A New Model of Menstruation and Uterine Regeneration

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Menstruation is a complex physiological process found only in a few mammalian species, including humans, where the inner lining of the uterus (endometrium) undergoes cyclic shedding and subsequent regeneration. Despite its clinical significance and relevance to various disorders, like endometriosis, our understanding of menstruation and endometrial regeneration remains limited since there is no established menstruating model organism.

In menstruating species, the endometrium undergoes a major transformation, characterized by massive cell proliferation and tissue growth, in response to rising progesterone levels after ovulation. This newly formed tissue, the decidua, is shed and discarded upon the fall of progesterone secretion towards the end of the menstrual cycle, a process accompanied by bleeding. Non-menstruating mammals, including *Mus*, also form decidua, but only during pregnancy, as their natural ovarian cycle does not lead to decidualization. These observations suggest that decidua formation without pregnancy is a prerequisite for menstruation. To test this hypothesis, we developed a new transgenic mouse model to induce decidualization on demand in the non-pregnant mouse by selectively activating the molecular steps required for decidualization. Characterization of this model revealed that these animals have a cycle mimicking human menstruation when progesterone levels decline, including endometrial bleeding and subsequent regeneration. We are currently characterizing the applications of this model for menstrual disorders, including endometriosis. Our novel mouse model of menstruation offers a unique platform for studying the intricate processes involved in endometrial shedding and regeneration, with important implications for advancing reproductive health and improving the quality of life for millions of women worldwide.