38. FUNCTIONAL CHARACTERISATION OF A LYMPHOCYTE-SUPPRESSING ACTIVITY IN GONADAL FLUID

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Protection of the developing gametes from attack by the immune system is essential for reproductive success, and autoimmune infertility represents a failure of this protection. The mechanisms are poorly understood, but there is evidence that local suppression of immune cell (i.e. T cell or antigen presenting cell) function by gonad-specific regulatory molecules is involved. Extracts of testicular and ovarian follicular fluid contain a potent inhibitor of T cell activation and proliferation as measured using a standard phytohemaglutinin (PHA) activated thymidine-incorporation assay. This activity has been partially purified from bovine follicular fluid, and initial characterisation indicates that it is a novel molecule. The inhibitor suppresses both basal and PHA-activated T cell proliferation *in vitro* within six hours in a dose-dependent manner. The suppression of proliferation does not appear to involve inhibition of the autocrine growth factor, interleukin-2. At sub-maximal inhibitory doses, the suppression of proliferation is reversible by withdrawal of the inhibitor, but at higher doses suppression is irreversible. This difference in reversibility is due to induction of T cell apoptosis at the higher doses, as indicated by Annexin V/propidium iodide dual-staining flow cytometry and DNA fragmentation analysis. In studies of the activity in several other cell types of different lineages, T cells and B lymphocytes (MPC-11 cell line) show a 10-fold or higher sensitivity to inhibition compared with non-lymphoid cells (HepG2 liver cells, NR8383 macrophages, NRK49F fibroblasts and K562 erythroid cells). These results indicate that the inhibitory mechanism involves T cell growth arrest leading to apoptosis, suggesting that the inhibitor triggers a specific lymphocyte deletion mechanism. Further characterisation of the function and immunoregulatory role of this inhibitor in the gonads is of great importance for understanding immune infertility, and more widely, has potentially significant clinical implications for improvement of transplant survival treatment of leukaemia and autoimmune diseases in general.

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