NIH HEAL Initiative: Program Update and Funding Opportunities for Pain Research Available through NIH

AAMC Webinar
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Pain is at the root of the opioid epidemic
Balancing Act of Treating Pain, Prescribing Opioids

100 million American adults have pain
- 40 million have severe pain
- 25 million report daily pain
- 8 million have pain that interferes with lifestyle

Source: NIDA, IMS Health, National Prescription Audit, years 1997-2011
Overdose deaths are increasing with influx of synthetic opioids.

Overdose Deaths Involving Opioids, by Type of Opioid, United States, 2000-2016

- Any Opioid
- Other Synthetic Opioids (e.g., fentanyl, tramadol)
- Heroin
- Natural & Semi-Synthetic Opioids (e.g., oxycodone, hydrocodone)
- Methadone

NIH Helping to End Addiction Long-term (HEAL) Initiative

• Funding of $500M/year provides opportunity to:
  – Improve prevention and treatment strategies, both in clinic and real world settings, for opioid misuse and addiction
  – Enhance pain management by furthering understanding of neurobiology of pain, developing non-addictive treatments, and building a Clinical Trial Network for pain
• Coordinating with the Surgeon General, our sister HHS agencies, local government officials

For more information on research programs related to opioid use disorder and overdose, please visit: www.nih.gov/heal-initiative
HEAL Research on Opioid Misuse and Addiction

• Develop new treatments for opioid addiction, including more flexible medications options and novel immunotherapies to opioids
• Advance clinical trials for Neonatal Opioid Withdrawal syndrome to improve short- and long-term outcomes for infants and children
• Enhance the NIDA Clinical Trials Network to build linkages with primary care, emergency departments, and the justice system
• Establish a Justice Community Opioid Innovation Network
• Optimize effective treatments for OUD in the field through the HEALing Communities Study
HEAL Research Priorities on Pain

Enhance Pain Management

- Understand the biological underpinnings of chronic pain
- Accelerate the discovery and pre-clinical development of non-addictive pain treatments
- Advance new non-addictive pain treatments through the clinical pipeline
- Inform best practices for effective pain management while minimizing risk of addiction

Read about the 2018 research plan:

www.nih.gov/heal-initiative

Collins, Koroshetz, Volkow; JAMA, 2018
In 2017, NIH invested $516 million on pain research

Pain cuts across all 27 NIH Institutes and Centers

NINDS leads the NIH Pain Consortium with the goal of enhancing pain research and promoting collaboration across NIH
HEAL Programs for Pain Under Consideration

Discovery
- Acute to Chronic Pain Signatures
- Discover and Validate Novel Targets for Safe and Effective Pain Treatment
- Preclinical Screening Platforms + Optimization of Non-addictive Therapies to Treat Pain

Preclinical Development
- Translating Discoveries Into Effective Stimulation Devices For Pain Treatment

Clinical Trials
- Discovery and Validation of Biomarkers, Biomarker Signatures, and Endpoints for Pain Indications
- Data and Asset Sharing Partnership
- Early Phase Pain Investigation Clinical Network
- Back Pain Research Consortium

Implementation/Dissemination
- Pain Effectiveness Research Trials + Network
- Pragmatic and Implementation Studies for the Management of Pain
The image shows a diagram of HEAL Programs for Pain Under Consideration. The stages of the process are labeled as Discovery, Preclinical Development, Clinical Trials, and Implementation/Dissemination. Below the diagram, there is a section titled "Acute to Chronic Pain Signatures."
Objective biosignatures to identify susceptibility or resilience to chronic pain

- Phenotyping
- Genotyping
- Sensory tests
- Imaging
- -omics

Outcomes

- Mechanisms
- Novel therapeutic targets
- Cohort stratification
- Prevention

Structure:
- Clinical Coordination Center
- Clinical Centers
- Omics Data Generation Centers
- Data Integration and Resource Center

Awards will be made in Spring 2019
Discover and Validate Novel Targets for Safe and Effective Pain Treatment

To promote the basic science discovery and validation of targets for the treatment of pain that can be used to develop treatments that have minimal side effects and little to no abuse/addiction liability

Basic biology target discovery projects

- Encourage collaboration from other fields
- Designed to reveal novel targets for small molecules, natural products, biologics, devices
- Devices: discovery of new sites for stimulation or electrophysiological signatures
- Open to all pain systems in CNS or periphery

Pain target validation

- Novel in vitro/ex vivo assays
- Animal model systems development
- Multidisciplinary tools
- Multisite validation; robustness; reproducibility
- Validation of pharmacodynamic and predictive biomarkers

RFA-NS-18-043 – R01
RFA-NS-18-042 – R21

NIH National Institute of Neurological Disorders and Stroke

Discover and Validate Novel Targets for Safe and Effective Pain Treatment

Preclinical Screening Platforms + Optimization of Non-addictive Therapies to Treat Pain

Acute to Chronic Pain Signatures

HEAL Programs for Pain Under Consideration
Develop human cell/tissue models
- Peripheral and central nervous system
- Normal and disease states
- iPSC-derived neurons, 3D printed organoids, tissue chips

Advance investigational drugs for new targets
- Human tissue constructs to identify new probes/drug leads
- Automated chemical synthesis
- Artificial Intelligence to identify new chemical structures

**IND-enabling studies: Optimization of Non-addictive Therapies [Small Molecules and Biologics] to Treat Pain**

**RFA-NS-19-010**

*The overall goal of this initiative is to support preclinical optimization and development of safe, effective, and non-addictive small molecule and biologic therapies to treat pain.*

[https://ncats.nih.gov/heal](https://ncats.nih.gov/heal)
Will establish a one-stop preclinical testing platform that promotes the testing and characterization of non-addictive modalities for the treatment of pain to accelerate discovery of non-addictive, effective therapies

- Incentivize both academia & industry
- Develop or refine animal models of pain conditions
- Generate high quality data to support partnerships, translational programs
- Provide access to research community

Preclinical Screening Platform

- In vitro µ-opioid receptor screening
- Acute pain models
- Chronic pain/disease models
- In vivo addiction screening

Successful compounds/devices move to clinical trials

2018: Work will start through the University of Utah Epilepsy Therapy Screening Program
2019: A new openly-competited contract will be awarded
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Clinical Trials

Implementation/Dissemination
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Effective Stimulation Devices for Pain Treatment: Program Under Consideration

The overall goal is to translate diagnostic and therapeutic devices into humans to address the opioid epidemic through the development of non-addictive therapies that improve patient outcomes and decrease or eliminate the need to prescribe opioids.

- Building on programs from the BRAIN Initiative, SPARC (Stimulating Peripheral Activity to Relieve Conditions), and HEAL
- Bridging the translational pipeline from mechanism to therapy by supporting late stage device development, verification, and validation
- Supports activities to achieve regulatory and IRB approvals
- Early clinical studies to de-risk these new and improved pain treatments in appropriate clinical populations.

Discovery and Validation of Biomarkers, Biomarker Signatures, and Endpoints for Pain Indications

Discover and Validate Novel Targets for Safe and Effective Pain Treatment

Preclinical Screening Platforms + Optimization of Non-addictive Therapies to Treat Pain

Translating Discoveries Into Effective Stimulation Devices For Pain Treatment

Acute to Chronic Pain Signatures

HEAL Programs for Pain Under Consideration
The overall goal is to facilitate the discovery and development of high-quality biomarkers to accelerate the development of non-addictive therapeutics for the treatment of pain conditions.

**Discovery of Biomarkers, Biomarker Signatures, and Endpoints for Pain**

**RFA-NS-18-041** – R61/R33

Goal is to facilitate the discovery of robust biomarkers, biomarker signatures and objective endpoints for pain conditions.

**Analytical and/or Clinical Validation of a Candidate Biomarker for Pain**

**RFA-NS-18-046** – R61/R33

Goal is to support the analytical and clinical validation of candidate biomarkers for use in the discovery and development of non-opiate alternatives to the treatment of pain conditions using retrospective and/or prospective methods.

NIH Workshop:

“Discovery of Biomarkers to Develop Transformational Non-Addictive Therapeutics for Pain”

November 14-15; Washington, DC
HEAL Programs for Pain Under Consideration

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**Implementation/Dissemination**
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Early Phase Pain Investigation Clinical Network

**Improve quality, consistency, efficiency of pain clinical trials**

- Clinical Coordination Center, Data Coordination Center, 10 specialized clinical sites (hub and spoke design)
- Incentivize, accelerate Phase II trials
- Focus on well-defined pain conditions with high-unmet need
- Reduce the time to start, enroll, run, and complete trials
- Test compounds and devices from industry, academia
- Incorporate biomarker studies
- Accommodate other platform trial designs

NOT-NS-18-069  
NOT-NS-18-057  
NOT-NS-18-058  
RFAs coming soon!
Early Phase Pain Investigation Clinical Network + Data and Asset Sharing Partnership

Clinical Coordination Center
- Clinical expertise
- Pain expertise
- Organizes hubs
- Protocol design (with hubs)

Data Coordination Center
- Statistical expertise
- Trial expertise

Repositories:
Industry and HEAL biosamples and data

Public Private Partnership:
Candidate therapeutics or devices from academia or industry

Biomarker studies

Deep phenotyping studies

10 Specialized Clinical Centers (hubs + spokes)
- Protocol design (with CCC)
- Trial execution

NOT-NS-18-058
NOT-NS-18-057
NOT-NS-18-058
NOT-NS-18-069
Patient-centric translational research initiative that will address the need for effective and personalized therapies for chronic low back pain by probing the biomedical mechanisms in a biopsychosocial context using interdisciplinary methods and innovative technologies.

Goals

- Expand the number of therapeutic options to improve pain and function
- Understand the mechanisms of low back pain
- Use novel technologies to identify new druggable disease mechanisms
- Develop precise diagnostic and treatment algorithms
- Tailor therapies to individual patients
- Test new therapies
Back Pain Research Consortium (BACPAC)
Program Under Consideration

Expected Outcomes

- Integrated model of low back pain through improved understanding of mechanisms, leading to new therapies
- Algorithms to match patients to best treatments based on extensive phenotyping
- Safety and Efficacy Data on new therapies that can move to Phase 3 Trials
- Clinical studies combining multimodal interventions with deep phenotyping and patient reported symptoms and outcomes

NOT-AR-19-022: Mechanistic Research Centers (U19)
NOT-AR-19-023: Data Integration, Algorithm Development and Operations Management Center (U24)
NOT-AR-19-024: Technology Research Sites (UH2/UH3)
NOT-AR-19-025: Phase 2 Clinical Trials (UG3/UH3)

More information and webinar slides available at: http://www.niams.nih.gov/grants-funding/BACPAC
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- Pain Effectiveness Research Trials + Network
Background

– Evidence for optimal pain management in many clinical situations is often insufficient, such as long-term opioid use for management of chronic pain.

Goals

– Establish the HEAL Pain Effectiveness Research Network (HEAL Pain-ERN) to conduct clinical trials and studies designed to establish effective interventions or programs to manage, reduce or prevent acute and chronic pain.
  
  • Initial studies will not be Phase III, placebo-controlled efficacy trials for approval of a new drug or device.

– Leverage the existing Clinical and Translational Science Award (CTSA) - Trial Innovation Network (TIN) to implement meritorious clinical trials/studies of interest to multiple NIH Institutes, Centers and Offices.

– Support studies that provide evidence to inform practice-based guidelines.
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Pragmatic and Implementation Studies for the Management of Pain to Reduce Opioid Prescribing (PRISM) Under Consideration

- Studies must be embedded in health care systems
- System changes to improve adherence to evidence-based guidelines for pain management
- Integration of evidence-based approaches for pain management into health care delivery
- Trials that will inform health care policy makers about coverage decisions and how to implement pain management approaches
- Support of a central resource center to assist trials improve rigor and achieve the project milestones

NIH
National Center for Complementary and Integrative Health

NOT-AT-19-004
NOT-AT-19-005 (acupuncture focus)
Follow HEAL and Find Funding Opportunities on our Website...

NIH HEAL INITIATIVE

About the NIH HEAL Initiative

In April 2018, NIH launched the HEAL (Helping to End Addiction Long-term) Initiative, an aggressive, trans-agency effort to speed scientific solutions to stem the national opioid public health crisis. This Initiative will build on extensive, well-established NIH research, including basic science of the complex neurological pathways involved in pain and addiction.
Thank You!

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