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Participation

Apoptosis...controlling nature's destructive process

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Apoptosis, or natural cell death, is a necessary process that occurs within living organisms in response to developmental signals or environmental cues. Cell death can be triggered and transmitted by cell surface receptors ("initiators") to impact the mitochondria, where the Bcl-2 family members of proteins ("mediators") regulate cytochrome C release and activate caspases ("executioners") to degrade components of the cell. An equilibrium is established within cells between excess proliferation and death and is regulated at one level by the mitochondrial-associating proteins Bax (promotes apoptosis) and Bcl-xL (inhibits apoptosis). Cancer arises when cells do not respond appropriately to normal external cues to undergo cell death; conversely, excess cell death can lead to pathologies such as loss of germ cells and infertility. The goal of this project is to determine whether Fas-mediated apoptosis occurs within the murine testis and other target organs. PCR analysis of mRNA from mouse testis shows that Fas ligand and Fas receptor are both expressed. Intraperitoneal injections of Jo2 antibody (100ug) was done to trigger Fas receptor-mediated apoptosis in mouse tissues; control mice received injections of phosphate-buffered saline. After 6 hours, tissues (liver, spleen, thymus, and testis) were collected from injected mice and analyzed for the induction of apoptosis. Out of the tissues examined, an increase in apoptosis was only found in the liver of Jo2-injected mice. Although previous work has speculated on the FasL-Fas pathway as being responsible for induction of apoptosis within the testis, especially in the context of responses to environmental toxicants, we did not find such an effect. Lower dose injections will be performed for longer time periods to find out whether the Fas-mediated apoptosis is important in controlling the maintenance of germ cells within the murine testis. If the pathway is found to be important, transgenic mice will be generated to effectively block this pathway in the testis in hopes of preventing infertility from exposure to environmental stresses and toxicants.