SEX DIFFERENCES IN GENETIC EFFECTS USING TWO GENE AGGREGATION TECHNIQUES: DEPRESSION AND COGNITION

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The state of science has increasingly valued interdisciplinary training and research. As an early-stage investigator, interdisciplinary research, such as that supported by the Research Centers Collaborative Network through the National Institute on Aging, provides valuable opportunities to connect researchers across disciplinary boundaries. This program encourages researchers use their diverse training experiences to tackle difficult questions in aging research and forge scholarly relationship that advance the state of science through creative problem-solving and a spectrum of interdisciplinary perspectives. This presentation describes a recently funded project to examine sex differences in aging outcomes using genetics, depression, and impaired cognition with polygenic and gene-region aggregation techniques. We will highlight the benefits and opportunities of the Research Centers Collaborative Network pilot grant to this highly interdisciplinary work, co-lead by early-stage investigators.

SESSION 7540 (SYMPOSIUM)

FROM THE NATHAN SHOCK CENTERS COORDINATING CENTER: BIOLOGY OF AGING FOR NONBIOLOGISTS

Chair: Steven Austad

Advances in the biology of aging that promise to dramatically extend the healthy length of human life are now appearing at a breathtaking rate. At the same time, baseless claims of research breakthroughs in maintaining youth have exploded on electronic media. It often difficult for people outside basic aging research to keep track of what is real, what is imaginary, progress. This symposium brings together four scientists working in some of the most exciting research areas to update attendees in terms that will be understandable to anyone. Our speakers were carefully selected both for their scientific achievements and for their outstanding skill as science communicators. Matt Kaeberlein (University of Washington) will discuss some of the most exciting emerging pharmacological interventions that delay or prevent multiple features of aging. Nathan LeBrasseur (Mayo Clinic) will update us on a specific type of pharmacological intervention – senolytics – which target aged, nonfunctioning cells distributed throughout the body to broadly improve and extend health. Morgan Levine (Yale) will discuss how newly discovered molecular clocks give us more accurate information on our real biological age than does our birth certificate and will explain the research significance of these clocks. Melissa Harris (UAB) will update us on progress in stem cell biology. The promise of stem cells to treat and possibly reverse multiple aspects of aging are real, but perhaps no area of research has been more abused by hyperbolic claims. Dr. Harris will separate the real hope from the false hype.

PHARMACOLOGICAL INTERVENTIONS THAT TARGET BIOLOGICAL AGING

Matt Kaeberlein, *University of Washington, Seattle, Washington, United States*

There is a high level of interest in drugs that may delay or even reverse the functional declines and disease risks that accompany biological aging. Several interventions have been shown to improve age-related outcomes and increase lifespan in laboratory animals by targeting the hallmarks of aging. A number of these small molecules are being clinically evaluated for age-related indications, including mTOR inhibitors such as rapamycin, the anti-diabetic drug metformin, and senescent-cell clearing senolytics. Others are being marketed to consumers outside of the federal regulatory process as "anti-aging" natural products with little information about safety or efficacy. Here I will provide an overview of the current state of "anti-aging drugs" with an emphasis on potential mechanisms of action and evaluation of the existing pre-clinical and clinical data.

TARGETING SENESCENT CELLS TO COUNTER AGING AND AGING-RELATED CONDITIONS

Nathan LeBrasseur, *Mayo Clinic, Rochester, Minnesota, United States*

In response to various forms of age-associated damage, cells can enter a state of senescence. Senescent cells can compromise the health and function of a tissue, and their accumulation with advancing age is believed to contribute to age-related diseases and geriatric syndromes. In preclinical models (i.e., mice), selective elimination of senescent cells through either genetic approaches or a new class of pharmacological agents, termed "senolytics", has been show to effectively delay, prevent, or reverse the onset and/or progression of pulmonary disease, osteoporosis, atherosclerosis, diabetes, cognitive decline, and several other conditions. Thus, considerable efforts are underway to optimize pharmacological strategies and test their effectiveness in human populations. This seminar will highlight the state-of-the-science of senolytic drugs, and the opportunities and challenges for early phase clinical trials in humans.

AGING CLOCKS

Morgan Levine, *Yale University School of Medicine, New Haven, Connecticut, United States*

While chronological age is arguably the strongest risk factor for death, disease, and disability, same-aged individuals remain heterogeneous in their susceptibilities to these various outcomes. One explanation is that chronological age is an imperfect proxy of the degree of biological aging an individual has undergone. Thus, defining measurable estimates of 'biological age' (in contrast to chronological age) has become a major initiative in Geroscience research. Such biomarkers of aging, or 'aging clocks' will 1) help identify underlying mechanisms of aging, 2) enable identification of at-risk individuals prior to disease onset, and 3) provide outcomes to assess efficacy of interventions. In this session, I will describe the various aging clocks, how they were developed, and what they track. I will also describe how aging clocks can facilitate research both within and outside of the biological sciences.