

Office of Portfolio Analysis and Strategic Initiatives:

Interdisciplinary Research Consortium in Geroscience

The Roadmap Interdisciplinary Research Program is intended to address significant research and health challenges by bringing together researchers from different fields to develop new approaches to solve problems. The Interdisciplinary Research Consortium in Geroscience will foster interdisciplinary collaborations that will help unravel the reasons why we age so that we can better understand what goes wrong in age-related diseases and disorders. Many avenues will be explored including how dietary restriction affects aging and why the aging brain recovers less easily from traumatic brain injury.

Lead Agency:

Office of Portfolio Analysis and Strategic Initiatives (OPASI) /
Common Fund, NIH Office of the Director

Agency Mission:

Strategic planning and implementation of trans-NIH initiatives that seek to transform the way health research is conducted

Development and distribution of tools and methodologies to NIH Institutes and Centers for analysis and evaluation of NIH programs

Principal Investigator:

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Partner Agencies:

All NIH Institutes and Centers participate in the planning and implementation of NIH Common Fund/Roadmap Programs. The NIDCR plays a lead role in implementing the Interdisciplinary Research Program. The Geroscience research program at the Buck Institute for Age Research is one of nine interdisciplinary research consortia funded by the NIH Director's Roadmap program.

General Description:

The Roadmap Interdisciplinary Research Program brings together scientists from numerous fields to develop new approaches that will address significant research and health challenges. The **Interdisciplinary Research Consortium in Geroscience** will foster interdisciplinary collaborations between cell and molecular biologists, biochemists,

geneticists, endocrinologists, physiologists, bioinformaticians, and chemists that will elucidate the fundamental mechanisms of aging in order to better understand what goes awry in age-related diseases and disorders. The research will be carried out at the Buck Institute for Age Research, which is an NIH-designed Center of Excellence, and the only independent research institute in the United States focused solely on aging research. The Geroscience Consortium will synergize research on the basic mechanisms of aging with research on age-associated diseases and with designing and optimizing new technologies that may be of great value to the geroscience community.

The research will include determining how cellular signaling pathways (e.g. TOR) increase longevity in response to environmental cues (e.g. dietary restriction) and how the same genes that control cell division and thereby suppress cancer (e.g. HUR) also promote neurodegeneration. Chemical compounds will be searched for that increase lifespan and also protect mammalian neurons from stressors. How proteins interact and how they change shape in an aging cell vs. a diseased cell will be explored since these processes are fundamental to the development of several neurodegenerative diseases. The role of histone deacetylase in aging and neurodegeneration will be investigated since this enzyme plays a critical role in modifying the epigenome of many cell types and may play a role in the development of Huntington's Disease and Parkinson's Disease. In addition, the research will explore why it is harder for the aged brain to recover from injury.

Excellence: What makes this project exceptional?

The nine interdisciplinary research consortia including the Geroscience Consortium were chosen through an incredibly competitive process. Each proposed consortium had to have a team of exceptionally accomplished scientists drawn from many disciplines who could address significant research challenges not amenable to existing uni- or multidisciplinary approaches. The Geroscience Consortium is located at a premier aging research institute – The Buck Institute for Age Research in Novato, CA – which has no academic departments and is therefore ideal for fostering interdisciplinary research at the interface of different fields. The Geroscience Consortium will integrate research on the molecular mechanisms of aging with age-associated disease research and with designing and optimizing new technologies of great potential value to the geroscience community.

Significance: How is this research relevant to older persons, populations and/or an aging society?

This research directly targets older persons. By determining what constitutes the “normal” aging process, one can better understand what biological processes go awry in age-related diseases and disorders, and find therapeutic agents to target these processes.

Effectiveness: What is the impact and/or application of this research to older persons?

Finding out how aging occurs at the molecular and cellular level will result in a better understanding of pathological processes associated with disease. The Geroscience Consortium has taken a multi-pronged approach to understanding aging and addressing age-related diseases from examining changes in the DNA (regulated epigenetic changes and stochastic oxidative damage), to looking at changing protein dynamics (including the formation of protein aggregates in Huntington's Disease and Parkinson's Disease), to

why aging brains do not recover well from trauma (may be a paucity of stem cells). Knowing the molecular players in the aging process and the factors that modulate their functions normally and during disease progression will allow for the development of therapeutic agents or adoption of lifestyle changes to increase longevity and combat disease.

Innovativeness: Why is this research exciting or newsworthy?

Much has yet to be elucidated with respect to the molecular pathways underlying aging in order to begin to get at what goes awry in these pathways during the development of age-related disease and to identify which molecules can be targeted by therapeutic agents or can be modulated by lifestyle choices - e.g., in diet.