Mechano-hydraulic control of mammalian ovarian follicle development

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The formation of functional eggs in the ovarian follicles is a critical process of early mammalian development. While genetic studies have revealed key genes for oocyte functions, the underlying mechanisms driving follicle growth remain enigmatic. Recent studies showed that follicle growth is sensitive to mechanical environment, calling for a need to understand mechanical signalling within follicles. Here, we investigate the mechanical functions of theca cells (TCs), which sit on a basement membrane encapsulating the follicles. Using a combination of biophysical, bioengineering, molecular and *ex vivo* approaches, we demonstrate that the TCs are highly contractile and exert active compressive stress to tune follicle pressure and mechanics, thereby regulating somatic cell signalling and follicle growth. We further found that the TC proliferation, migration and hormonal activities are mechanosensitive to stiffness, stretch and curvature, suggesting that changes in follicle geometry and basement membrane mechanics may in turn regulate TC functions *in vivo*. We hypothesise that such mechanical feedback is a key design principle for regulating follicle growth and oocyte functions through mechanotransduction pathways. Another long-standing question in the field is the mechanism driving the formation of fluid-filled cavity (lumen) in the antral follicle stage, failure of which is known to lead to infertility. Using label-free biophotonics and machine learning, we were able to, for the first time, characterise the spatiotemporal dynamics of lumen growth and cell motion during this phase. Our work will have profound implications for understanding infertility to help improve follicle health and IVF/IVM outcomes.

References:

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