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JOURNAL ARTICLE

Impairment of spermatogenesis in transgenic mice with selective overexpression of Bcl-2 in the somatic cells of the testis

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To explore the functional role of Bcl-2 in germ cell development, transgenic mice carrying 6 kilobases of the inhibin-alpha promoter were generated to express human bcl-2 gene product in the gonads. Although female transgenic mice demonstrated decreased follicle apoptosis, enhanced folliculogenesis, and increased germ cell tumorigenesis, the adult males exhibited variable impairment of spermatogenesis. The degree of damage ranged from tubules with intraepithelial vacuoles of varying sizes to near atrophied tubules consisting of Sertoli cells and a few spermatogonia. Although there was no significant change in body weight, an approximately 34% decrease in testicular weights was noted in transgenic animals compared with wild-type mice. Gamete maturation, assessed by determining the percentage of tubules with advanced (steps 13-16) spermatids, was decreased to 44.4% of the values measured in the wild-type animals. The incidence of germ cell apoptosis increased 3.8-fold in the transgenic animals and was associated with a marked loss of germ cells. Electron microscopy of the testes further revealed large vacuoles in the Sertoli cell cytoplasm and dilations of the intracellular spaces between adjacent Sertoli cells, spermatid malformations, and increased germ cell apoptosis in the transgenic animals. There was no evidence of Sertoli cell death either by terminal deoxynucleotidyl transferase-mediated dUTP nick end labeling (TUNEL) assay or electron microscopy. Leydig cell ultrastructure, cell size and numbers, and plasma levels of testosterone were not different between normal and the transgenic animals. Collectively, these results support the critical role of Bcl-2 in male germ cell development and are consistent with the gender-specific role of the Bcl-2 family members in reproduction.

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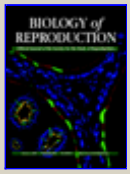

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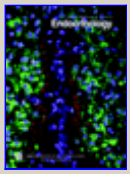

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