LEADING ARTICLE

INTERLEUKIN 2 — Quo Vadis?

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Molecular immunology is a hybrid, in which molecular biology techniques are used to dissect immunological networks, with the ultimate aim to better understand normal and disease states. Nowhere has there been such a great explosion of knowledge as in a group of proteins called lymphokines.

The Lymphokines are lymphocyte derived, genetically unrestricted peptides, that non specifically modulate immunologic and inflammatory response by regulating the growth and differentiation of a wide variety of leukocute and non leukocyte target cells.[1] There are at present six lymphokines and it is expected the list will grow.

Interleukin 2 (IL 2), formerly called T-cell growth factor has a molecular weight of 15,400 Kd is one such lymphokine. It is produced under suitable conditions by resting T-helper cells. Once produced the molecule has stimulatory effects on suppressor T-cells, B lymphocytes and cytotoxic T-cells. In addition it acts as an auto-stimulatory molecule, i.e. acts on the T-helper cell producing it, to further induce its own greater production. As previously mentioned the molecule acts on cell surfaces non-specifically but produces its stimulatory effect only when it binds to the IL receptor situated on cell surfaces.

The IL receptor has generated very considerable interest in recent years. It is now clear that it consists of two subunits 75 Kd and 55 Kd both of low affinity, but in combination become high affinity receptor of IL. The genes coding for the receptor and its ligand have been cloned and the amino acid sequence determined. IL2 can now be produced synthetically.

The ability to disrupt the synthesis of IL2, or to interfere with the interaction of IL2 with cellular receptors, could have considerable impact on clinical medicine. Animal studies show that the injection of anti IL2 antibodies lead to profound immunosuppression.[2] It is now known that cyclosporin A functions primarily by inhibiting the synthesis of IL2 by activated lymphocytes. A sub-population of peripheral blood lymphocytes, the large granular lymphocytes, on exposure to IL2 are able to kill tumour cells which are highly resistant.

Rosenberge[3] demonstrated that large quantities of peripheral lymphocytes can be safely removed, activated by IL2, and reinfused with minimal toxicity. Of the 222 patients treated with advanced cancer, 16 have undergone complete regression and 26 patients have undergone substantial reduction of tumour load. This therapy is now being combined with other cytokines like tumour necrosis factor. In some immunodeficiency states like AIDS, its efficacy remains to be demonstrated.

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