

SUMMARY

The molecular regulation of cell fate decision of the undifferentiated spermatogonia is not yet understood. Existing spermatogenic cells in the reproductive pole are due to a balance between cell survival and death. In the body, cells die either by apoptosis (programmed cell death) or necrosis. Apoptosis has been found to be the predominant mode of cell death in response to a diversity of physiological and pathological stimuli. Apoptosis differs from necrosis, in addition to its characteristic morphological and biochemical features, by being an active process that requires gene expression and protein synthesis (Ameisen, 1996). The body utilizes apoptosis as a protective mechanism. Elimination of damaged cells by necrosis will initiate an inflammatory reaction that could destroy the normal cells in the surrounding environment. Apoptosis on the other hand, is not associated with inflammatory response. In the seminiferous epithelium, apoptosis maintains a constant number of germ cells within the supportive capacity of Sertoli cells. A unique structural connection exists between Sertoli cells and the Differentiating spermatogenic cells in the testis. The interaction between the germ cells and their survival and apoptotic signals is mediated through a diversity of endocrine and paracrine pathways that may involve Sertoli cells. The cells in the body are kept in a living state by continuous survival signals. Elimination of such signals will result in cell death by apoptosis.

Cell fate decision in the mature testis during spermatogenesis is not yet understood. Understanding of the molecular basis that controls cell fate is important. The ability to inhibit and /or stimulate apoptosis has great therapeutic potentials. Suppression of apoptosis would help infertile patients with severe oligozoospermia and perhaps those with unexplained infertility. Meanwhile, stimulation of apoptosis can help fighting different types of cancer.

Cell survival and death are regulated through a number of pathways that mostly involve cell receptors. The tumor necrosis factor receptor (TNFR) family is one of the largest receptor family involved in cell fate decision. Stimulation of these receptors by their ligands will initiate either a survival or a death signal that propagate inside the cell. It has been demonstrated that stimulation of the Fas receptor will initiate the apoptotic cell death program. However, the role of the TNFRs is unclear. Stimulation of the TNFRs has been shown to initiate apoptotic cell death through caspase 8. On the other hand, the same receptors can initiate survival signals through the transcription activator nuclear factor NF- κ B. However, NF- κ B was found to be stimulated when apoptosis was induced in the seminiferous epithelium suggesting a role of NF- κ B in induction of apoptosis (Pentikainen et al., 2001). Furthermore, It has been suggested that the apoptotic effect of NF- κ B may require the transcription factor p53.

The aim of this study is: 1) Identification of the most vulnerable cells in the reproductive pool to apoptotic cell death. 2) Effects of induction of apoptosis on Sertoli cells within the cultured testicular tissue. 3) Role of NF- κ B activation and the overexpression of Fas and p53 on the degree of apoptosis in the testis.