ROLE OF INTERLEUKIN 2 AND INTERLEUKIN 3 IN HAEMOPOIESIS.

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by

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ABSTRACT

The hormones interleukin 2 (IL2) and interleukin 3 (IL3) can stimulate the growth of immature haemopoietic cells. These hormones are synthesised by mature thymus-derived (T) lymphocytes. The observation that the haemopoietic tissues of the bone marrow contain few T lymphocytes leads to the question of what role IL2 and IL3 have in haemopoiesis.

An original finding described in this thesis was that IL3 induced a population of haemopoietic cells to synthesise IL2, IL3, IL4 and GM-CSF when stimulated with complexes of antigen and antibody. This demonstrated that there were cells in the bone marrow which synthesised hormones normally considered T lymphocyte-derived. It was possible to correlate the production of IL2, IL3, IL4 and GM-CSF by IL3-dependent cells with Ag.Ab complex- and mast cell-associated inflammatory processes.

A second finding described in this thesis was that haemopoietic cell lines dependent on IL3 for growth could be stimulated to grow by IL2. A unique feature of these IL3-dependent cell lines was that they could be adapted to an IL2-dependent growth state without further differentiation occurring. Such cells provide a tool for dissecting the intracellular growth regulating pathways which are controlled by IL2 and IL3.

The influence of IL2 on the development of T lymphocytes in the microenvironment of the thymus was examined. It was

found that the normal programme of T lymphocyte differentiation was altered by IL2. IL2 was found to stimulate the growth of an immature class of thymocytes which expressed cytotoxic activity. These cells had the potential to participate in host immune and inflammatory responses.

The haemopoietic cell responses induced by IL2 and IL3 appear to reflect the differentiation of immature cells for roles in immune responses. This indicates that IL2 and IL3 may not have a role in normal haemopoietic cell development. The hormones which normally regulate the output of cells from the thymus and bone marrow may not yet be fully defined.

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ABBREVIATIONS

Ag.Ab	antigen-antibody complex
C′	complement
cDNA	complementary DNA
ConA	concanavalin A
FACS	fluorescence activated cell sorter
G-CSF	granulocyte-colony stimulating factor
GM-CSF	granulocyte-macrophage colony stimulating factor
HPLC	high performance liquid chromatography
Ig	immunoglobulin
IL1	interleukin 1
IL2	interleukin 2
IL3	interleukin 3
IL4	interleukin 4
IL2-R	interleukin 2 receptor
KLH	keyhole limpet hemacyanin
LGL	large granular lymphocytes
LPS	lipopolysaccharide
LAK	lymphokine activated killer
M-CSF	macrophage-colony stimulating factor
MHC	major histocompatibility complex
mRNA	messenger RNA
M_r	relative molecular weight

NK	natural killer cells
RAFT	rat spleen conditioned medium
sIg	surface immunoglobulin
TCR	T lymphocyte antigen-receptor
TCM	tonsil-conditioned medium

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