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REPRODUCTIVE ENDOCRINOLOGY

Circadian clock involved in embryo implantation

In mice, deletion of the gene that encodes Arntl (also known as Bmal1), leads to failure of embryo implantation, according to new findings. This protein in key for gene expression driven by circadian rhythms, which suggests that the circadian clock is involved in fertility.

Yan Liu and colleagues created a mouse model to determine whether particular cellular clocks in peripheral tissues are essential for specific aspects of reproductive biology. To create the model, *Arntl*^{fx} mice were crossed with mice expressing a *Cre* transgene driven by the promoter of steroidogenic factor 1 (SF-1), which resulted in deletion of the *Arntl* gene. The resulting mice were termed SF1-*Bmal1*$^{-/-}$.

The knockout mice underwent puberty as normal and had normal estrus cycles (including ovulation), but none delivered pups despite showing evidence of copulation. By contrast, ~95% of wild-type control mice delivered pups. SF1-*Bmal1*$^{-/-}$ mice displayed characteristic signs of early pregnancy loss. The embryo implantation sites in these mice were found to be abnormal, and no embryos were discovered on histological examination.

Transplantation of wild-type ovaries into the knockout mice rescued fertility, as did treatment with progesterone. The authors suggest that their data demonstrate the crucial role of Arntl in the intrinsic molecular clock of ovarian steroidogenic cells, which is in turn involved in regulating the production of progesterone.

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Original article Liu, Y. *et al.* Loss of BMAL1 in ovarian steroidogenic cells results in implantation failure in female mice. *Proc. Natl Acad. Sci. USA* doi:10.1073/pnas.1209249111