2026 IMPACT CIRCLE

Project Title: Beyond Estrogen: Discovering Novel Ovarian Factors that Shape Women's Health

Investigator: Bikem Soygur, PhD

Unmet Need/Primary Question:
Aging is not just about individual organs wearing out, but about the breakdown of communication in our bodies' sophisticated network, where organs constantly send signals to coordinate health and function. The ovary serves as a master regulator in this network throughout a woman's life, sending crucial messages that regulate metabolism, heart health, bone strength, and even brain aging. This communication role becomes strikingly clear with aging as loss of ovarian function at menopause increases risks for metabolic disorders, cardiovascular disease, osteoporosis, and dementia. Current understanding of ovarian aging centers almost entirely on estrogen deficiency and its downstream effects on target organs. However, this singular focus seems remarkably narrow: while human organs collectively secrete approximately 730 different proteins into blood circulation, only a handful of ovarian-derived proteins are functionally characterized. This represents not just a knowledge gap but a fundamental oversight in our understanding of ovarian function, as the limited characterization of ovarian secreted proteins (secretome) suggests we are missing critical mediators of female health and aging. Understanding the full repertoire of the ovarian secretome and its mechanism of action is a critical first step toward biomarker discovery and, ultimately, the development of targeted therapeutic interventions that preserve women's health across the lifespan.

Novel Hypothesis:
I hypothesize that the mouse ovary secretes novel age-dependent proteins that are detectable in blood and that target metabolic and neural tissues during aging.

Project Proposal:
I propose to identify circulating blood proteins secreted by ovarian follicles, the functional unit of the ovary, and study their effects on systemic health in young (2-month-old) and old (12-month-old) mice. Identification of the ovarian secretome requires genetic modification and tagging proteins in living organisms, which is impossible to do in humans. Therefore, I will leverage the mouse model which shares conserved ovarian steroid (i.e., estrogen and progesterone) and protein (i.e., AMH, inhibin, and activin) hormones with humans. I will leverage TurboID-based secretome profiling, a cutting-edge technology that labels secreted proteins in living mice. This approach will allow me to: (i) identify proteins secreted to the

bloodstream by ovarian follicles and (ii) map their distribution across target organs including the brain, muscle, adipose tissue, and bone. By linking ovarian secretions to systemic effects, this 2 unbiased approach will uncover previously unrecognized secreted proteins that mediate ovarian control of whole-body physiology.

Description of Potential Impact:
This study will be the first to systemically identify ovarianderived proteins that enter circulation and regulate systemic health, opening an entirely new frontier in women's health research. Future studies will validate candidate secreted proteins in human plasma from women across the pre-, peri-, and post-menopausal continuum, leveraging already banked human plasma samples at the Biospecimen Core at the Buck Institute. Success in this project positions us to decode the communication network of the ovary, potentially revealing therapeutic targets for extending women's healthspan and preventing age-related diseases.