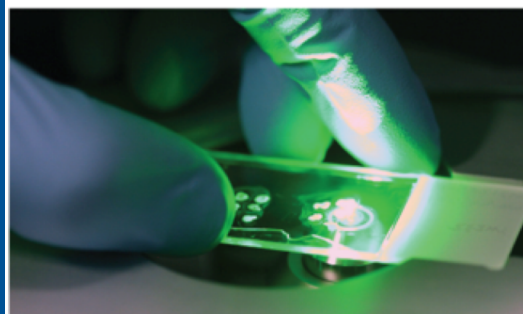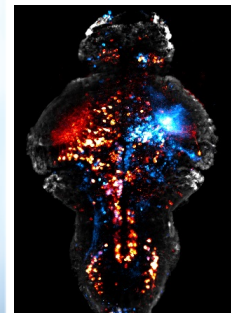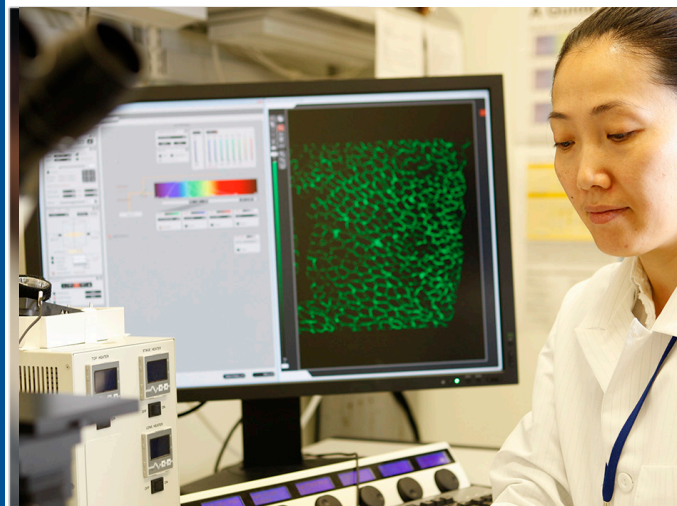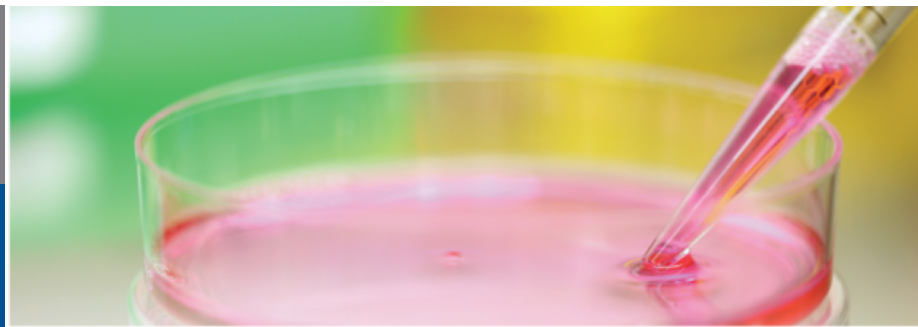# Opportunities in Pain Research with the NIH HEAL Initiative

Clinton Wright, M.D.

Director, Division of Clinical Research

National Institute of Neurological Disorders and Stroke, NIH

September 20, 2018

NIH HEAL: Pain Research Priorities

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

www.nih.gov/heal-initiative

JAMA   June 12, 2018   Opinion

VIEWPOINT

Helping to End Addiction Over the Long-term
The Research Plan for the NIH HEAL Initiative

Collins, Koroshetz, Volkow; JAMA, 2018

National Institute of
Neurological Disorders
and Stroke

Overview of current HEAL Programs for Pain

Discovery → **Preclinical Development** → **Clinical Trials**

Acute to Chronic Pain Signatures

Discover and Validate Novel Targets for Safe and Effective Pain Treatment

Trans-NIH Human-based Screening Platforms

Preclinical Screening Platform for Pain

Optimization of Non-addictive Therapies to Treat Pain ⭐

Translating Discoveries Into Effective Stimulation Devices For Pain Treatment ⭐

⭐ Brand new programs

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

Data and Asset Sharing Partnership

Early Phase Pain Investigation Clinical Network

Pain Effectiveness Research Trials + Network ⭐

NINDS HEAL Job Opportunities: https://www.ninds.nih.gov/About-NINDS/Jobs-At-NINDS/HEAL-Initiative-Employment-Opportunities

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

Clinical Coordination Center, **RFA-RM-18-035**
Multisite Clinical Centers, **RFA-RM-18-034**, **RFA-RM-18-033**
Omics Data Generation Centers, **RFA-RM-18-032**
Data Integration and Resource Center, **RFA-RM-18-031**

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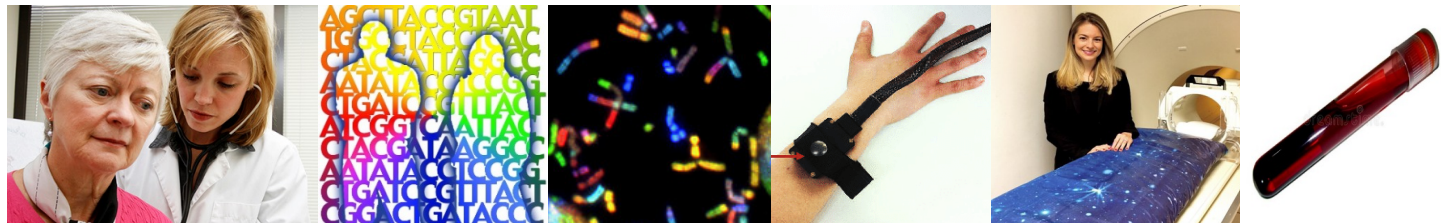
HEAL - Discover and Validate Novel Pain Therapies
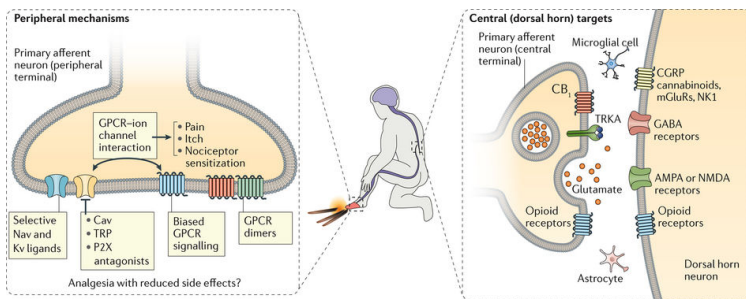
To promote the basic science discovery and validation of targets for the treatment of pain <u>that can be used to develop treatments with minimal side effects and little to no abuse/addiction liability</u>

Nat Rev Drug Discov. 2017 Aug;16(8):545-564.

[NOT-NS-18-073](#) – Administrative Supplements
[NOT-NS-18-080](#) – Notice of Intent to Publish (R01)

Previously identified targets

Basic biology target discovery projects

Pain target validation

- *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*

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

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HEAL - Human Cell-based Preclinical Screening Platforms

Develop human cell/tissue models

- Peripheral and central nervous system
- Normal and disease states
- iPSC-derived neurons, 3D printed organoids, tissue chips

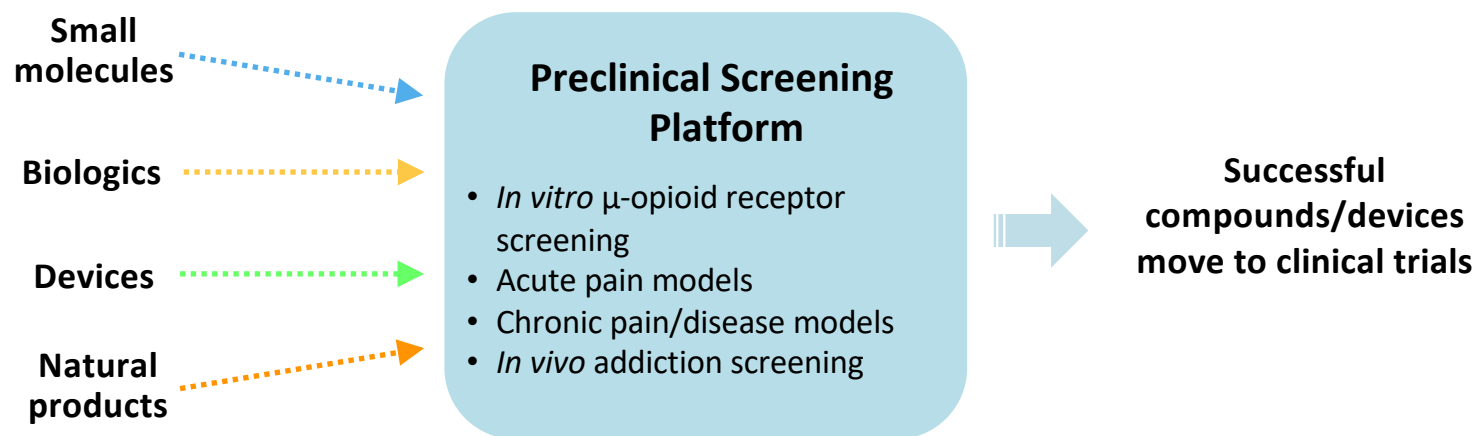Advance investigational drugs for new targets

- Human tissue constructs to identify new probes/drug leads
- Automated chemical synthesis
- Artificial Intelligence to identify new chemical structures
- IND-enabling studies

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https://ncats.nih.gov/heal

National Center for Advancing Translational Sciences

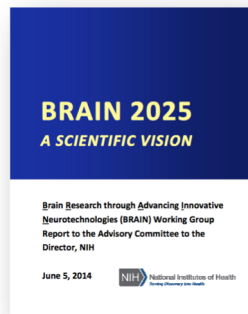# HEAL - Preclinical Screening Platform for Pain

A one-stop preclinical testing platform to promote the testing and characterization of non-addictive modalities for the treatment of pain

- <u>Incentivize academia & industry</u> to accelerate discovery of non-addictive, effective therapies
- Develop or refine animal models of pain conditions available to research community
- Generate high quality data to support partnerships, translational programs

Small molecules

Biologics

Devices

Natural products

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

NIH National I... Neurologi... and Strok...

HEAL – Translating BRAIN/SPARC/HEAL Discoveries into Effective Stimulation Devices for Pain Treatment

Brain
Research through
Advancing
Innovative
Neurotechnologies

BRAIN 2025
A SCIENTIFIC VISION

Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Working Group Report to the Advisory Committee to the Director, NIH

June 5, 2014

The overall goal of this initiative 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.

Stimulating
Peripheral
Activity to
Relieve
Conditions

Other Targets

➢ Goals

  ➢ Leverage ongoing mapping / target discovery activities in BRAIN, SPARC, and other HEAL Initiatives

  ➢ Expand Public Private Partnership efforts in SPARC & BRAIN to engage medical device industry to explore repurposing devices for new indications

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HEAL - Discovery and Validation of Biomarkers, Endpoints and Signatures for Pain Conditions

Define patient populations and treatment response to accelerate therapy development

Discovery of Biomarkers, Biomarker Signatures, and Endpoints for Pain

RFA-NS-18-041 – R61/R33

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

NINDS Funding Opportunity: Analytical and/or Clinical Validation of a Candidate Biomarker for Pain

NOT-NS-18-074 **(RFA coming soon) – R61/R33**

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

Registration now open!

NIH Workshop "Discovery of Biomarkers to Develop Transformational Non-Addictive Therapeutics for Pain"
November 14-15; Washington, DC

National Institute of Neurological Disorders and Stroke

HEAL - Data and Asset Sharing Partnership

Enable companies to access data that will speed development efforts

Data sharing

- Relevant clinical, preclinical, pharmacokinetic data

Asset Repurposing

- Accrue, analyze pharmacological assets from academia, pharma, device companies

Structured data repository
Data storage

Report generation and analysis
Develop dossiers on submitted assets

Data sharing of prior pain efforts
Industry partners review data from successful and failed pain therapy programs
to inform in-house strategies

Asset prioritization / scientific review
Prioritization and triaging to clinical trials network

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HEAL – 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 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!

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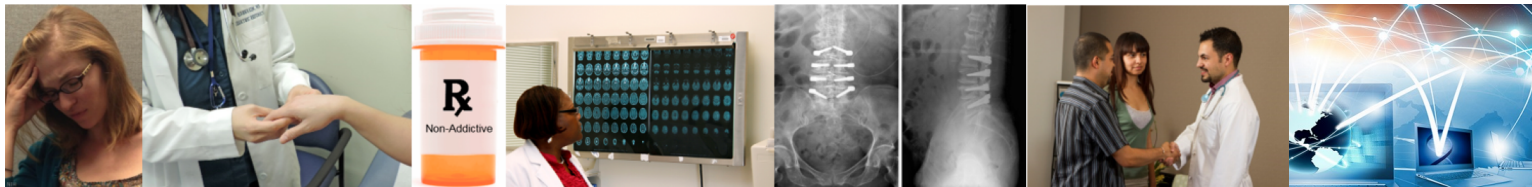
HEAL - Pain Effectiveness Research Network and Trials

To evaluate the effectiveness of pharmacologic and nonpharmacologic therapies for a broad array of pain conditions through phase 3 clinical trials

- Elucidate best treatment for different pain conditions, or best means of personalizing treatment for persons with similar pain conditions
- Focus of FOA(s):
  - Comparative effectiveness research (CER)
  - Trials of different pain therapies
  - Different pain treatment paradigms
- Inform patients and the medical community on how best to treat painful conditions while minimizing potential for addiction

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