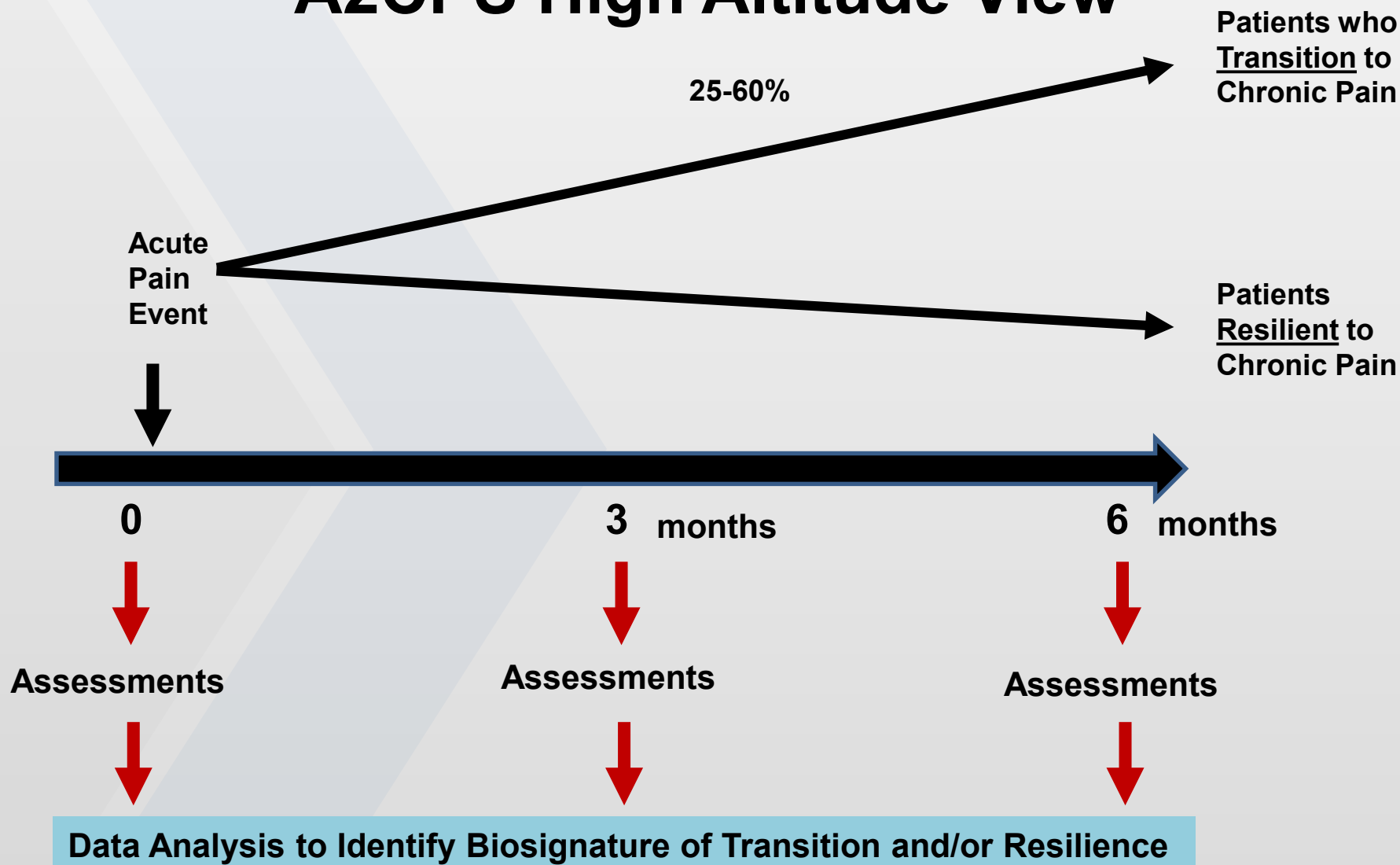
Goal: Identify *objective biosignatures* to predict

- 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)

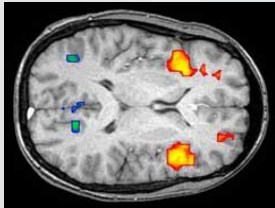
A2CPS High Altitude View



Potential Biomarkers

Circuit Changes: Imaging and QST:

- fMRI
- Resting State-MRI
- Thermal pain sensitivity
- Mechanical pain sensitivity
- Descending pain modulation



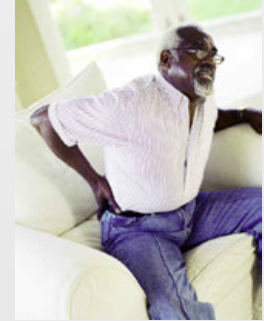
Psychosocial Characteristics

- Pain catastrophizing
- Depression
- Anxiety
- Prior trauma
- Sleep quality and quantity
- Disability



Pain Characteristics:

- Pain severity
- Physical activity level
- Assessment of widespread pain
- Co-occurring pain conditions

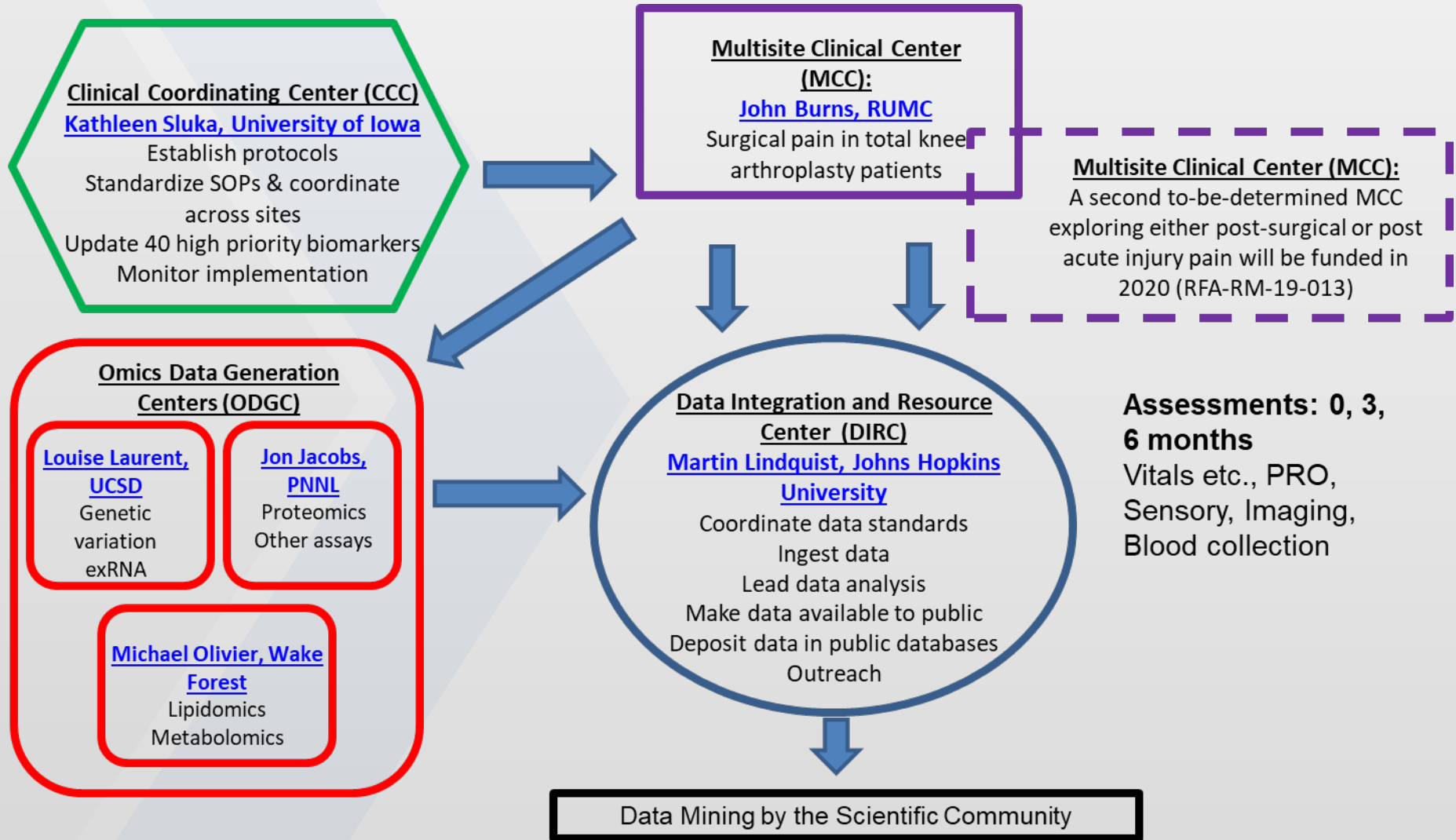


Omics/Bio-specimen Analyses:

- 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



Funded A2CPS Components

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

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.

RFA-RM-18-032: Omics Data Generation Centers (ODGCs) for Common Fund Acute to Chronic Pain Signatures Program (U54)

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.

Funded A2CPS Components, cont.

RFA-RM-18-034: Multisite Clinical Center Common Fund Acute to Chronic Pain Signatures Program: Acute Peri-operative Pain (UM1)

Support a Multisite Clinical Center to implement enrollment and multimodal longitudinal assessment of a large cohort of **acute peri-operative pain** patients (Total Knee Arthroplasty patients) to identify a biosignature for resilience to and the transition from acute to chronic pain.

RFA-RM-18-035: Clinical Coordination Center for Common Fund Acute to Chronic Pain Signatures (A2CPS) Program (U24)

Support a Clinical Coordination Center (CCC) for the Common Fund Acute to Chronic Pain Signatures (A2CPS) Program. The Clinical Coordinating Center will serve as the hub for the Multisite Clinical Centers 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.

MCC2 Integration with the Existing A2CPS Program

During the first (planning) year of the A2CPS program:

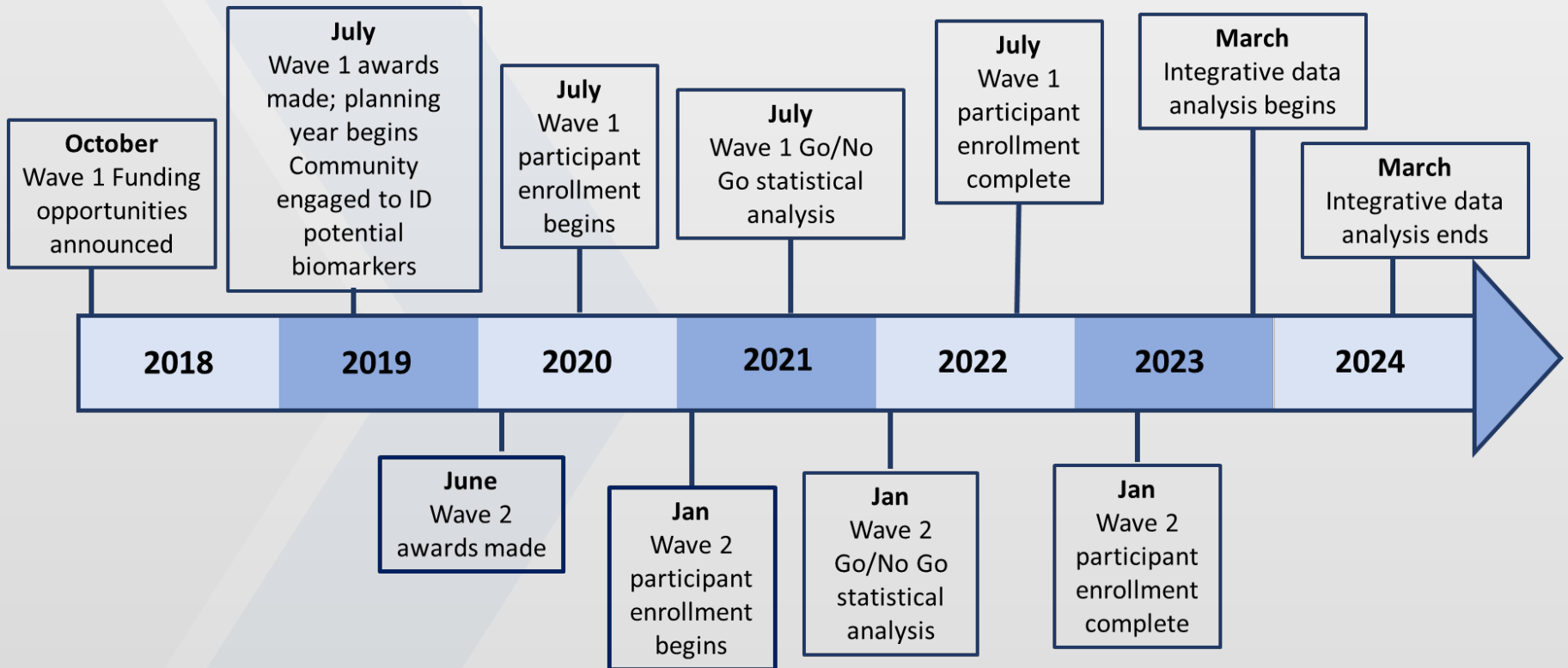
- External Program Consultants will be engaged to provide feedback on the program progress, and a Steering Committee consisting of A2CPS PIs and NIH Staff will be established to provide program governance.
- At the Kickoff Meeting in September 2019, an expert panel consisting of Consortium members, EPCs, and outside experts will recommend approximately 40 evidence-based candidate biomarkers.
- The A2CPS Consortium will establish workgroups to develop clinical protocols, standard operating procedures, staff training plans, recruitment plans, data standards, safety standards, and regulatory processes, identify biospecimen types and amounts to be collected and develop biospecimen collection and storage protocols.
- The Consortium will assess and refine the statistical analysis plan (including power analysis) for each cohort.
- **MCC2 Awardee will be expected to adhere to the existing Consortium standards and regulations.**

MCC2 Integration with the Existing A2CPS Program

MCC2 Awardee Timeline:

- After satisfactory completion of the 6 month planning period, the awardee from this FOA will begin patient enrollment (January 2021).
- In January 2022 or at approximately 50% completion of 6 month phenotyping, a futility assessment will be performed to determine whether the rate of transition to chronic pain and patient retention is adequate to meet the assumptions of the power analysis.
- In the event of lower than expected transition or poor retention of patients, the A2CPS Steering Committee with the EPCs will make recommendations to NIH to either increase enrollment or terminate the study. NIH leadership will make the final determination.
- We expect enrollment to be complete by January 2023, and clinical assessments to be complete by July 2023.
- Data analysis and public archiving of the data for data mining efforts by the scientific community should be complete by August 2024.

Anticipated A2CPS Timeline



Application Considerations

- **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 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 biannual meetings over the course of the A2CPS Program.

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 or Musculoskeletal Trauma(UM1)
Clinical Trial Optional**

[RFA-RM-19-013](#)

Linda Porter

(porterl@ninds.nih.gov)

RM19-013 Funding Opportunity Purpose

To support a Multisite Clinical Center to implement the enrollment and multimodal longitudinal assessment of a large cohort of patients that EITHER experienced an acute musculoskeletal trauma OR an acute peri-operative pain event to identify a biosignature for resilience to and/or the transition from acute to chronic pain.

Key Activities of the MCC

- Communicate effectively with other consortium members (CCC, DIRC, ODGC, and the companion MCC) and NIH staff to achieve the overall goals of A2CPS. The MCC is expected to work as a consortium with the CCC, ODGCs, DIRC and companion MCC. 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 care, including pain care.
- Capture opioid use, including whether patient is dependent on opioids at the 6-month assessment.
- Capture relevant details in the 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 OR a SINGLE specific type of musculoskeletal trauma (e.g. thoracotomy or other surgical procedure with expected 30% to 60% rate of transition from acute to chronic pain, or a 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-surgery.
- Justification for the selected surgical procedure OR musculoskeletal trauma 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 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.
- Propose and justify at least ten potential candidate biomarkers that you consider as the most compelling based on the scientific literature or from their own preliminary data.
- Include steps to avoid unconscious experimenter bias with respect to diagnosis of transition chronic pain.

U.S. Department of Health & Human Services



Center for
Scientific Review

Overview of Scientific Review Process

Jasenka Borzan, Ph.D.

Scientific Review Officer, Integrative, Functional and
Cognitive 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

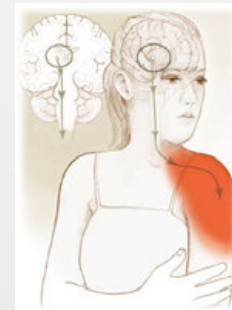
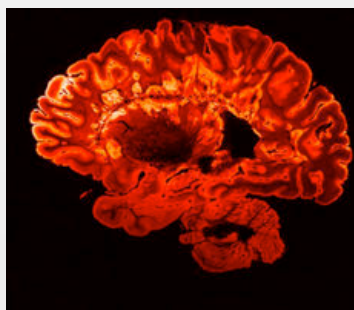
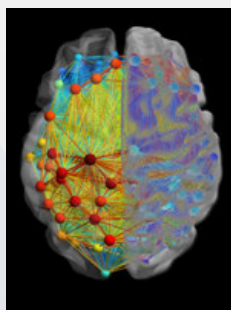
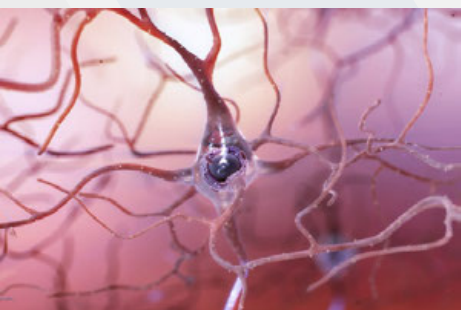
- Used when **substantial programmatic involvement is anticipated between the Federal agency and the recipient** during performance of the assisted activity.
- Supports and stimulates the recipients' activities by involvement in and working jointly with the award recipients in a **partnership role**; 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 the 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 Announcement:
 - Multisite Clinical Center: Acute Peri-operative Pain or Musculoskeletal Trauma [RFA-RM-19-013](#)



Important Contacts

Scientific/Research Contact(s)

RFA-RM-19-013

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

Peer Review Contact

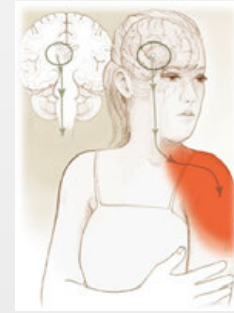
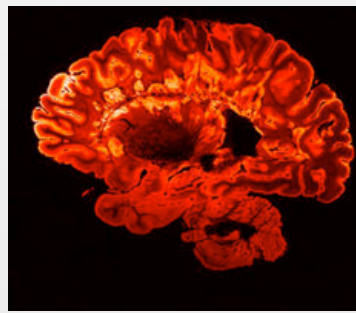
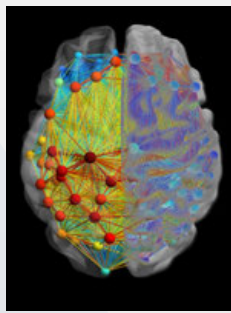
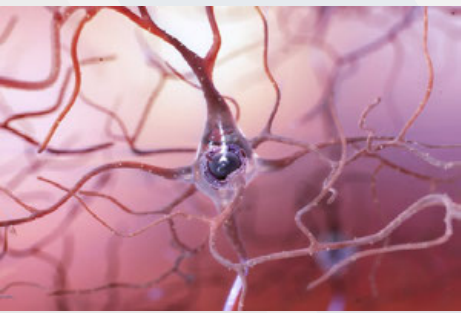
- Jasenka Borzan, Ph.D.; CSR
- Tel: 301.435.1260
- Email: jasenka.borzan@nih.gov

Grants Management

- Yvonne Talley; NINDS
- Tel: 301.496.7432
- 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.