Session 2: Selected Research on New Treatments for Pain

NIH · Helping to End Addiction Long-term

Discovery and Validation of New Targets and Biomarkers to Enhance Pain Management
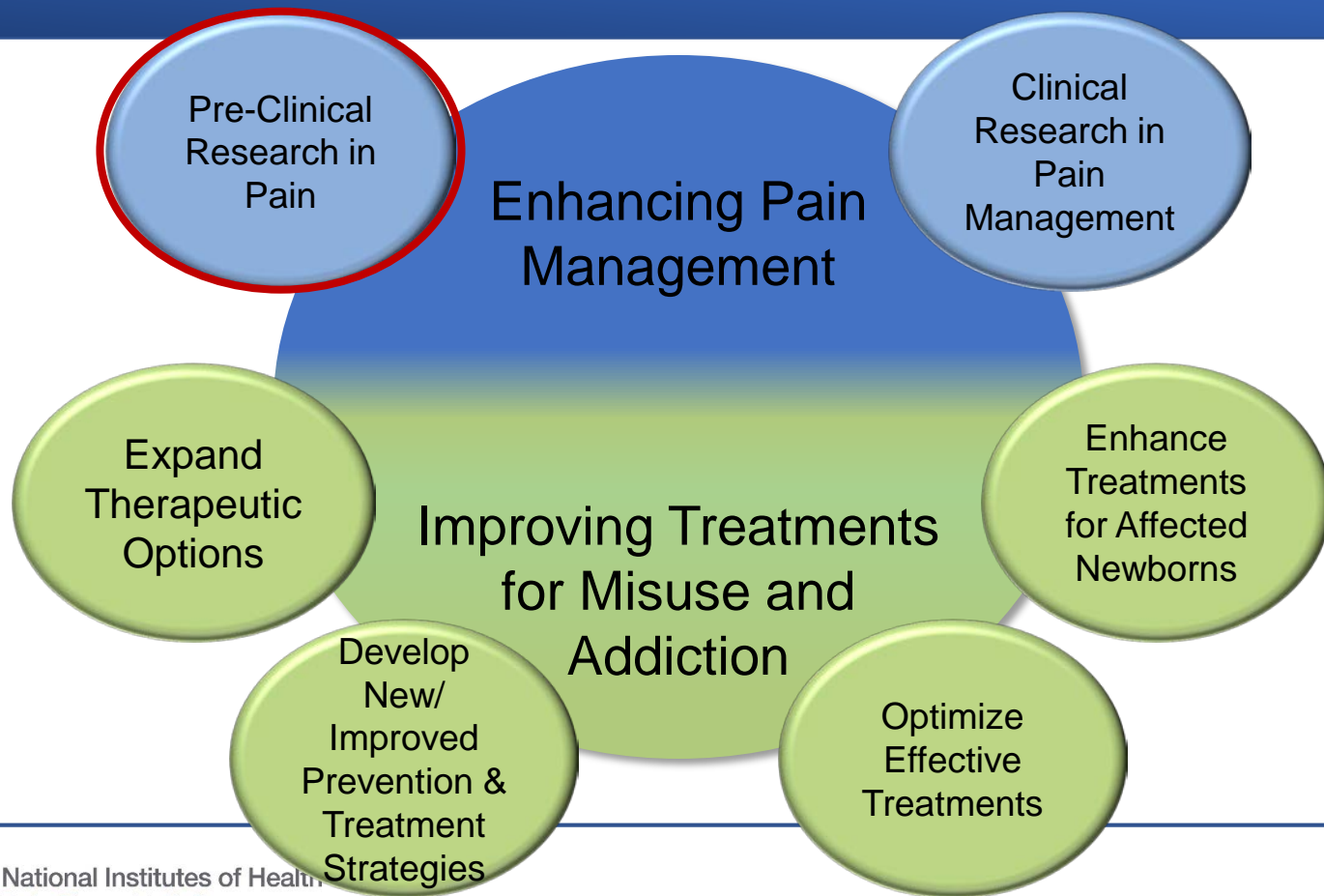
FOR MDWG Input

Michael Oshinsky, Ph.D.

Program Director, Pain and Migraine

National Institute of Neurological Disorders and Stroke

NIH National Institutes of Health
Turning Discovery Into Health

HEAL Initiative Research

Pre-Clinical Research in Pain

Clinical Research in Pain Management

Enhancing Pain Management

Expand Therapeutic Options

Enhance Treatments for Affected Newborns

Improving Treatments for Misuse and Addiction

Develop New/ Improved Prevention & Treatment Strategies

Optimize Effective Treatments

Enhancing Pain Management

- **Pre-Clinical Research in Pain Management**
  - Accelerate the discovery and development of non-addictive treatments for pain
    - Understanding the origins of chronic pain
      - Acute to Chronic Pain Signatures Program
    - Discovery and validation of novel targets for safe and effective pain treatment
    - Biomarkers, signatures and endpoints for pain
    - Translating discoveries into effective devices for pain treatment
    - Engineering preclinical screening platforms + novel drug development
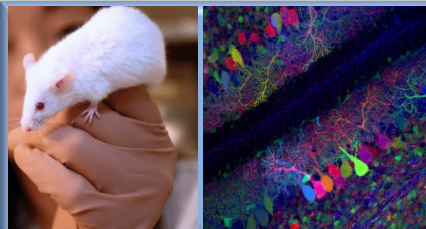
Overview of HEAL Pain Research Projects

Discovery → **Preclinical Development** → **Clinical Trials** → **Implementation/Dissemination**

Acute to Chronic Pain Signatures

Discover and Validate Novel Targets for Safe and Effective Pain Treatment

Preclinical Screening Platforms + Novel Drug Development

Translating Discoveries Into Effective Devices For Pain Treatment

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

Data & Asset Sharing Partnership

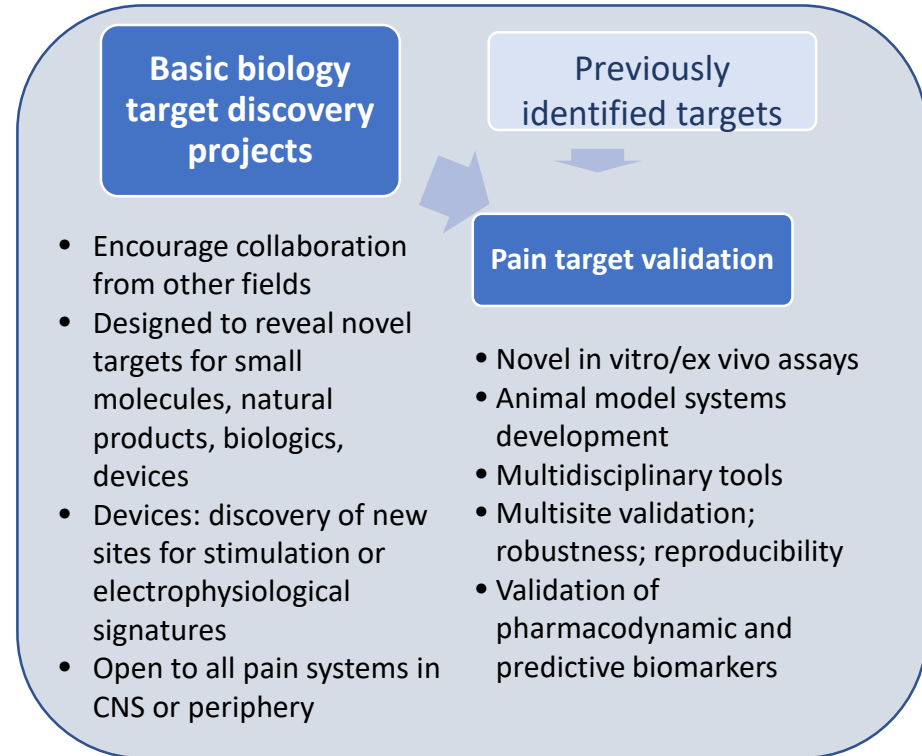Early Phase Pain Investigation Clinical Network

Back Pain Research Consortium

Hemodialysis Pain Management

Pain Effectiveness Research Network

Pragmatic and Implementation Studies for the Management of Pain

Target Discovery and Validation for Safe and Effective Pain Treatment

- Goal: 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
- RFA-NS-18-043 – R01
- RFA-NS-18-042 – R21
- NOT-NS-18-073 – Admin Sups
- Due Dates: February 11, 2019; July 11, 2019; November 12, 2019

Basic biology target discovery projects

Previously identified targets

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

TO BE DISCUSSED LATER TODAY

Biomarkers, Endpoints and Signatures for Pain Conditions

- Discovery of Biomarkers, Biomarker Signatures, and Endpoints for Pain
  - Goal: facilitate the discovery of robust biomarkers, biomarker signatures and objective endpoints for pain conditions
  - RFA-NS-18-041 – R61/R33
- Analytical and/or Clinical Validation of a Candidate Biomarker for Pain
  - Goal: 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
  - RFA-NS-18-046 – R61/R33

- Due Dates: March 7, 2019; November 25, 2019; March 12, 2020

**TO BE DISCUSSED LATER TODAY**

Optimization of Non-addictive Therapies [Small Molecules and Biologics] to Treat Pain

- Goal: Accelerate the optimization and development of promising small molecule and biologic hits/leads into therapeutic agents
  - Assembly of 2 Investigational New Drug (IND) Applications
- Entry Criteria:
  - A rigorous biological rationale for the intended approach
  - A promising small molecule or biologic starting point for optimization
  - Scientifically sound assays to optimize and test the agent
- Cooperative Agreement Mechanisms
  - (RFA-NS-19-010) (UG3/UH3) and SBIR RFA-NS-19-020 (U44 fast-track)
- Two-Stage Cooperative Agreement Mechanism
  - Plan to launch 6-8 projects in FY19, advance 2-3 in FY21 in phase 2
  - Funding will be a mix of grants and contract access
    - (PK/Tox & consultants)
  - Opportunity to utilize NCATS capabilities

Translating Discoveries into Effective Devices for Pain Treatment

enhanced targeting and reduced invasiveness of diagnostic and therapeutic devices to manage pain

Brain
Research through
Advancing
Innovative
Neurotechnologies
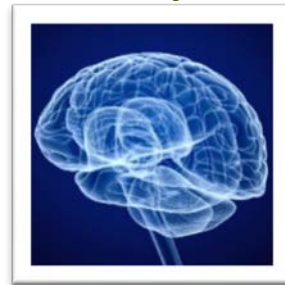
Stimulating
Peripheral
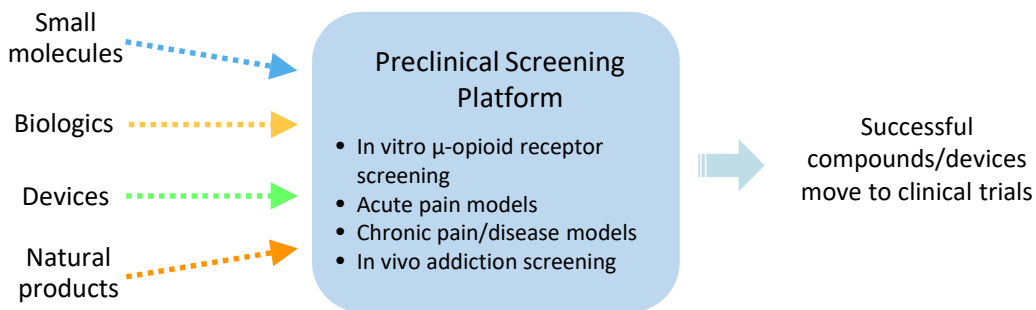**Activity to**
Relieve
Conditions

Other Targets

Funding Opportunities

- Translational Devices to Treat Pain (UG3/UH3 Clinical Trial Optional) - RFA-NS-19-016
- Translational Devices to Treat Pain (U44 Clinical Trial Optional) - RFA-NS-19-017
- Clinical Devices to Treat Pain (UH3 Clinical Trial Optional) - RFA-NS-19-018
- Stimulating Peripheral Activity to Relieve Conditions (SPARC): Anatomical and Functional Mapping of Pain-Related Visceral Organ Neural Circuitry (U01 Clinical Optional) - RFA-RM-19-001
- Translational Development of Devices to Treat Pain (U18 Clinical Trial Not Allowed) - RFA-EB-18-003

TO BE DISCUSSED LATER TODAY

Preclinical Screening Platform for Pain

- Preclinical animal behavioral testing platform for characterization of non-addictive modalities for the treatment of pain
- Incentivize academia & industry 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
- Provide access to research community

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