



PAR-27-045:

Whole Joint Health Program (R61/R33 Clinical Trial Required)

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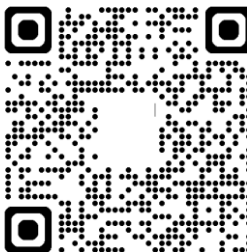
Acting Deputy Branch Chief & Acting Branch Chief, Basic and Mechanistic Research Branch, National Center for Complementary and Integrative Health

NIH Helping to End Addiction Long-term Initiative

- Since 2018, **>2,200** research projects in **all 50 states**, totaling over **\$4 billion**
- Collaboration across **18** NIH Institutes and Centers
- **>40** FDA approvals for investigational new drugs, biologics or devices
- Active ongoing partnerships with communities, federal, state, and local agencies, private sector companies, and academia



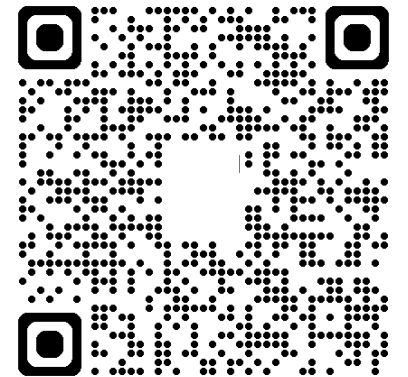
NIH
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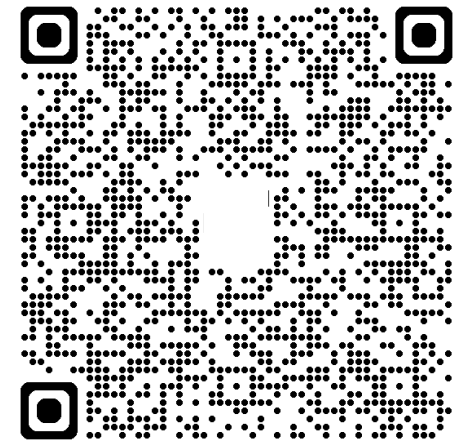
2023 NIH HEAL Workshop on Whole Joint Health

Objectives:

- Discussed failures of clinical trials that fail to evaluate the “whole joint,” including periarticular and articular tissues.
- Conceptualized the whole joint, including contributions of various articular and periarticular tissues and the pathologies that contribute to joint pain.
- Identified manipulations and interventions that may help to restore whole joint health.



Whole Joint Health PAR Goals



R61 phase: Identify multi-tissue mechanisms involving periarticular tissues (e.g., muscles, adipose, and connective tissues including ligaments, tendons, or fasciae) as well as their interactions with articular tissues (e.g., bone, synovium, cartilage) and/or the peripheral nervous system that result in joint pain and pathophysiology;

R33 Phase: Test mechanism(s) of action that non-pharmacological and/or multimodal interventions have on the identified multi-tissue mechanisms

Research Plan (12-page limit)

- Specific Aims (1 page):
 - Brief background describing state of knowledge of justification of proposed mechanism(s)
 - Rationale for proposed intervention proposed in R33 trial to test impact on measures of proposed mechanism(s) developed in R61 study
 - Clear aims defining how proposed hypotheses will be tested in both phases. **Use headers to distinguish R61 vs. R33 aims.**
 - Briefly detail innovation/impact of study's potential to advance understanding of whole joint pain
- Research Strategy (11 pages)
 - Importance of Research
 - Background and Research Objectives
 - Approach

Whole Joint Health Objectives and Approach

R61 Phase:

- Summarize one or more proposed quantitative measure related to whole joint pain.
- Develop a plan to complete one or more mechanistic study **with human subjects** to generate preliminary data for the R33 clinical trial (**pre-existing preliminary data is not required**)
- Provide clear and compelling rationale for proposed mechanisms- differentiate healthy whole joint function from clinical phenotypes of joint pain.
- Incorporate clear study design of proposed mechanistic study(ies)- patient population, primary outcomes, sample size, stat plan, and alternative approaches or contingencies

Whole Joint Health Objectives and Approach

R61 High Program Priorities:

- Projects should propose to measure **at least one** periarticular tissue and its interactions with one or more articular tissue and/or peripheral physiological or neural system.
- Examples of innovative mechanisms include (but are not limited to):
 - Measures of inter-tissue communication
 - Abnormal biomechanics or load across joint tissues
 - Concomitant indicators of tissue pathology
- Additional areas of specific research interest:
 - Use of innovative imaging, biomarker profiling, neuromuscular assessment, and/or behavioral or environmental measures of whole joint health.
 - Multimodal approaches that meet NIH standards for rigor and reproducibility

Whole Joint Health Objectives and Approach

‘Go/No-Go Criteria’ for R61 Section:

- Detail study benchmarks with well-defined “Go/No-Go” transition criteria (“milestones”) that demonstrate readiness for project to advance to the R33 trial phase.
 - Only include **key** quantitative and clinical enrollment milestones
 - Quantitative measures should demonstrate meaningful group differences in proposed measures of whole joint pain or pathophysiology from healthy tissue(s)
 - In addition to quantifying measures or participant enrollment in the milestones, provide brief rationales to justify the included metrics

Whole Joint Health Objectives and Approach

R33 Phase:

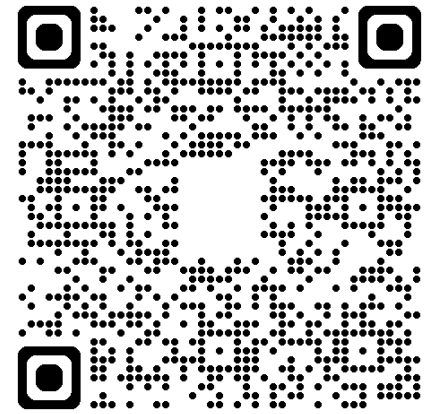
- Propose a rigorous, well-designed mechanistic clinical trial to test effect of proposed intervention(s) on mechanisms developed in the R61 phase.
- Rationale for intervention can be based on prior published work or preliminary data (**pre-existing preliminary data is not required**)
- Include a brief plan to extend the investigator team with clinical trials and intervention expertise for the R33 phase

Programmatic Priorities:

- Non-pharmacologic or multi-modal interventions for joint pain
- Other interventions that feasibly produce measurable mechanistic changes in identified tissues.

Required Elements

- Research Plan (Limit – 12 pages)
- Resource Sharing Plan
- Human Subjects and Clinical Trials Information
- Data Management and Sharing Plan **that follows HEAL Data sharing requirements** (QR code above)



Eligibility Information

- Higher Education Institution- All types
- Nonprofits with or without 501(c)(3) IRS Status
- For-Profit Organizations
- Local Governments
- Federal Governments
- Other Domestic Organizations enumerated in Section III of the PAR

Foreign Organizations/ International Collaborations are not allowed

Budget and Award Numbers

- Program will prioritize well-scoped projects that propose no more than \$500k direct costs (DC) per year for R61 phase (2-3 years).
- For 3-year R33 projects, no more than \$700k DC/year. For 2-year R33 projects, no more than \$800k DC/year.
- Maximum project period is 5 years:
 - 2-3 years for R61 phase
 - 2-3 years for R33 phase.
- Number of Awards contingent upon NIH appropriations and submission of meritorious applications.

Review

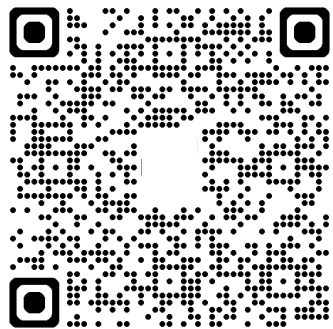
- Applications will be evaluated for scientific and technical merit by (an) appropriate Scientific Review Group(s) **convened by CSR**, in accordance with [NIH peer review policies and practices](#), using the stated review criteria.
- Assignment to a Scientific Review Group will be shown in the eRA Commons.
- Review anticipated in March 2027

Important!

- Applications will be **incomplete/not compliant** if they do not include required elements/attachments stated in Section IV of the PAR.
- Applications will be considered **non-responsive** if they propose to assess **clinical efficacy or effectiveness** of an intervention as a primary outcome measure.

HEAL Expectations

- NIH intends to maximize the impact of HEAL Initiative-supported projects through broad and rapid data sharing.
 - See HEAL Initiative Public Access and Data Sharing Policy-
<https://www.nih.gov/heal/heal-initiative-requirements/data-sharing-policy/complying-heal-public-access-data-sharing-policy>
 - All applications are required to include a **Data Management and Sharing Plan**



Key Dates

- Applications Due – October 30, 2026
- Scientific Review – March 2027
- Earliest Project Start Date – July 2027

Contacts

- National Center for Complementary and Integrative Health (NCCIH)
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Comments or Questions?