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Heat-Induced Apoptosis of Mouse Meiotic Cells Is Suppressed by Ectopic Expression of Testis-Specific Calpastatin

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Calpastatin is a naturally occurring inhibitor of calpain, a protease involved in apoptotic cell death. A testis-specific isoform of calpastatin (tCAST) has been identified that is transcribed in haploid germ cells but not in spermatocytes. To investigate the possible function(s) of tCAST, we tested the hypothesis that the ectopic expression of calpastatin in spermatocytes would suppress the death of these cells in response to an apoptosis-inducing stimulus in vivo. To this end, the 5'-flanking region of the mouse *Idhc* gene was linked to tCAST, and transgenic mice were generated. Immunohistochemical analysis revealed that, in contrast to control sections in which the signal for tCAST was seen in round spermatids, intense staining was visualized in pachytene spermatocytes in the transgenic animals, indicating that the strategy we used to generate the transgenic animals resulted in the ectopic expression of tCAST in spermatocytes. We then tested the effect of a short period of heating on germ cell apoptosis in the testes of wild-type and transgenic mice. Pachytene spermatocytes were the major germ cell type seen to undergo apoptosis after heat treatment. There were no differences in the number of apoptotic germ cells per seminiferous tubule between wild-type and tCAST transgenic control mice; thus, there was no apparent effect of the transgene on normal apoptosis. Heating resulted in increased numbers of TUNEL-positive germ cells in both wild-type and tCAST transgenic mice, as well as increased testicular DNA fragmentation. Heating the tCAST transgenic mouse testes resulted in significantly fewer apoptotic cells per seminiferous tubule than in wild-type mice at both 8 and 24 hours after treatment. Thus, as hypothesized, the ectopic expression of tCAST in pachytene spermatocytes suppressed germ cell apoptosis.

Key words: *Idhc* gene, tCAST, cell death, calpain, spermatocytes

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