2026 IMPACT CIRCLE

Project Title: Targeting the aging brain to preserve ovary function and extend healthspan

Investigator(s) and collaborations: Alison Kochersberger, Postdoctoral Fellow, and Ashley Webb, PhD

Unmet Need/Primary Question:
Aging of the reproductive system causes a decline in fertility and can negatively affect health in both men and women. Menopause — the loss of ovary function at midlife — drives an acceleration of aging in women, dramatically increasing risk for age-related diseases such as dementia and cardiovascular disease. Women who undergo menopause later in life live longer, and so do their brothers, demonstrating that the mechanisms driving ovary aging are fundamental to human longevity in both sexes. Targeting ovarian aging can extend healthspan of the entire body, reducing incidents of diseases that are leading causes of impairment, disability, and death. Despite recent increased effort in developing interventions to fix the aging ovary, few promising candidates have emerged.

Novel Hypothesis:
In young, healthy individuals, there is an ongoing back-and-forth conversation between the brain and the ovary, where the brain acts as the master regulator for healthy ovary function. During aging, a breakdown of brain-ovary communication begins before any changes are detected in the ovary, indicating that changes in the aging brain promote ovary decline. I have found that neuropeptides, a group of chemical messengers in the brain that are critical to brain-ovary communication, are significantly altered during aging in both mice and humans. My novel hypothesis is that alterations in the aging brain are driving ovary decline, and by targeting neuropeptides, we can restore brain-ovary communication and preserve ovary function. This research will shift the paradigm of ovarian aging research from ovary-targeted interventions to targeting the master regulator of ovary function, the brain.

Project Proposal:
Through bioinformatic analysis of aging mouse and human brains, I have identified a set of candidate neuropeptides to interrogate as intervention targets for ovary aging. Neuropeptide therapies act like a volume knob for the brain's communication, with therapeutics that can amplify a signal that has quieted with age or turn down a signal that has become too loud. I will test if using neuropeptide therapies to restore brain-ovary communication in aging mice preserves ovary function and overall health. As current biomarkers for ovary aging only detect changes after the ovary has been heavily impacted, I will also measure neuropeptides in human blood samples from the Buck's Clinical Research Core to establish if they can be used as novel early biomarkers to predict ovary decline.

Description of Potential Impact:
This project will identify targets for interventions that preserve brain-ovary communication with age to delay ovarian aging, and as a result delay the onset of many age-related diseases. There are many existing neuropeptide therapeutics, which will accelerate the translation of these findings into treatments. Additionally, I will have determined how neuropeptides in human blood are altered with age, motivating further development as novel biomarkers for ovary decline. This research will not only benefit women, since these same brain signals exist in men our findings will offer insights for improving healthy aging for everyone. Ultimately, this work will serve as the foundation for my own independent research career, studying how the brain drives aging of the entire body to develop novel biomarkers and interventions.