

## The Histone H3K9 Demethylase Kdm3b Is Required for Somatic Growth and Female Reproductive Function

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### Abstract :

Kdm3b is a Jumonji C domain-containing protein that demethylates mono- and di-methylated lysine 9 of histone H3 (H3K9me1 and H3K9me2). Although the enzyme activity of Kdm3b is well characterized in vitro, its genetic and physiological function remains unknown. Herein, we generated Kdm3b knockout (Kdm3bKO) mice and observed restricted postnatal growth and female infertility in these mice. We found that Kdm3b ablation decreased IGFBP-3 expressed in the kidney by 53% and significantly reduced IGFBP-3 in the blood, which caused an accelerated degradation of IGF-1 and a 36% decrease in circulating IGF-1 concentration. We also found Kdm3b was highly expressed in the female reproductive organs including ovary, oviduct and uterus. Knockout of Kdm3b in female mice caused irregular estrous cycles, decreased 45% of the ovulation capability and 47% of the fertilization rate, and reduced 44% of the uterine decidual response, which were accompanied with a more than 50% decrease in the circulating levels of the 17beta-estradiol. Importantly, these female reproductive phenotypes were associated with significantly increased levels of H3K9me1/2/3 in the ovary and uterus. These results demonstrate that Kdm3b-mediated H3K9 demethylation plays essential roles in maintenance of the circulating IGF-1, postnatal somatic growth, circulating 17beta-estradiol, and female reproductive function.

### Key Word :

knockout mice, IGFBP-3/IGF-1, ovulation, fertilization, decidulization

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