Request for Information on Themes for the NIAMS Strategic Plan for Fiscal Years 2025-2029

Deadline for response: January 1st, 2024
Maximum Length: unspecified

Purpose: The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) supports research into the causes, treatment, and prevention of arthritis and musculoskeletal and skin diseases; the training of basic and clinical scientists to carry out this research; and the dissemination of information on research progress in these diseases. NIAMS is updating its Strategic Plan to help guide the research, training, and information dissemination programs it supports between fiscal years 2025 through 2029.

Questions:

Please provide your perspective on the following potential cross-cutting themes (page two through eight), examples, and bold aspirations. NIAMS is particularly interested in suggestions for additional or alternative:

1. Cross-cutting themes that could be considered for the strategic plan.
2. General research that could be included as examples under the proposed themes.
3. Bold scientific or public health aspirations related to each proposed theme that could be accomplished by the end of the decade.

1 Link to full call. See full call for previous examples.
Theme: Molecular and cellular mechanisms of health and disease and resulting phenotypes for therapy development

Examples:

- Explore cell-cell, tissue, and interorgan interactions in model organisms and humans to understand how bone, immunologic, joint, muscle, and skin cells contribute to health and disease.
- Investigate how musculoskeletal function impacts metabolic, cognitive, immunologic, and other health outcomes. This could include exploring organ-organ crosstalk in the context of the health benefits of physical activity on conditions of interest to NIAMS.
- Understand the role of blood and lymphatic vasculature in arthritis and musculoskeletal and skin diseases. This could include studying how treatments that target the cardiovascular or lymphatic vascular system can impact the immune or musculoskeletal system in health and disease.
- Understand the role of immune cells in bone, cartilage, connective tissue, muscle, and skin health and deterioration due to injury or disease.
- Understand the roles of various microbiomes (e.g., skin, gut) in the prevention, development, and treatment of arthritis and musculoskeletal and skin diseases and conditions.
- Examine the interplay between inflammation, fibrosis, and tissue repair in healthy bone, cartilage, connective tissue, muscle, and skin and in various types of arthritis and musculoskeletal and skin diseases and conditions.
- Conduct comprehensive molecular mapping with ’omics technologies to identify unique and shared signaling pathways that provide mechanistic insights and therapeutic targets for diseases and conditions of interest to NIAMS.
- Identify additional biomarkers for arthritis and musculoskeletal and skin diseases and conditions. Biomarkers (e.g., molecules, images) can be instrumental in predicting disease development, assessing a disease’s existence and extent, guiding treatment decisions, and tracking people’s responses to therapy.
- Combine clinical and molecular data to redefine arthritis and musculoskeletal and skin phenotypes and conditions. These new definitions could be used for clinical trials and to guide treatment selection.

Bold Aspirations:

- Interdisciplinary research into the mechanisms of tissue or organ crosstalk will lead to treatments that address the whole patient instead of separate tissues or organ systems.
- Healthcare providers will be able to phenotype patients with heterogeneous forms of arthritis or musculoskeletal or skin diseases and use this knowledge to inform treatment decisions.
- Researchers will discover all human mutations that cause arthritis and musculoskeletal and skin diseases.

Theme: Data science, including artificial intelligence and machine learning, and computational biology
Examples:

- Improve the use of observational electronic health record data in studies of arthritis and musculoskeletal and skin conditions and their treatments.
- Develop and validate Common Data Elements related to pain in diverse populations and address biological and behavioral mechanisms that are driving pain and health outcomes in arthritis and musculoskeletal and skin diseases.
- Leverage datasets focused on areas such as aging, cardiovascular disease, or diabetes for the discovery of phenotypes for diseases and conditions of interest to NIAMS.
- Use data science approaches to explore the bidirectional interactions between systemic factors and the musculoskeletal system and skin in health, aging, and disease.
- Develop artificial intelligence tools with limited bias that integrate biomedical knowledge across the spectrum of pre-clinical research, clinical research, and clinical practice to increase the efficiency of research and accelerate advances that can benefit patients who have arthritis or a musculoskeletal or skin disease or injury.
- Ensure that artificial intelligence and machine learning approaches used for NIAMS-funded studies adhere to fairness, data diversity, statistical, privacy, reporting, and open access standards.
- Integrate computational biology methods and mechanistic clinical trials to inform the use of patient-specific therapeutics for arthritis or musculoskeletal or skin diseases and conditions across the lifespan.
- Integrate multidimensional human data, from molecular and cellular to population levels, to reduce the burden of arthritis and musculoskeletal and skin diseases and conditions.
- Mine large data sets to identify patients with undiagnosed rare diseases or treatable common diseases of interest to NIAMS to improve access to care.
- Develop clinical support tools that integrate polygenic risk scores with demographic and clinical data to predict the development and progression of arthritis or musculoskeletal or skin diseases.

**Bold Aspiration:**

- The application of data science tools to large data sets will allow researchers to distinguish among phenotypes for heterogeneous forms of arthritis or musculoskeletal or skin diseases.

**Theme: Health disparities and health equity**

Note: Efforts to identify and reduce health disparities and provide all Americans with equitable access to clinical and epidemiologic studies and healthcare should be considered for NIAMS-funded research projects whenever possible.

Examples:

- Identify the biologic, social, and environmental causes of disparate health outcomes in people from diverse backgrounds who have arthritis or a musculoskeletal or skin disease or condition. This includes research that explores the interaction between health
determinants, including the physical environment from urban planning, and the incidence and prevalence of diseases and conditions of interest to NIAMS.

- Assess genetic risks for arthritis and musculoskeletal and skin diseases across populations that include individuals from non-European ancestry.
- Increase participation of populations from diverse racial, ethnic, socioeconomic, and geographic backgrounds in NIAMS-funded clinical studies.
- Design and test low-cost, equitable interventions for diseases and conditions of interest to NIAMS.
- Develop approaches for effective outreach to underserved populations to improve access to treatment.
- Determine how underserved populations can benefit from proven interventions for arthritis and musculoskeletal and skin diseases through community engagement and implementation science efforts.
- Identify long-term outcomes of gender-affirming care on the bones, joints, muscles, and skin of transgender and non-binary persons.

**Bold Aspirations:**

- Researchers will identify social determinants of health that impact response to therapy for multiple types of arthritis or musculoskeletal or skin disease.
- All Americans with arthritis or a musculoskeletal or skin disease will have equitable access to research, trials, and therapies that improve their outcomes and quality of life.

**Theme: Pain in arthritis and musculoskeletal and skin conditions**

**Examples:**

- Explore the molecular and cellular origins of pain in people with arthritis and musculoskeletal and skin diseases, including those who have no structural abnormalities.
- Map neuron subtypes to individual cell types in skin, muscles, joints, and bones.
- Study the central nervous system’s role in the pain experience and responses to treatment for diseases and conditions within the NIAMS mission.
- Define the molecular and cellular underpinnings of neuro-inflammation seen in arthritis and musculoskeletal and skin diseases.
- Examine how psychological and social factors influence the biomedical mechanisms of pain in arthritis and musculoskeletal and skin diseases and conditions.
- Determine pain’s influence on motor learning behaviors (e.g., in the context of osteoarthritis, back pain, or autoimmune disease) and how pain prevents the learning of healthy movement patterns.
- Translate findings related to the mechanisms of exercise-induced hypoalgesia (a decreased sensitivity to painful stimuli) into potential non-addictive pain relief medications.
- Study interventions for arthritis and musculoskeletal and skin diseases and conditions that combine pain relief strategies and regenerative medicine.

**Bold Aspiration:**
Researchers will understand the mechanism of pain in patients with arthritis or musculoskeletal or skin conditions who have no obvious structural abnormalities.

**Theme: Lifestyle factors and environmental exposures that affect health and related interventions**

Note: Consistent with the note under *Health disparities and health equity*, studies of lifestyle factors and environmental exposures should include efforts to identify and reduce health disparities and provide all Americans with equitable access to clinical and epidemiologic studies and healthcare whenever possible.

Examples:

- Evaluate the impact of lifestyle factors such as diet and physical activity on onset, severity, and treatment of arthritis and musculoskeletal and skin diseases.
- Assess the impact of sleep and circadian rhythm disturbances on arthritis and musculoskeletal and skin diseases and conditions and responses to treatments.
- Discover disease-exacerbating environmental exposures (e.g., compounds, organisms) and environmental triggers for arthritis and musculoskeletal and skin diseases and investigate how they interact with a person’s biology in various disease states.
- Identify biomarkers of environmental exposures leading to heightened susceptibility to arthritis and musculoskeletal and skin diseases.
- Investigate the social determinants of health, including the built environment, that influence susceptibility and responses to treatment of arthritis and musculoskeletal and skin diseases.

**Bold Aspiration:**

- Evidence-based integrated multidisciplinary patient education and nutritional and behavioral health programs will be available to improve the bone, muscle, joint, and skin health of patients of all ages.

**Theme: Clinical and epidemiologic research and preclinical studies necessary for translating basic findings into interventions**

Note: Consistent with the note under *Health disparities and health equity*, clinical and epidemiologic research should include efforts to identify and reduce health disparities and provide all Americans with equitable access to clinical and epidemiologic studies and healthcare whenever possible.

Examples:

- Enhance the translation of preclinical studies of arthritis and musculoskeletal and skin diseases and conditions into humans.
- Translate promising tissue regeneration technologies into clinical practice. This could include identifying and removing barriers to successful cell therapy delivery to the joints, muscles, and skin.
• Improve precision immunotherapies for autoimmune, musculoskeletal, and skin diseases.
• Develop drug delivery technologies such as nanomedicine for arthritis and musculoskeletal and skin diseases and conditions.
• Develop and test primary and secondary prevention strategies based on disease mechanisms for arthritis and musculoskeletal and skin diseases in people who are at-risk for disease due to genetic, environmental, and other biologic markers. Care should be taken to include participants from diverse backgrounds to ensure the interventions are appropriate for everyone.
• Understand the psychosocial burdens of arthritis and musculoskeletal and skin diseases and conditions and develop strategies to overcome them.
• Develop holistic treatments targeting all aspects of the patient to accelerate recovery from or prevent development of arthritis and musculoskeletal and skin conditions. Integrated care that considers neurobehavioral, endocrine, and other factors will reduce pain, inform patient and provider decisions, and improve recovery from injury or disease.
• Determine effective care strategies and the optimal sequence of therapies in arthritis and musculoskeletal and skin diseases and conditions. This could include the combination of medications and physical and rehabilitation interventions.
• Identify strategies to incorporate shared decision-making into clinical care for arthritis or musculoskeletal or skin diseases or conditions.
• Promote the application of the best evidence for prevention or treatment of arthritis or musculoskeletal or skin diseases and conditions in health care settings.
• Refine recruitment strategies for studies of arthritis and musculoskeletal and skin diseases and conditions to be more intentionally inclusive of diversity and equity so that ancillary studies of treatment barriers and outcomes can be conducted.
• Develop and apply genetic and genomic predictive tools to arthritis and musculoskeletal and skin diseases with pediatric onset. This includes projects addressing ethical and pragmatic considerations of using genetic and genomic data in the care of children in clinical settings.
• Develop innovative and validated pediatric outcome measures such as patient-reported outcomes and clinical, imaging, and cellular and molecular biomarkers that are objective, accurate, and sensitive to disease change for studies of children who have arthritis or musculoskeletal or skin diseases.
• Explore how responses to treatment for arthritis and musculoskeletal and skin diseases that begin in childhood evolve at the mechanistic and whole-person level during maturation to adulthood.
• Determine the best mechanisms to support transitions from pediatric to adult health care to realize the best possible long-term health outcomes and quality of life for people who experience arthritis or chronic musculoskeletal or skin diseases.

Bold Aspiration:

• Research will allow health care providers to know the general physical and psychosocial characteristics that distinguish patients who will respond well to medical, lifestyle, rehabilitation, or surgical therapies (or a combination of treatments) for a given type of arthritis or musculoskeletal or skin disease or condition.
Theme: Interdisciplinary research, team science, and partnerships

Examples:

- Encourage research on *the cross-cutting thematic topics noted above* by fostering collaboration among scientists who study autoimmune, skin, bone, joint, and muscle and those who study complementary basic, clinical, social science, or public health disciplines.
  - Such specialties can range from non-biological disciplines such as data science, chemistry, or engineering; other biomedical fields such as neuroscience, microbiology, or stem cell biology; clinical fields that focus on co-occurring conditions; and social science and public health focus areas that can explain and help to reduce health disparities and implement proven interventions at a community or systems level.
- Increase community engagement and community-based participatory research in arthritis and musculoskeletal and skin studies to enhance the quality, outcomes, and value of the research questions being answered.
- Develop cross-institutional, cross-agency, and global efforts to leverage strengths and resources within NIAMS and other activities such as is being done through the NIAMS Core Centers for Clinical Research (P30), Accelerating Medicines Partnership® (AMP®) Autoimmune and Immune-Mediated Diseases, and Clinical and Translational Science Awards (CTSA) programs. Such partnerships could facilitate access to data, biospecimens, and technological resources to advance the NIAMS mission.
- Expand the topics being studied through public-private partnerships such as AMP or through the NIH Common Fund to include additional musculoskeletal and skin diseases.

Bold Aspiration:

- Specialists in bioinformatics, molecular and cellular biology, and bioengineering will collaborate to develop organ on-a-chip models to study arthritis and musculoskeletal and skin diseases.

Theme: Training and workforce

Note: Training and workforce efforts are essential for the pursuit of all cross-cutting thematic research areas in the new NIAMS Strategic Plan.

Examples:

- Encourage and support scientists at all career levels to pursue research in NIAMS mission areas.
- Develop a robust workforce addressing arthritis and musculoskeletal and skin diseases and conditions with demographics that mirror society. Efforts may include partnering with professional societies or student organizations to recruit and support additional researchers at various career levels.
- Build institutional diversity into NIAMS' large-scale research efforts such as the Centers’ programs. This could include establishing collaborations for NIAMS-focused research
and training opportunities between institutions that have considerable funding and those with less support.

- As noted under the Interdisciplinary research, team science, and partnership theme, foster collaboration among scientists who study autoimmune, skin, bone, joint, and muscle and those who study complementary basic, clinical, social science, or public health disciplines.

**Bold Aspiration:**

- The demographics of the biomedical workforce supported by awards from NIAMS will more closely mirror society.

**Theme: Enabling technologies and model systems**

**Examples:**

- Develop in vitro systems that model the complex physical and biological microenvironments for the design and testing of potential therapeutics and the exploration of disease mechanisms. Such research could include the development of models for musculoskeletal or skin microenvironments to overcome hurdles blocking the development and testing of regenerative strategies.
- Develop animal models that better mimic human diseases and conditions. Examples identified by the community include models of facioscapulohumeral muscular dystrophy and other skeletal muscle diseases that accurately reflect mechanisms of disease onset and progression, models of autoimmune diseases that mimic host immunity and gut microbiota, and models of musculoskeletal conditions such as chronic low back pain or aging-associated osteoarthritis.
- Screen high throughput medicinal libraries for potential drug targets and therapies for rare diseases of interest to NIAMS.
- Include musculoskeletal tissues in new or existing ‘omics resources. These efforts could include projects from other federal or private-sector entities or could be a stand-alone resource that includes standardized clinical phenotyping of sequenced patients with musculoskeletal diseases.
- Develop scalable and economic protocols to generate complex tissues from stem cells for studies of arthritis or musculoskeletal or skin diseases and the generation of replacement tissue for regenerative medicine approaches to treat diseases and conditions of interest to NIAMS.
- Explore the intersection of cell therapy and gene therapy.

**Bold Aspirations:**

- Researchers will develop in vitro skin tissue from stem cells that contain multiple cell lineages and appendages (e.g., nails, sweat glands).
- Research teams will develop multifactorial models based on two-dimensional and organoid systems and computational biology with machine learning components to study arthritis or musculoskeletal or skin diseases.