

Our laboratory studies molecular and cellular mechanisms that drive the phenotypes and pathologies of aging. We study cell fate decisions, with an emphasis on cellular senescence. Cells constantly assess their functional state and their tissue microenvironment and attempt to repair or overcome molecular and cellular damage which increase with age. While these responses often benefit young organisms, they can become maladaptive during aging. Many diseases are driven by senescent cells, which cause age-related chronic inflammation (inflammaging), including cancer, arthritis and osteoporosis, dementia and frailty, among others. We primarily use human and mouse cells and organoids in culture, and mouse models.

Possible research project options include:

1. During genotoxic or cytotoxic cancer therapy, normal and malignant cells can undergo a cellular response termed therapy-induced senescence (TIS). TIS is characterized by an essentially irreversible proliferation arrest but also by the secretion of a plethora of inflammatory and other factors, collectively termed the senescence-associated secretory phenotype (SASP). SASP factors include growth factors, inflammatory cytokines, extracellular matrix (ECM) components and ECM degrading enzymes, all of which can promote activation and/or aggressiveness in neighboring cancer cells. More recent studies show that TIS can promote cancer relapse *in vivo*. We are investigating mechanisms governing the SASP intensity during senescence induction, with the ultimate goal of developing new combinatorial therapeutic regimens to minimize the long-term adverse effects of TIS in cancer patients.

2. Age-related visual impairment affects the physical, psychological, and social function of the elderly. 80% of our sensory impressions are perceived through the eyes. Therefore, it is essential to maintain healthy vision for a good quality of life. The ocular surface protects the cornea, keeping it smooth and wet for proper eyesight, cooperating with structures that include the conjunctiva and lacrimal glands. The retina is at the eye posterior and plays a major role in vision. Aging can change the ocular microenvironment as corneal epithelial stem cells decline. Tear fluid can also change, photoreceptor density can decline, and the retinal microvasculature can promote inflammation through the infiltration of macrophages and microglia.

Our hypothesis is that cellular senescence is a prime cause of age-related eye disease, including dry eye disease (DED), corneal stem cell deficiency, and macular degeneration. It was recently reported that as cells enter senescence, they acquire an inflammatory phenotype called the senescence-associated secretory phenotype (SASP), which includes many inflammatory cytokines, matrix metalloproteases (MMPs), chemoattractants, and even bioactive lipids. These deleterious molecules that senescent cells secrete can cause tissue degeneration, resulting in pathologies and diseases associated with aging. We are studying the pathology of senescence-related eye diseases and aim to discover novel options for treatment based on interventions that reduce the deleterious effects of senescent cells.

Desired Skills or Experience: Western blot, qRT-PCR, and ELISA

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