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NUS researchers identify how ovarian tissue stiffness can impair egg development

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Preclinical experiments link disrupted cellular connections to reduced egg maturation and identify a potential research target

Researchers at the National University of Singapore (NUS) have identified how a stiffer ovarian environment can disrupt communication between developing eggs and their supporting cells, offering insight into reproductive ageing.

The study was led by Assistant Professor Jennifer Young from NUS' Department of Biomedical Engineering and Professor Rong Li from its Department of Biological Sciences, working with the Mechanobiology Institute. The findings were published in Aging Cell.

Using mouse models, the researchers found that ovarian supporting tissue became approximately 2.5 times stiffer with age, alongside increased collagen content. The follicles containing developing eggs did not show the same age-related change in stiffness.

To examine the effect of the surrounding environment, the team cultured young follicles in hydrogels designed to reproduce younger and older tissue conditions.

Follicles in stiffer gels grew more slowly. The proportion of eggs reaching maturity was approximately one-third of that observed in softer gels.

The researchers also found about 28% fewer transzonal projections—thin cellular connections through which granulosa support cells exchange molecules and signals with the egg.

Further analysis implicated SMAD7, a protein that inhibits transforming growth factor beta signalling. Increased SMAD7 activity in the stiff environment was associated with reduced formation of these connections.

Treating cultured follicles with Mongersen, which suppresses SMAD7 production, helped restore cellular connections and partially improved follicle growth, egg maturation and mitochondrial function.

“Our findings suggest that some of the effects of ovarian tissue stiffening on egg development may be targetable,” said Assistant Professor Young.

The findings remain preclinical. Further work is needed to test the approach in follicles from older models and establish its relevance to potential fertility treatments.