

NANO-COMPUTED TOMOGRAPHY 3D MAPPING OF PRIMARY-TO-PREOVULATORY FOLLICLES IN THE MOUSE OVARY ACROSS LIFESPAN

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Folliculogenesis involves profound cyclic remodeling of the ovary 3D architecture. However, the spatial organization of follicles at different maturation stages, and how growth and atresia dynamics change throughout lifespan remain unsolved.

Here, we used computed tomography with nanometric isotropic resolution (nanoCT) to investigate the 3D organization of folliculogenesis in the mouse ovary from birth and prepuberty (0-25 days post-birth, dpb) to adulthood (2-4 months post-birth, mpb) and ageing (9-16mpb).

This approach enabled classification of all follicle types, from primary to preovulatory, and assessment of their health or atretic status.

Total follicle number increased 3-fold from 4dpb to 4mpb,

followed by a ~50% decline by 9mpb and subsequent stabilization. Total number of primary-antral follicles remained constant from 22dpb to 4mpb, and, after a sharp reduction, during aging (9-16mpb).

Atresia was first detected at 19dpb, affecting follicles from the secondary stage, and stabilized at 30-50% from late prepuberty onwards. While the healthy/atretic follicle ratio remained stable until 14mpb, atresia in antral and preovulatory follicles increased with aging, becoming significant by 16mpb, indicating impaired folliculogenesis.

Overall, this study establishes a novel approach to 3D mapping each follicle stage and presents the first comprehensive 4D atlas of the ovary, that quantifies primary-to-preovulatory follicle dynamics from birth through aging, providing a basis to uncover organizing rules of ovarian activity.