# The Inhibition of the NLRP3 Inflammasome via Autophagy Regulation Mitigates Ovarian Fibrosis in Reproductively Aged Mice

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The microenvironment within the ovary plays a crucial role in follicle growth and ovulation but undergoes age-related changes. Fibrosis emerges as a hallmark of aging ovaries, accompanied by the establishment of an inflammatory environment, such as the activation of the NLRP3 inflammasome. Autophagy, an essential cellular homeostatic process for cell survival, is related to fibrosis by regulating NLRP3 inflammasome. However, the exact relationships between age-associated ovarian fibrosis and autophagy are poorly understood. In this study, we investigate the influence of autophagy on ovarian fibrosis through the modulation of the NLRP3 inflammasome. Here, we observed collagen deposition and fibronectin, both fibrosis markers, were increased within the ovarian tissue with advancing age. Also, diminished autophagic flux was observed in aged ovaries, compared to young ovaries, and this implies a functional impairment of autophagy with aging. In reproductively aged mice, the treatment with autophagy inducer reduced collagen deposition and increased the number of ovulated oocytes in aged ovaries, in association with alleviated NLRP3 inflammasome. Additionally, the administration of the NLRP3 inflammasome inhibitor (MCC950) attenuates ovarian fibrosis, concurrently restoring ovulatory function. Our studies demonstrate dysfunctional autophagy as a hallmark of the aging ovarian stroma and suggest that modulation of autophagy may contribute as a potential therapeutic intervention for ovarian function recovery by inhibiting ovarian fibrosis.