

Knockout of the Histone Demethylase Kdm3b Decreases Spermatogenesis and Impairs Male Sexual Behaviors. ^[1]

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Abstract

Kdm3b is a JmjC domain-containing histone H3 (H3) demethylase and its physiological functions are largely unknown. In this study, we found that Kdm3b protein is highly expressed in multiple cell types in the mouse testes, including Leydig cells, Sertoli cells, spermatogonia and spermatocytes at different differentiation stages. We also observed Kdm3b protein in the epithelial cells of the caput epididymis, prostate and seminal vesicle. Breeding tests revealed that the number of pups produced by the breeding pairs with Kdm3b knockout (Kdm3bKO) males and wild type (WT) females was reduced 68% because of the decreased number of litters when compared with the breeding pairs with WT males and females. Further analysis demonstrated that Kdm3bKO male mice produced 44% fewer number of mature sperm in their cauda epididymides, displaying significantly reduced sperm motility. No significant differences in the circulating concentration of testosterone and the expression levels of androgen receptor and its representative target genes in the testis were observed. However, the circulating levels of 17 β -estradiol, a modulator of sperm maturation and male sexual behaviors, was markedly reduced in Kdm3bKO male mice. Strikingly, abrogation of Kdm3b in male mice significantly increased the latencies to mount, intromit and ejaculate and decreased the number of mounts and intromissions, largely due to their loss of interest in female odors. These findings indicate that Kdm3b is required for normal spermatogenesis and sexual behaviors in male mice.

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