NATHAN SHOCK CENTERS OF EXCELLENCE IN THE BASIC BIOLOGY OF AGING

PILOT AWARDEE SPOTLIGHT

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A single-cell atlas of the aging lacrimal gland to understand the mechanisms underlying age-associated dry eye disease

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How did you become interested in aging?

I have always found it fascinating to understand how genetic and environmental factors can influence the way we age. Indeed, common mechanisms may lead to different responses/pathologies depending on the biological context. During my PhD, I was working on the impact of a longevity gene on cancer aggressiveness. Now, for my postdoctoral training in the Makarenkova lab at Scripps, my research focus is about the degeneration of exocrine glands during aging. In particular, I am interested in the changes affecting the crosstalk between secretory cells and the immune system in response to intrinsic and external stressors.

Briefly describe your project in non-scientific terms. What questions are you trying to answer?

The lacrimal gland secretes aqueous tears to keep the cornea wet and clear from debris, but also tear-specific proteins that promote cornea healing and have anti-microbial properties. For the defense of the ocular surface, the secretory cells of the lacrimal gland also closely interact with the immune system. With aging, chronic inflammation and cellular damages can alter tear secretion and trigger dry eye disease. Dry eye affects the quality of life of millions of aged Americans and, as for now, only palliative treatments attenuating symptoms are available. Our project aims at understanding the common mechanisms involved in the pathological aging of the mouse lacrimal gland at the single cell level, in both males and females, to gain new insights into therapeutic strategies restoring its function in humans.

What previous research or experience informed the development of this proposal?

It is known that the lacrimal gland exerts sexual dimorphism and that some age-related alterations tend to be sex-specific. We previously established the first single cell atlas of the aging lacrimal gland in female mice. We found both common and unique features in old females and thus, sought to find out if these alterations could also be observed in males.

What's exciting about your project's potential impact?

Beyond the biology of the lacrimal gland, our results provide a wealth of new data about exocrine gland aging, sex-specific features and the individual heterogeneity of aging. As exocrine glands are at front line of defense against environmental pathogens, they are of exceptional interest to understand the interplay between the epithelium and the immune system and how it is affected by aging.

If your project is successful, what is the next step?

Next, we will test treatments that we think will improve age-related chronic inflammation and epithelial dysfunction. Ultimately, our results could provide new insights for the management of dry eye.

How has support from and collaboration with the NSCs helped further this project and/or your research overall?
The collaboration with the genomics core of the SD-NSC has been very easy and successful, I received good guidance from them and my mentor. Thanks to this grant, I could perform the study about sexual dimorphism that would have been otherwise impossible. The results obtained help me to apply for other fundings, and the publications I am working on will be essential to build my career as an independent investigator. The workshops were also a good opportunity to discover the resources and new technologies available in the community.