

Immunomodulation by Colony-Stimulating Factors

Thomas Hartung

University of Konstanz, Biochemical Pharmacology, D-78457 Konstanz

Contents

Introduction	6
I G-CSF	10
1 General Information	10
1.1 Molecular Biology and Endogenous Production	10
A The Molecule G-CSF	10
B Endogenous Production of G-CSF	11
C Receptors and Signal Transduction	19
1.2 Role in Hematopoiesis	20
2 Effects on Granulocytes	23
2.1 Effects on the Functions of Neutrophilic Granulocytes	23
A Phagocytosis	24
B Oxidative Burst	25
C Adhesion and Chemotaxis	26
D Cytotoxicity	27
E Mediator and Enzyme Synthesis	28
F Degranulation	29
G Expression of Surface Molecules	30
H Microbial Killing	31
I Other	32
2.2 Effects on Eosinophilic and Basophilic Granulocytes	32
3 Effects on Mononuclear Cells	33
3.1 Effects on the Functions of Monocytes/Macrophages	33
A Synthesis of Mediators and Enzymes	33
B Expression of Surface molecules	34

C Other	34
3.2 Effects on the Functions of Lymphocytes	35
A Mediator and Enzyme Synthesis	35
B Expression of Surface Molecules	36
C Other	36
4 Effects on the Functions of Other Cells	37
5 Infections	38
A Bacterial Infections	38
B Viral, Fungal and Parasitic Infections	40
6 Potential Clinical Applications	40
 II GM-CSF	 44
1 General Information	44
1.1 Molecular Biology and Endogenous Production	44
A The Molecule GM-CSF	44
B Endogenous Production of GM-CSF	45
C Receptors and Signal Transduction	55
1.2 Role in Hematopoiesis	57
2 Effects on Granulocytes	59
2.1 Effects on the Functions of Neutrophilic Granulocytes	59
A Phagocytosis	59
B Oxidative Burst	60
C Adhesion, Chemotaxis and Migration	61
D Tumor Cytotoxicity	62
E Synthesis of Mediators and Enzymes	63
F Degranulation	64
G Expression of Surface Molecules	65
H Other	66
2.2 Effects on the Functions of Eosinophilic Granulocytes	67
A Phagocytosis	67
B Oxidative Burst	67
C Adherence, Chemotaxis and Migration	67
D Cytotoxicity	68
E Synthesis of Mediators	68
F Degranulation	68
G Expression of Surface Molecules	69
H Microbial Killing	69
I Other	69
2.3 Effects on the Functions of Basophilic Granulocytes	70

A	Histamine Release	70
B	Chemotaxis	70
C	Other	70
3	Effects on Mononuclear Cells	71
3.1	Effects on the Functions of Monocytes/Macrophages	71
A	Maturation of Monocytes to Macrophages	71
B	Phagocytosis	71
C	Oxidative Burst	72
D	Adhesion, Chemotaxis and Migration	73
E	Tumor Cytotoxicity	73
F	Synthesis of Mediators and Enzymes	74
G	Expression of Surface Molecules	78
H	Microbial Killing	79
I	Other	80
3.2	Effects on the Functions of Lymphocytes	80
4	Effects on the Functions of Other Cells	80
5	Infection	82
A	General	82
B	Specific Pathogens	84
6	Potential Clinical Applications	85
III	M-CSF	92
1	General Information	92
1.1	Molecular Biology and Endogenous Production	92
A	The Molecule M-CSF	92
B	Endogenous Production of M-CSF	92
C	Receptors and Signal Transduction	98
1.2	Role in Hematopoiesis	99
2	Effects on Granulocytes	100
3	Effects on Mononuclear Cells	100
3.1	Effects on the Functions of Monocytes/Macrophages	100
A	Maturation of Monocytes to Macrophages	101
B	Phagocytosis	101
C	Oxidative Burst	101
D	Chemotaxis and Migration	101
E	Tumor Cytotoxicity	101
F	Synthesis of Mediators and Enzymes	102

G Expression of Surface Molecules	104
H Microbial Killing	104
I Other	105
3.2 Effects on the Functions of Lymphocytes	105
4 Effects on the Functions of Other Cells	106
5 Infection	106
6 Possible Role of M-CSF In disease	106
7 Potential Clinical Applications	107
IV IL-3	107
1 General Information	107
1.1 Molecular Biology and Endogenous Production	107
A The Molecule Interleukin-3	107
B Endogenous Production of IL-3	108
C Receptors and Signal Transduction	110
1.2 Role in Hematopoiesis	111
2 Effects on Granulocytes	112
2.1 Effects on the Functions of Neutrophilic Granulocytes	112
2.2 Effects on the Functions of Eosinophilic Granulocytes	113
A Phagocytosis	113
B Chemotaxis and Migration	113
C Synthesis of Mediators	113
D Degranulation	113
E Expression of Surface Molecules	114
F Microbial Killing	114
G Other	114
2.3 Effects on the Functions of Basophilic Granulocytes	114
A Histamine Release	114
B Expression of Surface Molecules	115
C Adhesion and Chemotaxis	115
D Other	115
3 Effects on mononuclear cells	115
3.1 Effects on the Functions of Monocytes/Macrophages	115
A Maturation of Monocytes to Macrophages	115
B Phagocytosis	116
C Oxidative Burst	116
D Tumor Cytotoxicity	116

E Synthesis of Mediators and Enzymes	116
F Expression of Surface Molecules	117
G Microbial Killing	118
H Other	118
3.2 Effects on the Functions of Lymphocytes	118
A Migration	118
B Mediator Synthesis	119
4 Effects on the Functions of Other Cells	119
5 Role of IL-3 in Disease	120
6 Potential Clinical Applications	120
Conclusion	120
Acknowledgment	122
References	122
List of Abbreviations	163

CSF	homology in %	conservatively
G-CSF	73%	yes
GM-CSF	35%	no
M-CSF	81%	no > mo
IL-3	73%	no