SESSION 830 (POSTER)

BIOLOGY OF AGING III

PROLONGATION OF HUMAN LIFESPAN BY IMMATURE PEAR EXTRACT MEDIATED SIRTUIN-RELATED GENE EXPRESSION

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Demographics of the world are changing rapidly with older populations growing at an unprecedented rate. Cellular senescence, a decline of cellular function due to aging, causes gradual loss of physiological functions. Several cellular senescence-related chronic diseases, such as metabolic syndrome, cardiovascular disease, cancer, osteoporosis, diabetes, and hypertension, negatively affect the quality of human life. Intervention in the cellular senescence process may reduce these incidences and slow the progression of age-related diseases, while contributing to the longevity of healthy human lifespans. Saccharomyces cerevisiae, the budding yeast, is a simple model system that can provide significant insights into the human genetics and molecular biology of senescence and is considered suitable as a cellular model for research on mammalian cells. The aim of our study was to investigate the anti-aging effects of immature pear fruit extract (IPE) on yeast cells and its possible application to extend healthy lifespan in humans. Anti-aging effects of IPE were investigated using a chronological lifespan assay on S. cerevisiae cells. The chronological lifespan of the yeast treated with IPE at 1% (v/v) was significantly extended than that of untreated cells ($p < 0.05$). The expression of sirtuin-related genes, which regulate cellular senescence, was examined by reverse transcription-polymerase chain reaction and found to be significantly increased following IPE treatment. These results suggest that sirtuin-related genes have important roles in IPE-regulated lifespan extension, which provides a mechanism by which IPE could affect mammalian cells and potentially extend healthy human lifespans.

CAENORHABDITIS ELEGANS AS A MODEL OF AIR POLLUTION TOXICITY DURING DEVELOPMENT AND LIFESPAN

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Air pollution (AirPoll) is among the leading human mortality risk factors and yet little is known about the molecular mechanisms of this global environmental toxin. Our recent studies using mouse models even showed genetic variation and sex can alter biological responses to air pollution. To expand genetic studies of AirPoll toxicity throughout the lifespan, we introduced Caenorhabditis elegans as a new AirPoll exposure model which has a short lifespan, high throughput capabilities and shared longevity pathways with mammals. Acute exposure of C. elegans to airborne nanosized AirPoll matter (nPM) caused similar gene expression changes to our prior findings in cell culture and mouse models. Initial C. elegans responses to nPM included antioxidant, inflammatory and Alzheimer homolog genes. The magnitude of changes was dependent on the developmental stage of the worms. Even short term exposure of C. elegans to nPM altered developmental and lifespan hormetic effects, with pathways that included skn-1/Nrf family antioxidant responses. We propose C. elegans as a new and complementary model for mouse and cultured cells to study AirPoll across the lifespan. Future chronic nPM exposure and high throughput genetic screening of C. elegans can identify other major regulators of the developmental and lifespan effects of air pollution. This work was supported by grants R01AG051521 (CEF); R21AG05020 (CEF); Cure Alzheimer's Fund (CEF); R01GM109028 (SPC), F31AG051382 (HMD) and T32AG000037 (HMD), T32AG052374 (AH).

THE EFFECTS OF INDY ON FLY HEALTH

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Indy (I'm not dead yet) gene encodes a plasma membrane transporter of Krebs' cycle intermediates with highest affinity for citrate. Indy is the fly homolog of a mammalian mIndy (SLC13A5), which has the same physiological function. Reduced expression of the Indy gene extends longevity in fruit flies and worms. Genetic and pharmacological INDY reduction affects metabolism in flies, worms, mice, rats and non-human primates by affecting the levels of cytoplasmic citrate. In flies, INDY is predominantly expressed in the midgut, fat body and oenocytes, all tissues with a key role in metabolism. Our first goal was to examine our working hypothesis that INDY reduction in the midgut regulates citrate levels leading to metabolic changes that preserve intestinal stem cell (ISCs) homeostasis and slows aging by modifying Insulin/Insulin-like signaling (IIS). ISC homeostasis is vital for midgut homeostasis and contributes to health and longevity. We found that reduction of Indy preserves ISC homeostasis and intestinal integrity. The IIS is a key nutrient sensing pathway, which regulates growth, metabolism and longevity. Indy reduction is associated with decreased IIS activity. Our second goal was to examine the role of IIS in Indy mediated changes in ISC homeostasis and health. We found that at least some of INDY's beneficial effects on fly health are mediated by the IIS.