

Cambridge University Press

0521425034 - Monoclonal Antibodies: Production, Engineering and Clinical Application

Edited by Mary A. Ritter and Heather M. Ladyman

Table of Contents

[More information](#)

## Contents

<b>1</b>	<b>Introduction</b>	<b>1</b>
	<i>M. A. Ritter</i>	
1.1	Introduction	1
1.2	Generation of an immune response	1
1.3	Antibody structure	2
1.4	Generation of the B cell repertoire	4
1.5	What is a monoclonal antibody?	6
1.6	The aim of this book	8
1.7	References	8
<b>2</b>	<b>Production of monoclonal antibodies</b>	<b>9</b>
	<i>H. M. Ladyman and M. A. Ritter</i>	
2.1	Introduction	9
2.2	Antigens and immunization	9
2.3	Cell fusion	15
2.4	Growth and selection of hybrids	18
2.5	Cloning techniques	22
2.6	Cell maintenance and bulk production of antibody	24
2.7	Characterization and purification of antibody	26
2.8	Storage	30
2.9	Analysis of the structure of the antigen to which your monoclonal antibody binds	31
2.10	Summary	32
2.11	References	32
<b>3</b>	<b>Antigen–antibody interactions: how affinity and kinetics affect assay design and selection procedures</b>	<b>34</b>
	<i>R. J. Morris</i>	
3.1	Introduction	34
3.2	What is affinity?	34
3.3	Kinetics of association and dissociation	37
3.4	Sensitivity, and its relationship to affinity	41
3.5	Other parameters affecting affinity	44
3.6	The nature of a protein epitope and its influence on antibody binding	50

		<i>Contents</i>
3.7	So what is antibody specificity?	53
3.8	Summary	56
3.9	References	57
<b>4</b>	<b>Production and characterization of synthetic peptide-derived antibodies</b>	<b>60</b>
	<i>K. M. Price</i>	
4.1	Introduction	60
4.2	Prediction and selection of antigenic determinants	61
4.3	Conjugation	63
4.4	Immunization	66
4.5	Screening	66
4.6	Epitope detection and analysis	69
4.7	Appendix	78
4.8	References	82
<b>5</b>	<b>Human monoclonal antibodies: production, use, problems</b>	<b>85</b>
	<i>A. Sa'adu and A. Zumla</i>	
5.1	Production of human monoclonal antibodies	85
5.2	Use of human monoclonal antibodies	90
5.3	Problems with human monoclonal antibody production	97
5.4	Conclusion	106
5.5	References	106
<b>6</b>	<b>Bispecific monoclonal antibodies</b>	<b>121</b>
	<i>S. Songsivilai and P. J. Lachmann</i>	
6.1	Introduction	121
6.2	Production of bispecific monoclonal antibodies	123
6.3	Applications of bispecific antibodies: current status and future development	132
6.4	References	136
<b>7</b>	<b>Production of antibodies using phage display libraries</b>	<b>142</b>
	<i>A. J. T. George</i>	
7.1	Introduction	142
7.2	Filamentous phage	143
7.3	Filamentous phage as expression vectors	144
7.4	Antibody selection on phage	146
7.5	Recombinant antibody fragments	154
7.6	Conclusions	159
7.7	References	160
<b>8</b>	<b>Genetic manipulation of monoclonal antibodies</b>	<b>166</b>
	<i>N. S. Courtenay-Luck</i>	
8.1	Introduction	166
8.2	Humanization	166
8.3	Recombinant antibody fragments	170
8.4	Discussion	175
8.5	References	177

	Contents	ix
<b>9</b>	Monoclonal antibodies in diagnostic immunoassays <i>D. B. Cook and C. H. Self</i>	180
9.1	Introduction	180
9.2	Advantages and pitfalls of using monoclonal antibodies	183
9.3	Specificity	185
9.4	Small molecular weight analytes	188
9.5	Endogenous interference in immunoassays	190
9.6	High-dose hook phenomenon	193
9.7	Use of established labelling technology	194
9.8	Sensitivity	194
9.9	Speed	195
9.10	Convenience	196
9.11	Methods of detection	197
9.12	Fibre optic sensors	201
9.13	Future of monoclonal antibodies in diagnostics	201
9.14	References	203
<b>10A</b>	Monoclonal antibodies in oncology: diagnostic pathology <i>A. Colfor and P. A. Hall</i>	209
10A.1	Introduction	209
10A.2	Genotype and phenotype	209
10A.3	Use of immunohistochemistry in diagnostic pathology	210
10A.4	Use of immunohistochemistry in diagnosis	210
10A.5	Immunohistochemistry as an educational aid	214
10A.6	Use in prognosis	214
10A.7	Histogenesis versus differentiation	216
10A.8	Future prospects	218
10A.9	Conclusion	219
10A.10	References	219
<b>10B</b>	Monoclonal antibodies in oncology: <i>in-vivo</i> targeting for immunoscintigraphy and therapy of human malignancies <i>A. Bamias and A. A. Epenetos</i>	222
10B.1	Introduction	222
10B.2	Immunoscintigraphy	223
10B.3	Immunotherapy	229
10B.4	Conclusion	238
10B.5	References	238
<b>11A</b>	Monoclonal antibodies in infectious disease: diagnosis <i>T. G. Wreggitt and J. J. Gray</i>	247
11A.1	Introduction	247
11A.2	Respiratory infections	247
11A.3	Gastroenteritis	248
11A.4	Hepatitis	249
11A.5	Neurological/congenital infections	250
11A.6	Meningitis	250
11A.7	Encephalitis	251
11A.8	Sexually transmitted disease	252

Cambridge University Press

0521425034 - Monoclonal Antibodies: Production, Engineering and Clinical Application

Edited by Mary A. Ritter and Heather M. Ladyman

Table of Contents

[More information](#)

x

*Contents*

	<i>Contents</i>
11A.9 Infection in the immunocompromised host	253
11A.10 References	255
<b>11B Monoclonal antibodies in infectious disease: prophylaxis and therapy</b>	<i>J. Cohen</i>
11B.1 Introduction	260
11B.2 Bacterial infections	261
11B.3 Viral and chlamydial infections	266
11B.4 Additional applications of monoclonal antibodies	268
11B.5 Conclusions	268
11B.6 References	269
<b>12A Monoclonal antibodies in transplantation: immunohistology</b>	<i>M. L. Rose</i>
12A.1 Introduction	274
12A.2 Nature of the infiltrate	274
12A.3 Major histocompatibility complex antigens	276
12A.4 Adhesion molecules	285
12A.5 Cytokines	287
12A.6 References	288
<b>12B Experimental studies on <i>in-vivo</i> immunosuppression</b>	<i>N. M. Parish and A. Cooke</i>
12B.1 Introduction	292
12B.2 Monoclonal antibody treatments directed towards T cell surface markers	294
12B.3 Monoclonal antibody therapies targeted at antigen-presenting cells	304
12B.4 Monoclonal antibody therapies targeting cytokines	305
12B.5 Monoclonal antibody therapies targeting adhesion molecules	308
12B.6 Monoclonal antibodies directed towards miscellaneous cell markers	309
12B.7 References	310
<b>12C Monoclonal antibodies in transplantation: prophylaxis and treatment of graft-versus-host disease after bone marrow transplantation</b>	<i>L. Boström and O. Ringden</i>
12C.1 Introduction	317
12C.2 Prevention of GVHD with <i>in-vitro</i> use of monoclonal antibodies	319
12C.3 Randomized clinical studies comparing pharmacological GVHD prophylaxis with T cell depletion	324
12C.4 Monoclonal antibodies <i>in vivo</i> for prevention of GVHD	325
12C.5 Treatment of GVHD with monoclonal antibodies	326
12C.6 Monoclonal antibodies in the diagnosis of GVHD	328
12C.7 Outlook	329
12C.8 References	329

Cambridge University Press

0521425034 - Monoclonal Antibodies: Production, Engineering and Clinical Application

Edited by Mary A. Ritter and Heather M. Ladyman

Table of Contents

[More information](#)*Contents*

xi

<b>12D</b>	Monoclonal antibodies in transplantation: use as therapeutic agents in clinical organ transplantation <i>M. Giral, J. Dantal, D. Cantarovich, M. Hourmant, R. Baatard, B. Le Mauff, Y. Jacques and J. P. Soulillou</i>	340
12D.1	Introduction	340
12D.2	Monoclonal antibodies reacting with all T lymphocytes	341
12D.3	Antibodies that react against a subset of T lymphocytes	346
12D.4	Monoclonal antibodies against interleukin-2 receptors	347
12D.5	Engineered monoclonal antibody molecules: chimeric, 'humanized' and fusion proteins	351
12D.6	Comments	352
12D.7	Acknowledgements	353
12D.8	References	353
<b>13</b>	Monoclonal antibodies and the skin <i>A. C. Chu and E. Tsele</i>	362
13.1	Introduction	362
13.2	Structure of the skin	362
13.3	The keratinocyte	362
13.4	Melanocytes	366
13.5	Langerhans cells	367
13.6	Basement membrane zone	368
13.7	Dermal infiltrates	370
13.8	Cutaneous T cell lymphoma	371
13.9	Benign cellular infiltrates	371
13.10	Adhesion molecules	372
13.11	References	373
<b>14</b>	Monoclonal antibodies in endocrinology <i>E. Hillhouse and C. H. Self</i>	380
14.1	Introduction	380
14.2	Assays of hormones	380
14.3	Generation of suitable monoclonal antibodies	382
14.4	Use of monoclonal antibodies	383
14.5	Specific modification	393
14.6	References	396
<b>15</b>	Monoclonal antibodies in rheumatology <i>J. D. Isaacs</i>	403
15.1	Introduction	403
15.2	Normal immune response	403
15.3	Monoclonal antibodies to control immune responsiveness	406
15.4	Animal models of rheumatological disorders	408
15.5	Monoclonal antibodies in human rheumatic diseases	410
15.6	Adverse effects of monoclonal antibodies	417
15.7	The future	419
15.8	Summary	420
15.9	Acknowledgements	421
15.10	References	421

Cambridge University Press

0521425034 - Monoclonal Antibodies: Production, Engineering and Clinical Application

Edited by Mary A. Ritter and Heather M. Ladyman

Table of Contents

[More information](#)

xii

*Contents*

<b>16</b>	Technical appendix: monoclonal antibody production methods	429
	<i>H. M. Ladyman and M. A. Ritter</i>	
16.1	Immunization	429
16.2	Media and general cell culture	429
16.3	Contamination in tissue culture	430
16.4	Cryopreservation of cells	431
16.5	The fusion	433
16.6	Cloning techniques	436
16.7	Bulk production of monoclonal antibodies	440
16.8	Screening techniques	441
16.9	Monoclonal antibody characterization and purification	449
16.10	SDS-PAGE and Western blotting	459
<b>Index</b>		467