SESSION 6540 (SYMPOSIUM)

SENESCENCE AND SENOLYTICS: STATE OF THE ART ON CELLULAR SENESCENCE, SENOLYTICS, AND HEALTHSPAN

Chair: Judith Campisi

Cellular senescence is a cell fate decision that is made by many mammalian cell types in response to damage, stress or certain physiological signals. Senescent cells arrest proliferation, essentially permanently, and develop a complex multi-component senescence-associated secretory phenotype (SASP). Recent studies using human and rodent cells, tissue samples and transgenic mouse models have defined a causal role for senescent cells, acting largely through the SASP, in a surprisingly large and diverse number of age-related diseases. Subsequently, several synthetic and natural compounds have been identified that have the ability to selectively kill senescent, but not non-senescent, cells. These compounds, termed senolytics, are now of intense interest to both basic research groups and biotechnology companies because they hold promise for postponing, ameliorating or, in some cases, reversing certain age-related pathologies. A related group of compounds, termed senomorphics, hold similar promise and act by selectively suppressing certain modules of the SASP. This symposium will feature presentations on some of the latest developments in the fields of cellular senescence and the SASP and how these cellular responses affect organismal health span. The symposium will particularly emphasize recent findings on the identification and activities of senolytic and senomorphic agents that have the potential to significantly extend the health span of mammalian organisms.

CELLULAR SENESCENCE AND MAMMALIAN HEALTHSPAN

Judith Campisi, *The Buck Institute for Age Research, Novato, California, United States*

Cellular senescence is a complex cell fate, often induced by stress or damage, that can be beneficial or deleterious, depending on the physiological context and age of the organism. A prominent feature of senescent cells is a multi-faceted senescence-associated secretory phenotype (SASP), which includes growth factors, cytokine and chemokines, growth factors, proteases, bioactive lipids and metabolites. Senescent cells increase with age in most, if not all, mammalian tissues. Through the use of transgenic mouse models, senescent cells are now known to causally drive numerous age-related pathologies, largely through the SASP. Eliminating senescent cells, genetically or through the use of senolytic/senomorphic agents, can improve the health span, at least in mice, and hold promise for extension to humans in the near future.

UNCOVERING THE MOLECULAR UNDERPINNINGS OF OXIDATIVE STRESS-INDUCED SENESCENCE

Melissa Carpenter, Laura Corrales-Diaz Pomatto, Jonathan Kato, Sarah Wong, Oye Bosompra, Michel Bernier, and Rafael de Cabo, *National Institute on Aging, Bethesda, Maryland, United States*

The aging process is sexually dimorphic, with males having higher occurrence rates of cancer and facing a greater risk of mortality. Sexual dimorphism in the response to cellular damage may account for distinct phenotypic changes with age as they relate to the accumulation of cellular damage leading to cancer. Cellular senescence triggers permanent cell cycle arrest in order to protect against malignant growth. However, organismal senescence increases with age and is associated with the release of pro-inflammatory signals (cytokines, chemokines, and proteases) known as the 'senescence-associated-secretory-phenotype' (SASP) that, if unchecked, accelerates tissue damage and creates a microenvironment ripe for cancer development. In this study, we hypothesized that sexual disparities in mortality and cancer prevalence stems from differences in the rate of accumulation of senescent cells in mice. Male and female C57BL/6J mice were fed ad libitum or subjected to 30% calorie restriction, a nutritional intervention known to delay the onset of various cancers and prevent senescent cell accumulation. Primary skin fibroblasts were collected longitudinally to allow measurement of cell proliferation, wound healing and the release of SASP factors. The results indicate that when compared to males, fibroblasts of CR-fed females showed significant improvements in cell growth rate, wound healing and SASP markers vs. AL controls. Work is underway to determine how sex influences cellular protective pathways. Thus, like other cell processes, cellular senescence is unequal between males and females and CR delays the emergence of the senescence phenotype.

DNA DAMAGE, CELLULAR SENESCENCE IN HEALTH AND DISEASE

Laura Neidernhofer

TARGETING CELLULAR SENESCENCE IN CANCER, HEALTH AND DISEASE

Daohong Zhou

SESSION 6545 (SYMPOSIUM)

EPIGENETICS: THE MANY FACES OF EPIGENETICS IN AGING

Chair: Shelley Berger

EPIGENETICS OF HUMAN NEURODEGENERATION

Shelley Berger, *University of Pennsylvania - Perelman School of Me*

EPIGENETICS AND AGING IN KILLIFISH

Anne Brunet, *Stanford School of Medicine, Stanford, California, United States*

DNA DAMAGE: EPIGENETICS, AGING AND REJUVENATION

David Sinclair, *Paul F. Glenn Center for Biology of Aging Research at Harvard Medical School, Boston, Massachusetts, United States*

SESSION 6550 (SYMPOSIUM)

STEM CELLS: THE FUTURE PROMISE OF STEM CELLS IN HEALTHSPAN

Chair: Ashley Webb

Tissue specific stem cells are critical for maintenance and repair of tissues and organs throughout life. However, during