Concept Proposal for a Common Fund Program

Acute-to-Chronic Transition Signatures (ACTS) for Pain

Patricia Labosky, Ph.D.
Office of Strategic Coordination
Division of Program Coordination, Planning, and Strategic Initiatives
Council of Councils Concept Clearance
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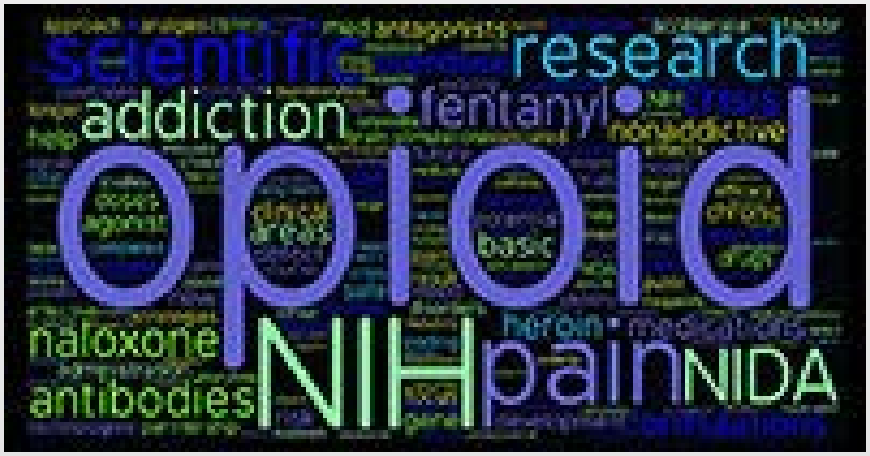
Why a Common Fund Program on Pain?

Need: Nearly 26 million Americans report pain every day. Their sole treatment is often opioids. Deaths from opioid overdoses exceeded 33,000 in 2015 and are on the rise. Patients with chronic pain need safer and more effective treatments.



Scientific Gap: There are no objective signatures of the transition from acute to chronic pain. This study will enable identification of patients at risk for chronic pain and may guide pain prevention management plans.

Why a trans-NIH Program: Chronic pain is a symptom of many diseases and can be a disease in of itself. It cuts across the IC spectrum. This project will involve scientists from diverse areas of research and will bring in advanced technologies. We foresee 'omics, neuroimaging, sensory testing, psychosocial behavioral assessments, metabolomics, etc.. This effort will require NIH coordination.

External Input

Medications Development for Opioid Use Disorders and Overdose Prevention/Reversal
June 5, 2017

Development of Safe, Effective, and Non-Addictive Pain Treatments
June 16, 2017

Understanding the Neurobiological Mechanisms of Pain
July 7, 2017

External Input

Key themes emerged during the meetings:

- Linkages between industry and academic can promote effective use of limited resources;
- Pain research would benefit from **leveraging available neuroscience technologies** and encouraging more neuroscientists to enter the pain field;
- Pain processing is complex throughout brain and periphery. **Need for multidisciplinary efforts to understand pain at the molecular, cellular, circuit, and system levels;**
- ***Standardized, objective biomarkers*** **are needed that will predict the response to treatment in animal models and in humans;**
- ***Extensive patient phenotyping*** **is needed to develop objective biomarkers** to enable precision medicine approaches to more effectively treat patient pain, and factors affecting patient's experience of pain;
- Need for **objective screens** based on the neurobiology of pain to accelerate the drug development process;
- Research gaps regarding prolonged effects of chronic pain, long term impacts of treatment (e.g. hyperalgesia due to chronic opioid use), ***and the transition from acute to chronic pain.***

External Input

Federal Pain Research Strategy

The Federal Pain Research Strategy -- effort of the Interagency Pain Research Coordinating Committee and the National Institutes of Health to **oversee development of a long-term strategic plan** for those federal agencies and departments that support pain research. A diverse and balanced group of scientific experts, patient advocates, and federal representatives **identified and prioritized research recommendations** as a basis for this long-term strategic plan to coordinate and advance the federal pain research agenda. Key research priorities were identified across groups as “top priorities”.

NIH The Interagency Pain Research Coordinating Committee

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

External Input

The 2017 Federal Pain Research Strategy
Acute to Chronic Pain Research Priorities

FPRS Top Priority: ***Understand and Address Plasticity Mechanisms that Promote Persistent Pain and (Endogenous) Resolution Mechanisms that May Reverse Persistent Pain.***

FPRS Top Priority: ***Prospective Studies for Susceptibility and Resilience Factors Underlying the Transition from Acute to Chronic Pain***

FPRS Top Priority: ***Develop Approaches Incorporating the Principles of Precision Medicine to Prevent and Effectively Treat Chronic Pain.***

Proposed CF Pain Program

Discovery-focused clinical trial to identify objective signatures (genetic, imaging, molecular, biochemical) that associate with transition from acute to chronic pain.

- Recruit patients with **clear T=0 acute pain event** with known incidence of transition to chronic pain
  - T=0 surgery, trauma, injury, other?
- Follow for ~6 months to identify factors in those who **transition to chronic pain vs who is resilient**
  - Clinical records
  - Psychosocial and psychophysical assessment
  - Neuroimaging
  - Multi'omic phenotyping: Genomics, Metabolomics, Proteomics, secreted RNA transcriptomics

Parallel discovery-focused clinical study to identify objective signatures (genetic, imaging, molecular, biochemical) that associate with chronic pain lasting more than one year.

- Recruit patients with selected acute pain event, who have established chronic pain > 1 year
- Assess factors as in the transition cohort

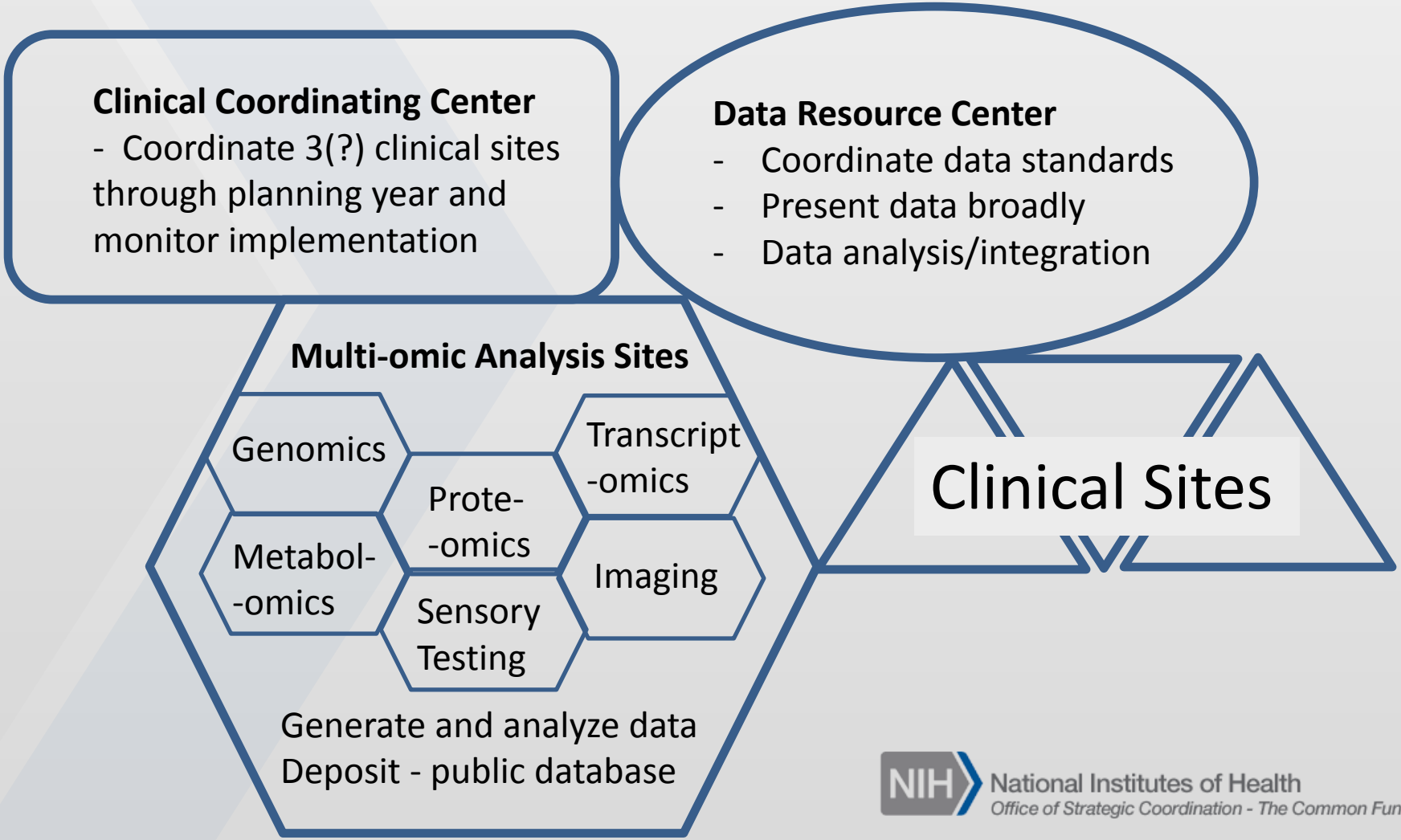
Data Coordination and Analysis

- Signatures that predict transition to chronic pain
- Signatures that define established chronic pain
- Signatures that predict efficacy of pain management strategies

Proposed CF Pain Program

- **Clinical projects** (~3 projects, each of which would be multi-site)
  - **Applicants** would justify the acute pain event to study, describe recruitment capacity and clinical assessments to be conducted in both the transition and established chronic pain cohort
  - **Peer review** would consider the appropriate types of pain and clinical assessment strategies proposed
  - **Awardees would work together during an initial planning year** to determine collectively consortium protocols so that signatures from all patient groups can be compared
    - Pain management protocols
    - Clinical measures, types/timeframe for sample/data collection
    - Psychosocial assessments
    - Imaging protocols
    - Sample collection protocols

Proposed CF Pain Program



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Trans NIH Working Group

Walter Koroshetz (NINDS)
Nora Volkow (NIDA)

Lauren Atlas (NCCIH)
Inna Belfer (OD/ORWH)
Stephanie Courchesne-Schlink (OD/OSC)
Patricia Labosky (OD/OSC)
Rebecca Lenzi (OD/OSC)
Lucie Low (NCATS)
Martha Matocha (NINR)
Leah Pogorzala (NINDS)
Linda Porter (NINDS)
Coryse St Hillaire-Clark (NIA)
John Satterlee (NIDA)
David Shurtleff (NCCIH)
David Thomas (NIDA)
Yolanda Vallejo (NIDCR)