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ROLE OF INTERLEUKIN 2 AND INTERLEUKIN 3
IN HAEMOPOIESIS.

Thesis submitted in partial fulfilment of
the requirements for the degree of
Doctorate in Philosophy.


by

Graham S. Le Gros
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.
ACKNOWLEDGEMENTS

I would like to thank my supervisors Jim Watson and John Marbrook for their scientific guidance. I thank Janette Le Gros for performing the molecular analysis described in this thesis. I thank Gaynor Borthwick and the Department of Cell Biology for their help in preparing this thesis. I thank the Medical Research Council of New Zealand, Leprosy Trust Board and the Cancer Society for funding the experiments carried out in the Department of Immunobiology. I thank my parents Helen and Steve for all their support.
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>TITLE PAGE</th>
<th>PAGE NUMBER</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABSTRACT</td>
<td></td>
</tr>
<tr>
<td>ACKNOWLEDGEMENTS</td>
<td></td>
</tr>
<tr>
<td>TABLE OF CONTENTS</td>
<td></td>
</tr>
<tr>
<td>LIST OF FIGURES</td>
<td></td>
</tr>
<tr>
<td>LIST OF TABLES</td>
<td></td>
</tr>
<tr>
<td>ABBREVIATIONS</td>
<td></td>
</tr>
</tbody>
</table>

## CHAPTER ONE : INTRODUCTION.

1.1 GENERAL INTRODUCTION. 1
1.2 HAEMOPOIESIS.
   ONTOGENY. 2
   ORGANISATION. 3
1.3 CELL GROWTH REGULATING HORMONES.
   INTERLEUKIN 1. 4
   INTERLEUKIN 2. 5
   INTERLEUKIN 3. 7
   INTERLEUKIN 4. 10
   GM-CSF. 11
   B LYMPHOCYTE GROWTH REGULATORS.
   M-CSF. 12
   G-CSF. 12
   THROMBOPOIETIN. 13
   ERYTHROPOIETIN. 14
   GENERAL FEATURES OF GROWTH REGULATORS 14
1.4 WHAT REGULATES HAEMOPOIETIC CELL GROWTH IN THE BONE MARROW? 16
1.5 THE EFFECT OF INTERLEUKIN 3 ON HAEMOPOIETIC CELLS. 17
1.6 WHAT REGULATES THYMOCYTE DEVELOPMENT?
   THYMOCYTE DEVELOPMENT. 19
   GROWTH HORMONES AND CELL SURFACE ANTIGENS REGULATE THYMOCYTE DEVELOPMENT. 21
1.7 EXPERIMENTAL AIMS OF THIS THESIS.

CHAPTER TWO : MATERIALS AND METHODS.

2.1 ANIMALS.

2.2 REAGENTS.

CULTURE MEDIUM.
MITOGENS.
GROWTH HORMONES.
CONDITION MEDIUM.

2.3 ANTIBODY REAGENTS.

MONOCLONAL ANTIBODIES.
PREPARATION OF IMMUNOGLOBULIN.
PREPARATION OF ANTIGEN-ANTIBODY COMPLEXES.
PEPSIN CLEAVAGE OF IMMUNOGLOBULIN.
PREPARATION OF HYPERIMMUNE SERUM.

2.4 CELL CULTURE.

CELL LINES.
ORGAN-CULTURE OF FETAL THYMUS LOBES.

2.5 CELL GROWTH ASSAYS.

MICROCULTURE GROWTH ASSAYS.
LONG-TERM GROWTH ASSAYS.
CLONING OF CELL LINES.

2.6 CELL PHENOTYPING.

FLUORESCENT STAINING.
COMPLEMENT-MEDIATED LYSIS.
CYTOCHEMICAL STAINING.
CELL CYCLE ANALYSIS.
CYTOTOXIC ASSAYS.

2.7 PREPARATION AND PURIFICATION OF GROWTH HORMONES.

PREPARATION OF CONDITIONED MEDIUM.
PURIFICATION OF GROWTH HORMONES.
GEL FILTRATION CHROMATOGRAPHY.
ION EXCHANGE CHROMATOGRAPHY.
HIGH PERFORMANCE LIQUID CHROMATOGRAPHY.

2.8 ISOLATION OF mRNA.

NORTHERN BLOT ANALYSIS.
CHAPTER THREE: THE SYNTHESIS OF GROWTH FACTORS BY IL3-DEPENDENT CELLS.

3.1 INTRODUCTION.

3.2 ANTIGEN-ANTIBODY COMPLEXES STIMULATE THE GROWTH OF IL3-DEPENDENT CELL LINES.

3.3 ANTIGEN-ANTIBODY COMPLEXES STIMULATE FD.C/1 CELLS TO SYNTHESISE GROWTH FACTORS.

3.4 EFFECT OF $F(ab')_2$ ANTIGEN-ANTIBODY COMPLEXES ON FD.C/1 CELLS.

3.5 BIOCHEMICAL CHARACTERISATION OF GROWTH FACTORS SYNTHESISED BY FD.C/1 CELLS.

3.6 ANTIGEN-ANTIBODY COMPLEXES STIMULATE THE SYNTHESIS OF IL2, IL3, IL4 AND GM-CSF mRNA.

3.7 BONE MARROW, SPLEEN AND FETAL LIVER CELLS RESPOND TO ANTIGEN-ANTIBODY COMPLEXES.

3.8 ANTIGEN-ANTIBODY COMPLEXES IN IMMUNE SERA.

3.9 DISCUSSION.

CHAPTER FOUR: EFFECT OF IL2 ON THE GROWTH OF IL3-DEPENDENT CELL LINES

4.1 INTRODUCTION.

4.2 THE EFFECT OF HUMAN TONSIL-CONDITIONED MEDIUM ON THE GROWTH OF FD.C/1 CELLS.

4.3 PURIFICATION OF THE GROWTH FACTOR(S) IN HUMAN TONSIL CONDITIONED MEDIUM.

4.4 RESPONSE OF FD.C/1 TO RECOMBINANT INTERLEUKIN 2.

4.5 THE DEVELOPMENT OF FD.C/2 CELLS IN LONG TERM CULTURES OF FD.C/1 CELLS.

4.6 GROWTH RESPONSE OF FD.C/1 AND FD.C/2 CELL LINES TO IL2 AND IL3.

4.7 RESPONSE OF THE IL3-DEPENDENT CELL LINES 32Dc1-23 AND GM TO IL2.
4.8 RESPONSE OF IL3- AND IL2- DEPENDENT CELLS TO IL1, IL2, IL3, IL4, GM-CSF, G-CSF AND M-CSF. 61
4.9 EXPRESSION OF IL2 RECEPTORS BY IL3-DEPENDENT AND IL2-DEPENDENT CELL LINES. 62
4.10 REGULATION OF IL2 RECEPTORS BY IL2 AND IL3. 63
4.11 PHENOTYPE OF IL3- AND IL2- DEPENDENT CELLS. SURFACE MARKER EXPRESSION. T LYMPHOCYTE ANTIGEN-RECEPTOR EXPRESSION. FUNCTIONAL ACTIVITIES. 64
4.12 THE RESPONSE OF BONE MARROW CELLS TO IL2. 67
4.13 DISCUSSION. 68

CHAPTER FIVE : EFFECT OF IL2 ON FETAL THYMOCYTE DEVELOPMENT
5.1 INTRODUCTION. 72
5.2 EFFECT OF IL2 ON THE GROWTH OF THYMOCYTES IN FETAL THYMUS LOBE ORGAN CULTURES. 73
5.3 EFFECT OF IL2 ON THE PHENOTYPE OF THE DEVELOPING FETAL THYMOCYTE POPULATIONS. 74
5.4 DEVELOPMENT OF CYTOTOXIC CELLS IN FETAL THYMUS ORGAN CULTURES. 76
5.5 EXPRESSION OF CYTOTOXIC ACTIVITY BY ORGAN-CULTURED FETAL THYMOCYTES. 77
5.6 THE SURFACE ANTIGENS EXPRESSED BY CYTOTOXIC FETAL THYMOCYTES. 78
5.7 EFFECT OF IL1, IL2, IL4 AND T LYMPHOCYTE MITOGENS ON CYTOTOXIC THYMOCYTES. 79
5.8 DISCUSSION. 80

CHAPTER SIX : DISCUSSION.
6.1 IL3-DEPENDENT CELLS SYNTHESISE GROWTH FACTORS. 83
6.2 IL2 REGULATES THE GROWTH OF IL3-DEPENDENT CELLS. EFFECT OF IL3 ON IL2 RECEPTOR DENSITY. 88
EFFECT OF IL2 ON IL3-DEPENDENT CELL MATURATION. 91
6.3 THE EFFECT OF IL2 ON FETAL THYMOCYTE DEVELOPMENT. 93
IL2-STIMULATED FETAL THYMOCYTES EXPRESS
CYTOTOXIC ACTIVITY. 96

REFERENCES 99
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ag.Ab</td>
<td>antigen-antibody complex</td>
</tr>
<tr>
<td>C'</td>
<td>complement</td>
</tr>
<tr>
<td>cDNA</td>
<td>complementary DNA</td>
</tr>
<tr>
<td>ConA</td>
<td>concanavalin A</td>
</tr>
<tr>
<td>FACS</td>
<td>fluorescence activated cell sorter</td>
</tr>
<tr>
<td>G-CSF</td>
<td>granulocyte-colony stimulating factor</td>
</tr>
<tr>
<td>GM-CSF</td>
<td>granulocyte-macrophage colony stimulating factor</td>
</tr>
<tr>
<td>HPLC</td>
<td>high performance liquid chromatography</td>
</tr>
<tr>
<td>Ig</td>
<td>immunoglobulin</td>
</tr>
<tr>
<td>IL1</td>
<td>interleukin 1</td>
</tr>
<tr>
<td>IL2</td>
<td>interleukin 2</td>
</tr>
<tr>
<td>IL3</td>
<td>interleukin 3</td>
</tr>
<tr>
<td>IL4</td>
<td>interleukin 4</td>
</tr>
<tr>
<td>IL2-R</td>
<td>interleukin 2 receptor</td>
</tr>
<tr>
<td>KLH</td>
<td>keyhole limpet hemacyanin</td>
</tr>
<tr>
<td>LGL</td>
<td>large granular lymphocytes</td>
</tr>
<tr>
<td>LPS</td>
<td>lipopolysaccharide</td>
</tr>
<tr>
<td>LAK</td>
<td>lymphokine activated killer</td>
</tr>
<tr>
<td>M-CSF</td>
<td>macrophage-colony stimulating factor</td>
</tr>
<tr>
<td>MHC</td>
<td>major histocompatibility complex</td>
</tr>
<tr>
<td>mRNA</td>
<td>messenger RNA</td>
</tr>
<tr>
<td>$M_r$</td>
<td>relative molecular weight</td>
</tr>
<tr>
<td>Acronym</td>
<td>Description</td>
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<tr>
<td>--------</td>
<td>--------------------------------------------------</td>
</tr>
<tr>
<td>NK</td>
<td>natural killer cells</td>
</tr>
<tr>
<td>RAFT</td>
<td>rat spleen conditioned medium</td>
</tr>
<tr>
<td>sIg</td>
<td>surface immunoglobulin</td>
</tr>
<tr>
<td>TCR</td>
<td>T lymphocyte antigen-receptor</td>
</tr>
<tr>
<td>TCM</td>
<td>tonsil-conditioned medium</td>
</tr>
</tbody>
</table>
LIST OF FIGURES

Figure 3.1. Ag.Ab Complexes Stimulate the Growth of IL3-Dependent Cell Lines.

Figure 3.2. Ag.Ab Complexes Stimulate FD.C/1 Cells to Synthesise Growth Factors.

Figure 3.3. Effect of F(ab')2 Ag.Ab Complexes on FD.C/1 Cells.

Figure 3.4. Size Fractionation of Growth Factors Synthesised by FD.C/1 Cells.

Figure 3.5. HPLC Fractionation of Growth Factors Synthesised by FD.C/1 Cells.

Figure 3.6. The Synthesis of IL2, IL3, IL4 and GM-CSF mRNA by FD.C/1 Cells Stimulated with Ag.Ab Complexes.

Figure 3.7. Ag.Ab Complexes in Immune Sera.

Figure 4.1. Growth Response of FD.C/1 and FD.C/2 Cell Lines to TCM or IL3.

Figure 4.2. Purification of Growth Factors in TCM.

Figure 4.3. Development of FD.C/2 Cells in Long Term Cultures of FD.C/1 Cells.

Figure 4.4. The Growth Response and Cell Cycle Distribution Profile of FD.C/1 and FD.C/2 Cells to IL2 and IL3.

Figure 4.5. The Growth Response of 32Dcl-23, 32Dcl-23(IL2) and GM Cells to IL2.

Figure 4.6 Growth Response of IL3- and IL2- Dependent Cell Lines to IL1, IL2, IL3, IL4, GM-CSF, G-CSF, M-CSF

Figure 4.7 Expression of IL2 Receptors by IL3- and IL2- Dependent Cell Lines.

Figure 4.8 Regulation of IL2 Receptors by IL2 or IL3.

Figure 4.9 Expression of T Lymphocyte Antigen Receptor (TCR) α, β and γ Chain mRNA.

Figure 5.1 The Effect of IL2 on Cell Growth in Fetal Thymus Organ Cultures.

Figure 5.2 Effect of IL2 Concentration on Thymocyte Growth.
Figure 5.2  Effect of IL2 Concentration on Thymocyte Growth.
Figure 5.3  Effect of IL2 on the Phenotype of Cells Which Develop in Fetal Thymus Organ Cultures.
Figure 5.4  Kinetics of Appearance of Cytotoxic Activity in Fetal Thymus Organ Cultures.
Figure 5.5  Specificity of Cytotoxic Activity.
Figure 5.6  Expression of J11d, CD4 and CD8 Antigens by Cytotoxic Fetal Thymocytes.
Figure 5.7  Growth Response of Cytotoxic Thymocytes to IL1, IL2, IL4 and T lymphocyte Mitogens.

TABLES

Table 3.1  The Synthesis of Growth Factors by Bone Marrow, Fetal Liver and Spleen Cells.
Table 4.1  The Development of IL2-Dependent F.D.C/1 Cell Lines.
Table 4.2  Surface Antigen and Enzyme Phenotype of IL2- and IL3- Dependent Cell Lines.
Table 4.3  Expression of Functional Activities by IL3- and IL2- Dependent Cell Lines.
Table 4.4  Effect of IL2 on the Phenotype of IL3-Cultured Bone Marrow Cells.
Table 5.1  Surface Antigen Phenotype of Anti-J11d Antibody and Complement Treated 14 Day Fetal Thymocytes.
Table 5.2  Phenotype of Cytotoxic Fetal Thymocytes.