

Old mice expressing mitochondrial catalase have decreased lung cancer

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This presentation will focus on new data showing that old transgenic mice expressing the human catalase gene targeted to mitochondria (mCAT) have decreased cancer of the lungs. Patients with lung cancer have a devastating five-year survival rate of 15 percent, with adenocarcinoma of the non-small cell type representing 40 per cent of the cases and frequently expressing activated K-ras mutations. The incidence of lung adenocarcinomas occurs with increasing frequency (up to 70 per cent) with increasing age in male Balb/c X C57BL/6 F1 mice, also with frequently associated K-ras mutations. When these mice express mCAT, the incidence decreases to 40 per cent, with mostly adenomas rather than adenocarcinomas. Fibroblasts isolated from the lungs of old mCAT mice have increased expression of senescence markers beta-galactosidase, p16 and p53, compared to fibroblasts from lungs of old wild type (WT) mice. In addition, phospho-p38 MAP kinase is attenuated in mCAT lung fibroblasts treated with hydrogen peroxide compared to WT lung fibroblasts. We suggest that the anti-tumor activity of mCAT is associated with an increased senescence phenotype of stromal fibroblasts in conjunction with decreased p38MAP kinase activity and decreased ROS signaling. In addition to these novel findings, attendees will be familiarized with a spontaneously occurring lung cancer model in old mice that is clinically relevant to lung cancer in older people.

Biography

Warren Ladiges has studied the relationship between cancer and aging for over 20 years during which time he has contributed more than 100 peer-reviewed reports. He has served on the editorial boards of *Mechanisms of Aging and Disease*, *Gerontology*, and is Editor-in-Chief of *Pathobiology of Aging and Age-related Diseases*. He has served on various review committees for NIH including aging systems and geriatrics study section, and the Veterans Administration including oncology B study section.

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