

NIH HEAL INITIATIVE

PRECISION Human Pain Network (RFA-NS-22-018 & RFA-NS-22-021)

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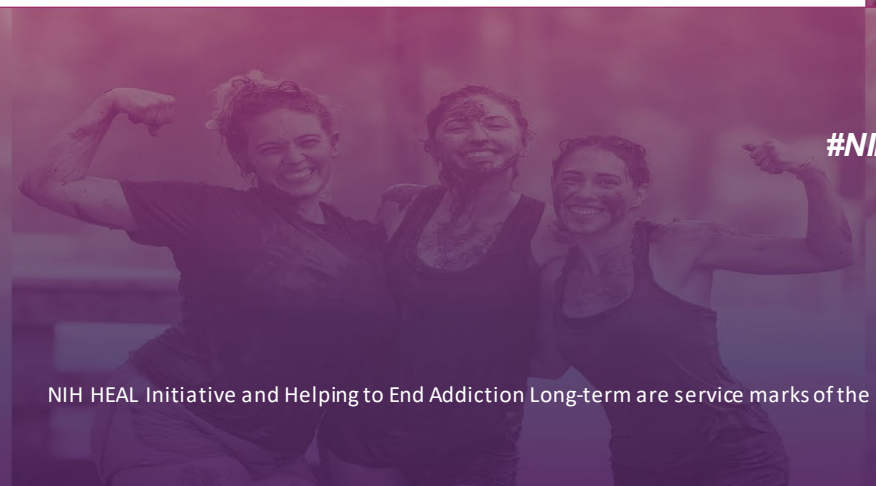
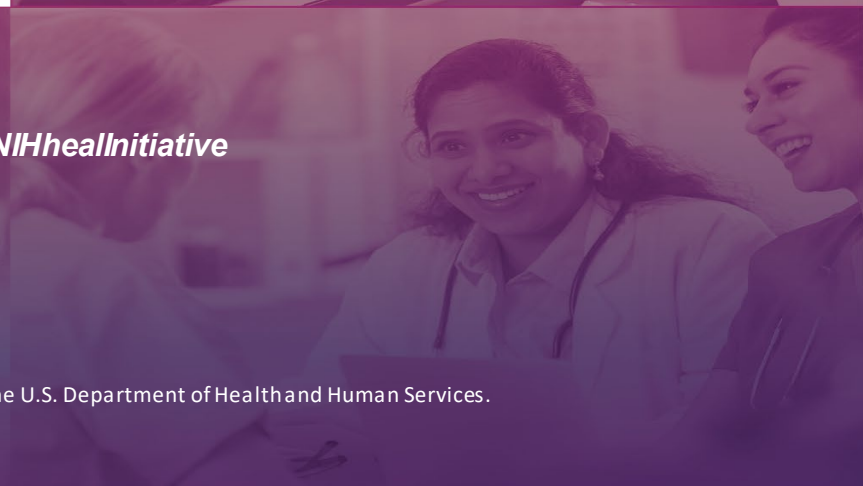
#NIHhealInitiative

NIH National Institutes of Health
HEAL Initiative

NIH HEAL Initiative: PRECISION Human Pain Network

Webinar Logistics

- This webinar will be recorded
- The webinar recording and slides will be posted on the NIH HEAL website
- PDF of slides will be emailed to registered attendees
- Please use chat box to post all questions
- Questions will be answered following the presentation

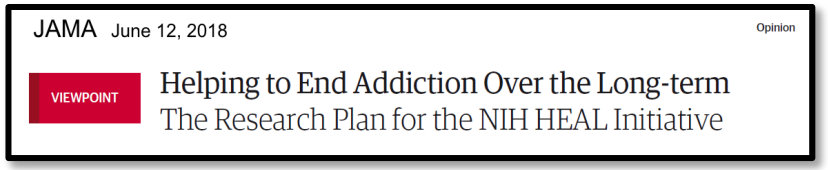
NIH Helping to End Addiction Long-term (HEAL) Initiative: Pain Research Priorities

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

Read about the research plan:

www.nih.gov/heal-initiative


JAMA June 12, 2018 Opinion

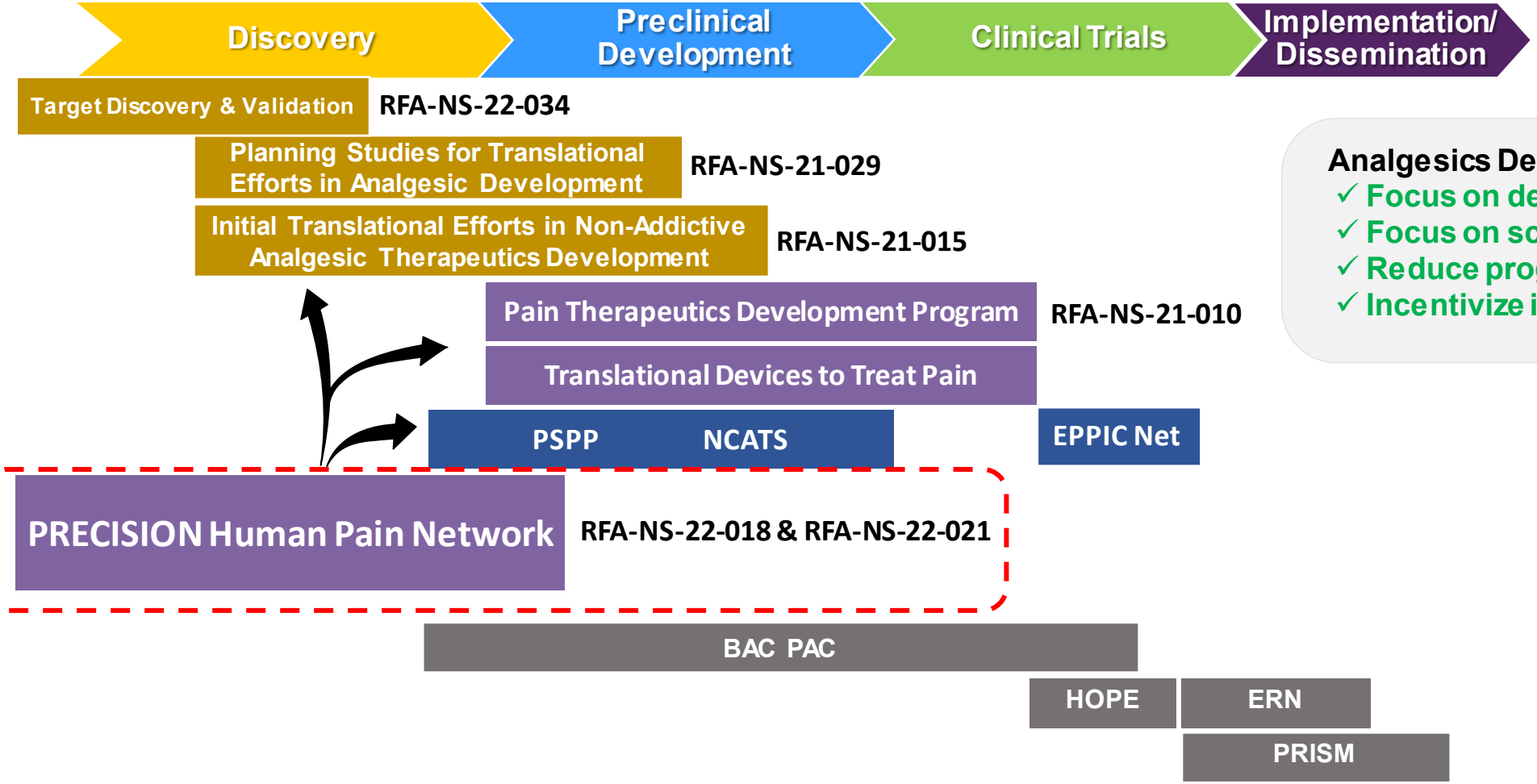
VIEWPOINT

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

Collins, Koroshetz, Volkow; JAMA, 2018

NIH HEAL Initiative Programs for Enhancing Pain Management

Grants | Grants & Contracts/Co-OP | Grants, Contracts & Intramural Resources



Analgesics Development:

- ✓ Focus on deliverables
- ✓ Focus on scientific challenges
- ✓ Reduce program complexity
- ✓ Incentivize industry to reinvest

NIH HEAL INITIATIVE

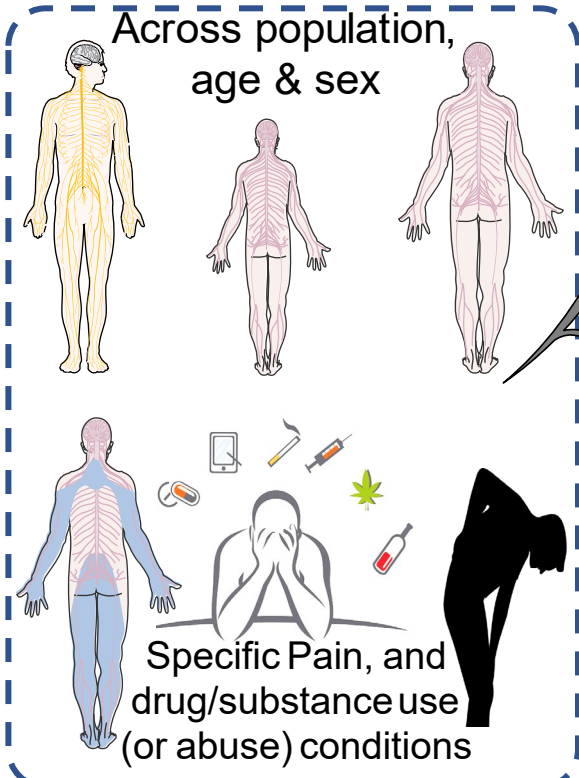
NIH HEAL Initiative: PRECISION Human Pain Network

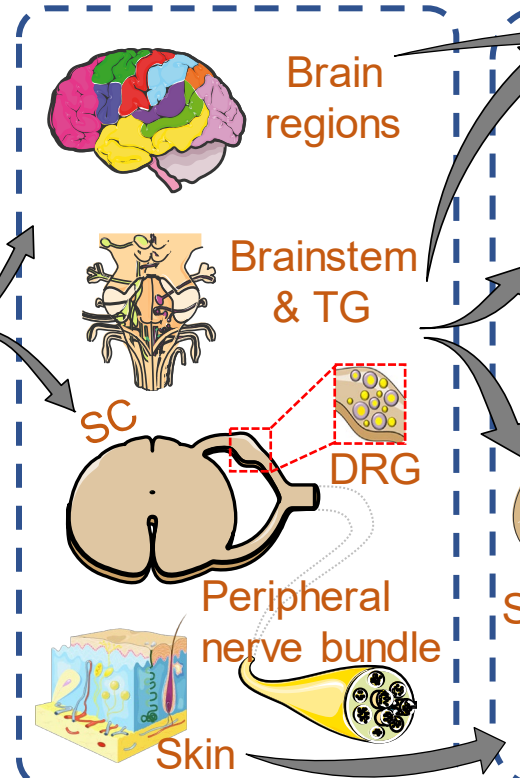
PRECISION Human Pain - *P*rogram to *R*eveal and *E*valuate *C*ells-to-gene *I*nformation that *S*pecify *I*ntricacies, *O*rigins and the *N*ature of **Human Pain**

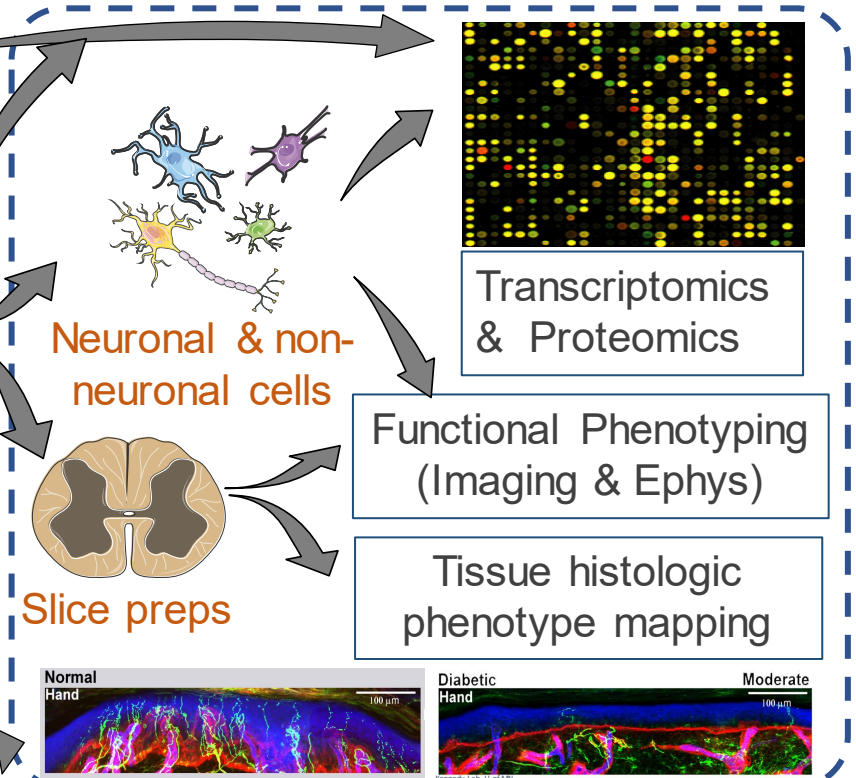
Objectives: To build up comprehensive datasets of molecular signatures, cell types, and cellular function phenotypes or signatures that underlie human pain signal transduction, transmission, and processing, by using primary human tissues and cells.

Tissue Resources:

- Local transplant centers
- Consortium of transplant centers
- National Disease Research Interchange (NDRI)
  - NINDS supported
- NIH NeuroBioBank Brain Bank Network







NIH HEAL INITIATIVE

NIH HEAL Initiative: PRECISION Human Pain Network

RFA-NS-22-018: HEAL Initiative: Discovery and Functional Evaluation of Human Pain-associated Genes & Cells (U19 Clinical Trial Not Allowed)

RFA-NS-22-021: HEAL Initiative: Human Pain-associated Genes & Cells Data Coordination and Integration Center (U24 Clinical Trial Not Allowed)

Team-based U19 Centers
- Research Projects (indv.)
- Admin & Resource Cores
- Human Tissue Procurement & Processing Core
- Data management Core

- 2-3 Center grants in FY22
- Duration: ~4-5 yrs

Steering Committee
- Individual U19 Center Leads
- NIH HEAL & IC Programmatic Staff
- U24 Data Coordination & Integration Center Lead

NIH-HEAL Data Ecosystem

NIH-HEAL Public Access & Data Sharing

U24 Data Coordination & Integration Center
- Coordinate, curate, harmonize, integrate comprehensive datasets across U19 centers for transcriptome, proteome, cellular function phenotypes, and disease/condition-specific cellular & tissue phenotypes.
- Dedicated staff - computational & bioinformatics expertise

- 1 Center grant
- Duration: 5 yrs

Next Receipt Date: March 17, 2022

NIH HEAL INITIATIVE

***Receipt Dates*: March 17, 2022, July 7, 2022, October 11, 2022, and March 09, 2023**

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PRECISION Human Pain Network: Goals & Expected Outcomes

- Elucidation of comprehensive single-cell datasets underlying human pain transduction, transmission, and processing in different pain types, conditions and/or diseases
  - * functional genetic elements
  - * epigenetic signatures
  - * proteome and/or metabolome signatures,
  - * molecular/cellular functions & phenotypes
  - * single-cell, network and tissue analyses
- Identification of cellular bases underlying individual human susceptibility to different pain conditions, including conditions of chronic analgesic use, other drug use, SUDs and other co-morbidities and/or overlapping pain conditions.
- Development of optimized, machine-readable experimental protocols and functional assays utilizing primary human cells and tissue (including neuronal cultures and co-cultures with ganglionic non-neuronal cell types as well as SC and brainstem slices).
- Cross-inform and complement other NIH-supported research programs and networks on optimization of iPSC-derived cells and organoids for pain therapeutic target validation and screening, with the standards and datasets from the PRECISION Human Pain network.

PRECISION Human Pain Network: U19 Centers

- Elements of Successful U19 Center:
  - Clear set of overall goals that are aligned with the PRECISION Human Pain network's objectives and outcomes
    - Preliminary data and literature-based evidence
    - Approach & Feasibility
    - Coordination with other U19 centers in this network
  - Multidisciplinary team
    - Evidence it has expertise AND can work together
    - Team coordination plan with other U19 centers in this network
- U19 is up to 5 years (if milestones are met)
  - Direct costs up to $1.5 million per year including all consortium and subaward costs
  - 2-3 U19 centers in FY22 for the PRECISION Human Pain Network

Individual U19 Center Components

Component	Component Type for Submission	Page Limit	Required/ Optional	Minimum	Maximum
Overall	Overall	12	Required	1	1
Administrative Core	Admin Core	6	Required	1	1
Human Tissue Procurement and Processing Core	Core	6	Required	1	1
Data Core	Core	6	Required	1	1
Resource Core	Core	6	Optional	0	2
Research Project	Project	12	Required	1	3

These page limits refer to the research strategy section only.

A separate "Specific Aims" page for each individual component of the U19 application should be submitted [per SF424 (R&R) Application Guide Instructions].

U19 Application: Overall Component

The central scientific, data and resource production goals of the U19 Center

- Comprehensiveness of Center's data

Rationale and brief research approach/plan for individual research projects and cores

- Interdisciplinary nature, synergy and integration across Research Projects and Cores
- Unique contribution of Research Projects and Cores to the overall aims of the U19 Center
- Coordination with other U19 Centers → PRECISION Human Pain network overarching goals

Multidisciplinary Team

- Expertise for proposed approaches and team science; Strive to include diversity in team members
- Input from patients/caregivers encouraged

Data Management and Coordination with U24 Center

- Support and coordinate data for Research Projects and Cores in the U19 Center
- Coordinate with other U19 Centers, and wit the U24 DCIC

Milestones

- Quantifiable

U19 Application: Milestones

- Annual quantitative milestones **must** be proposed
- Quantifiable, Objective Criteria, Well-defined, Scientifically justified, and should establish feasibility for all aspects of U19 center
- Specific Aims or a list of activities are not milestones!

U19 Application: Milestones Review

- Proposed milestones: peer reviewed
- **Prior to award**, NIH program staff will contact you to finalize milestones based on review recommendation and RFA goals
- **Annual milestone evaluation** will be done via administrative review by NIH
  - Successful achievement of milestones
  - The overall feasibility of program advancement towards the goals and outcomes of the PRECISION Human Pain network, considering data that may not have been captured in milestones

U19 Application: Human Tissue Procurement and Processing Core

Core contribution to U19 Center goals and to the overarching goal of the NIH HEAL Initiative PRECISION Human Pain network

Core will conduct and coordinate with other U19 centers in the network to develop and optimize experimental protocols:

- Extraction and processing of human tissues for pain signal transduction, transmission, and processing
- Dissociation and cell sorting; Processing of tissue for histological and other analysis
- Dissociation and cultures of neuronal and non-neuronal cells and co-cultures with ganglionic non-neuronal cell types
- Preparation of SC and brainstem slices, if applicable

Feasibility, General and background preliminary findings, Team and Expertise

Coordinate with other U19 centers on dissemination of resources generated

Coordination on tissue procurement, quality, quantity, devolving consent forms & SOPs, screening, ethical aspects, inclusion/exclusion criteria, and timeline

U19 Application: Data Core

Contribution of the data core to U19 Center and PRECISION Human Pain Network goals

- Overview & approach

Detailed plan on data management and analysis practices

- Database infrastructure, information management & monitoring, complex multimodality data management, statistical analysis, data integration and registration to a common tissue and cell coordinate systems
- Data analysis methods and procedures, including analysis algorithms and data hierarchy
- Bioinformatics expertise, data integration & analysis support, study design & statistical support/services
- Evidence of feasibility

Team

- Expertise for proposed data approaches; evidence of team/coordination and feasibility.
- Input from patients/caregivers encouraged

Data Management and Coordination with U24 Center

- Support and coordinate data for Research Projects and Cores in the U19 Center
- Coordinate with other U19 Centers, and wit the U24 DCIC

U19 Application: Resource Core

Core contribution to one or more of the Research Projects and Cores of the U19 Center

- Broad activities and services of the proposed Core
- Should not duplicate resources already available at the institution

Facilities, services and/or types of resources provided and managed

- How they will meet the specific needs of each Research Project and/or Cores
- Rationale for centralizing activities in Resource Core rather than including in Research Projects
- Facilitate dissemination of technology, expertise, materials, experimental models or modalities

Core objectives - to improve technologies, tools, and or reagents

- Limitations and gaps of the current technologies and tools in throughput, sensitivity, selectivity, scalability, spatiotemporal resolution and reproducibility in tissue, cells and gene analyses.
- Improvements proposed address the current limitations and gaps, and how it will enhance the goals of the U19 Center and network.

Team

- Expertise for proposed approaches, facilities and services to be provided
- Resource Core coordination and management plan

U19 Application: Research Projects

Contribution of research projects to the goals of U19 Center, and goals of the network

- Generate data on molecular signatures, cell types, and cellular function phenotypes or signatures

Rationale and detailed research approach/plan for individual research projects

- Comparative view of other/existing data pertaining to similar questions; Outline preliminary data
- Comprehensiveness or breadth and depth
- Unique contribution of Research Projects and Cores to the overall aims of the U19 Center
- Coordination with other U19 Centers → PRECISION Human Pain network overarching goals

Multidisciplinary Team

- Expertise for proposed approaches and team science; Strive to include diversity in team members
- Input from patients/caregivers encouraged

Data Management and Coordination with U24 Center

- Support and coordinate data for Research Projects and Cores in the U19 Ce
- Coordinate with other U19 Centers, and wit the U24 DCIC

U19 Application Reviews: Review Criteria

Data Core:

- Approach, coordination (intra- & inter-U19, and U24)
- Coordination with U24 DCIC and HEAL Data Ecosystem

Administrative Core:

- Leadership
- Admin Management
- Planning & Evaluation
- Component integration
- Communication with Data Core

Human Tissue Procurement and Processing Core:

- Experience & Expertise of Core Lead and Team
- Develop and Optimize
- Coordination

Research Projects:

- Significance
- Investigators
- Innovation
- Approach
- Environment
- Contribution to PRECISION Human Pain Network goals

Resource Core(s):

- Centralized facility & services for projects

Overall U19 Center Goals & Strategy:

- Significance
- Investigators
- Innovation
- Approach
- Environment
- Overall Coordination (intra- and inter-U19, and U24)
- Milestones

Overall Impact of the Proposed U19

PRECISION Human Pain Network: U19 Application Components

Activities that are Not Responsive:

Research areas are considered outside the research scope of this FOA.

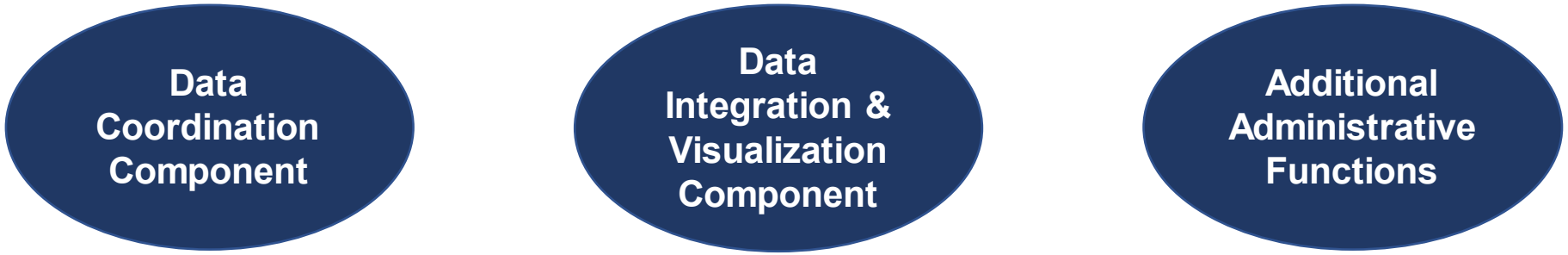
- Studies conducted on primary tissues that are from non-human species.
- Studies with a major focus on analyses comparing data from human and non-human species (including theoretically modeled and extrapolated data).
- Studies utilizing cultured human cell lines, including human iPSCs, organoids, and micro-physiological systems.
- Studies with a major focus on development of tools, reagents, and technologies for analysis of human tissue.
- Applications lacking milestones or any of the required core components.

Applications with any of these activities will be considered non-responsive

PRECISION Human Pain Network
Data Coordination and Integration Center (DCIC)

RFA-NS-22-021 HEAL Initiative: Human Pain-associated Genes & Cells Data Coordination and Integration Center (U24 Clinical Trial Not Allowed)

- Curate, harmonize, and integrate comprehensive datasets across U19 centers
- Adopt and promote standard terminology, data acquisition protocols, quality control metrics, and metadata requirements to enhance data interoperability and harmonization
- Dedicated staff - computational & bioinformatics expertise



PRECISION Human Pain Network
Data Coordination and Integration Center (DCIC)

RFA-NS-22-021 HEAL Initiative: Human Pain-associated Genes & Cells Data Coordination and Integration Center (U24 Clinical Trial Not Allowed)

- **Funds Available and Anticipated Number of Awards**
  - NIH HEAL Initiative intends to fund an estimated direct cost of $1M per year, to fund 1 award, starting in fiscal year 2022 or 2023.
- **Award Project Period: Max 5 years**
- **Receipt Date(s): March 17, July 7, Oct. 11, 2022**

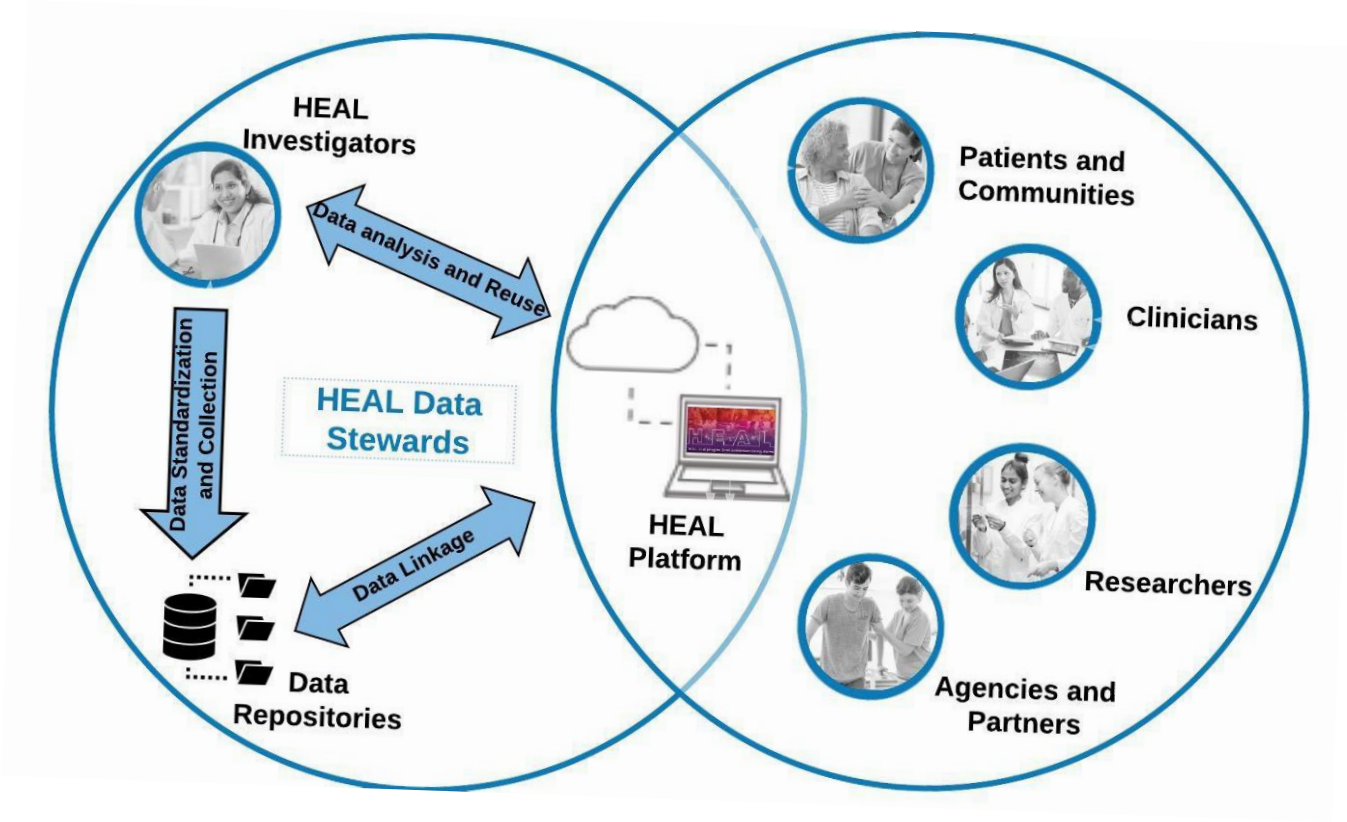
Data Coordination Component - (b/n U19 Centers)

- **Interface with the U19 Centers** to **define data and metadata** types to be collected in support of the overall network goals
- Develop a **secured database** that can **receive data from the U19 Centers and allows for private collaboration** among researchers prior to public release (leveraging the HEAL Platform as appropriate)
- Develop a **quality control** and **quality assurance pipeline** for **data and metadata** generated by the network
- **Integrate, link, and display datasets** in space and time; **give U19 users** the **ability to easily browse and navigate datasets based on key metadata fields**
- **Work with U19 awardees to collect and archive datasets** in HEAL-recommended existing repositories, where appropriate
- **Work with the research community to adopt and promote a standard terminology** to describe experiments and datasets by leveraging existing resources (e.g., Neuroscience Information Framework, BAMS, Allen Brain Atlas)

Data Integration and Visualization Component

- **Process and register data to common neural tissue coordinate systems, generate digital neural tissue atlases, link multiple data elements**
- **Implement user-friendly data registration tools** for the network to interact with the digital neural tissue atlases to share and cross validate the data.
- Lead efforts to **establish spatial and semantic standards** that will incorporate multiple ways to define a location in the pain neuraxis
- Develop tools that provide analytical and visualization capabilities to its end users.
- **Develop a database that is broadly accessible to anyone with a web browser** to view and access data, tools, protocols, etc.
  - Some datasets may require controlled access
  - Can leverage the NIH STRIDES Initiative as appropriate
- To the extent allowable, **digital assets** crucial to reproducibility **should be made shareable and accessible**
- **Promote broad discovery and reuse of data and tools** - support their accessibility through the HEAL Platform

HEAL Data Ecosystem



HEAL Platform
University of Chicago
Access, query, computational services and tools, metrics, security infrastructure

CONNECT BUILD LEARN

NIH HEAL INITIATIVE | Data Stewardship Group

RENCI/RTI
Consulting on storage, management, and security processes; engagement; harmonization via use cases

Visit HEALdataFAIR.org for more information

DCIC: Additional Administrative Functions

DCIC will facilitate and coordinate both internal network communication and activities as well as external partnerships and outreach.

Meeting organization: Planning/logistics associated with PRECISION Human Pain network meetings

- Monthly on-line and annual in-person Steering Committee meetings
- Subcommittee meetings involving informatics efforts such as developing and implementing spatial and semantic standards, data/metadata submission and deposition, etc.

PRECISION Human Pain network communication: across the network and with the HEAL Data Ecosystem

- Provide resources such as mailing lists, forums, or wikis to enable discussion
- Provide computational and data analysis support to identify knowledge gaps, prioritize research, and prepare reports

Education and Outreach: To facilitate the data use by the broad scientific community (e.g., develop tutorials, conduct user workshops, use of social media outlets, etc.)

PRECISION Human Pain Network DCIC Considerations

- HEAL data must be Findable, Accessible, Interoperable, and Reusable
- Align with HEAL Data Ecosystem and HEAL Platform wherever possible
- Align with similar existing efforts in this space
- Leverage use of existing infrastructures and standards
- Scalability to incorporate relevant datasets in the future
- Sustainability of generated resources beyond the 5-year grant period
- DCIC applications must also include proposed milestones for the project

NIH HEAL Initiative: PRECISION Human Pain Network

RFA-NS-22-018: HEAL Initiative: Discovery and Functional Evaluation of Human Pain-associated Genes & Cells (U19 Clinical Trial Not Allowed)

RFA-NS-22-021: HEAL Initiative: Human Pain-associated Genes & Cells Data Coordination and Integration Center (U24 Clinical Trial Not Allowed)

Questions after the webinar is completed?

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