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Determine the developmental dynamics of primordial follicles in the mouse ovary

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ABSTRACT

Ovarian follicles are the basic functional units of the mammalian ovary. Progressive activation of primordial follicles serves as the source of fertilizable ova. In this thesis, by generating the *Foxl2-CreER*^{T2} and *Sohlh1-CreER*^{T2} mouse models, I have specifically labeled and traced the *in vivo* development of two classes of primordial follicles, the first wave of primordial follicles that are activated immediately after they are formed and the adult primordial follicles that are activated gradually in later life. The time-lapse tracing study has shown that the first wave of primordial follicles exist in the ovaries for about 3 months and contribute to the onset of puberty and to early fertility, whereas the adult primordial follicles gradually replace the first wave and dominate the ovary after 3 months of age, providing fertility until the end of reproductive life. Moreover, the two follicle populations also exhibit diverged minimal and maximal *in vivo* ripening times. Thus the two classes of primordial follicles follow distinct, age-dependent developmental paths and play different roles in the mammalian reproductive lifespan. Next I have verified whether primordial follicles can be regenerated from the purported female germline stem cells in the postnatal mouse ovary. We have created a multiple fluorescent *Rosa26*$^{rbw/+}$*;Ddx4-Cre* germline reporter mouse model for *in vivo* and *in vitro* tracing the development of female germline cell lineage. Through live cell imaging and neo-folliculogenesis experiments, we have shown that the Ddx4-expressing cells from postnatal mouse ovaries do not divide during the *in vitro* culture, nor do they differentiate into oocytes following transplantation into the recipient mouse. Such experimental evidence supports the classic view that there is neither follicular replenishment nor female germline stem cell in the postnatal mammalian ovary. In summary, I have determined the developmental dynamics of two distinct populations of primordial follicles in the mouse ovary and confirmed that there is no spontaneous follicle regeneration. Such knowledge will hopefully lead to a more in-depth understanding of how different types of primordial follicles contribute to physiological and pathological alterations of the mammalian ovary.

Key words: ovary, primordial follicles, germline stem cell, cell lineage tracing.

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