The findings of this study also highlight that, by itself, high gene expression level in the testis is not a perfect indicator of an essential role in male fertility. Such studies, however, are important for our understanding of gene function in spermatogenesis as a portion of the genes from these larger screens will have essential roles for male fertility (and will presumably be published independently).

In addition, and as highlighted by the authors, this study was useful in generating knockout mice that could be used to investigate gene/protein function in other tissues or organ systems. The publishing of these results also prevents duplication of studies and narrows down the list of novel genes for which contraceptive targets could/should be designed.

Male infertility is a complex, multifactorial condition, and the interplay between genetics and environment in the etiology of male infertility requires further comprehensive studies. Notwithstanding the hundreds to thousands of studies with clear genetic diagnoses, it is probable that in a subset of cases, the cause of male infertility is more complicated than whether an individual gene is functional.

**COMPETING INTERESTS**

The author declares no competing interests.

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Commentary on “CRISPR/Cas9-mediated genome editing reveals 12 testis-enriched genes dispensable for male fertility in mice”

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Several thousand genes (17 000–19 000) are expressed in the human/mouse testis and a sizeable number of these are testis-enriched. However, the function of many of these genes in spermatogenesis is yet to be investigated. In a recent study by Oyama et al., the essential nature of 12 testis-enriched genes in male fertility was tested using knockout mouse models generated by clustered regularly interspaced short palindromic repeats (CRISPR-associated protein 9) technology. The authors performed basic male fertility analyses for three knockout lines (Tmem210, 4921539E11Rik, and 4930558C23Rik) and determined that spermatogenesis was normal, motile and morphologically normal sperm were produced, and knockout males were fertile. For the remaining nine lines (Cby2, Ldhal6b, Rasef, Scl25a2, Scl25a41, Smim8, Smim9, Tomm20l, and 1700057G04Rik), the authors simply investigated fertility via mating. Thus, there is a small chance that subtle roles of these genes in spermatogenesis or optimal fertility were overlooked. Altogether, despite a biased testis expression, each gene was dispensable for male fertility.

The research groups involved in the current study are world leaders in generating mouse models to ascertain the role(s) of unstudied genes in male fertility. This study, along with their previous work (e.g., Miyata et al.), emphasizes that while many genes are testis-enriched and evolutionarily conserved, they are not absolutely essential for male fertility. However, the absence of any fertility phenotypes may reflect the differences in environment for mice in animal houses, and men, who have varied diets, live in environments with pollution and exposure to other physical factors and may take medication, etc. Numerous environmental factors are known to be detrimental to male fertility, but the extent to which they interact with genetic variants is virtually unexplored. Thus, high-confidence genetic variants in these genes may contribute to infertility in men.