Infertility with defective spermatogenesis and hypotestosteronemia in male mice lacking the androgen receptor in Sertoli cells

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摘要

Abstract

Androgens and the androgen receptor (AR) play important roles in male fertility, although the detailed mechanisms, particularly how androgen/AR influences spermatogenesis in particular cell types, remain unclear. Using a Cre-Lox conditional knockout strategy, we generated a tissue-specific knockout mouse with the AR gene deleted only in Sertoli cells (S-AR-/y). Phenotype analyses show the S-AR-/y mice were indistinguishable from WT AR mice (B6 AR+/y) with the exception of testes, which were significantly atrophied. S-AR-/y mice were infertile, with spermatogenic arrest predominately at the diplotene premeiotic stage and almost no sperm detected in the epididymides. S-AR-/y mice also have lower serum testosterone concentrations and higher serum leuteinizing hormone concentrations than B6 AR+/y mice. Further mechanistic studies demonstrated that S-AR-/y mice have defects in the expression of anti-Müllerian hormone, androgen-binding protein, cyclin A1, and sperm-1, which play important roles in the control of spermatogenesis and/or steroidogenesis. Together, our Sertoli cell-specific AR knockout mice provide in vivo evidence of the need for functional AR in Sertoli cells to maintain normal spermatogenesis and testosterone production, and ensure normal male fertility.