

Project name: Role of CD38 in female reproductive aging

Project Description: Aging is accompanied by a gradual decline in tissue and cellular NAD⁺ levels, and this decline is linked causally to numerous age-associated diseases, including cognitive decline, cancer, metabolic disease, sarcopenia and frailty. Many of these ageing-associated diseases can be slowed down and even reversed by restoring NAD⁺ levels. Therefore, targeting NAD⁺ metabolism has emerged as a potential therapeutic approach to ameliorate age-related disease. However, much remains to be learnt about how NAD⁺ influences female reproductive health and ovarian aging. Ovarian aging is an irreversible process characterized by decreased oocyte quantity and quality which has negative impacts on fertility and endocrine function. Ovaries undergo an accelerated aging process that sets the pace for multi-organ female aging. Interestingly, recent evidence showed a strong association between ovarian aging and NAD⁺ decline, suggesting a pivotal role of NAD⁺ metabolism in reproductive healthspan. However, the mechanisms underlying ovarian NAD⁺ decline and the contribution of NAD⁺ consuming enzymes are still unknown. Our recent work in metabolic tissues (i.e. liver and adipose tissue) shows a link between age-dependent NAD⁺ decline and increased CD38, the major NAD⁺ consuming enzyme. CD38 is a multifunctional ecto-enzyme that degrades NAD⁺ and is ubiquitously expressed in immune cells. CD38 expression has been shown to increase with age in multiple tissues leading to NAD⁺ decline. However, CD38 expression in female reproductive tissues and its role in ovarian aging is unknown. The aim of this project is to investigate the role of CD38 in female fertility and ovarian health. We are seeking undergraduate students to join our team and work with our postdoctoral scholar in the lab to elucidate the contribution of CD38 as a negative regulator of ovarian aging and define the age-related ovarian metabolic profile. We will use C57BL6 (WT) and CD38 KO mouse strains to define CD38 expression pattern within the ovary, how this changes with age and how this impacts the NAD⁺-related metabolic profile.

Desired Skills or Experience: Completed coursework in biology, biochemistry and genetics desired but not necessary. Familiarity and proficiency with the following techniques desirable but not necessary: IHC, microscopy, WB, PCR, mass spectrometry.

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