

Contents

<i>List of contributors</i>	xv
<i>Abbreviations</i>	xvii

1 Targeting precursor proteins to mitochondria	1
TREVOR LITHGOW and GOTTFRIED SCHATZ	
1 Introduction	1
2 Targeting sequences	3
2.1 N-terminal targeting sequences	4
2.2 C-terminal sequences	6
2.3 Internal sequences	7
3 Precursor subclasses	8
3.1 Some precursors seem to have exposed presequences	8
3.2 Some precursors need ATP in the cytosol to enter the mitochondria	9
4 Cytosolic factors	11
4.1 Hsp70	11
4.2 Cytosolic DnaJ homologues	11
4.3 Chaperones specific for mitochondrial precursors	12
5 The import machinery on the mitochondrial surface decodes targeting signals	13
5.1 Mitochondrial protein import receptors	13
5.2 Do Mas70p and Mas20p function as hetero-oligomers?	15
6 Future directions	16
6.1 Dissection of the targeting process	16
6.2 A full-circle: what is sufficient to target a protein to the mitochondria?	18
Acknowledgements	18
References	18

2 Protein transport to the nucleus and its regulation	25
DAVID A. JANS	
1 Introduction: nuclear–cytoplasmic processes in the eukaryotic cell	25
2 The nucleus	26
2.1 The nuclear pore complex as a molecular sieve	26
2.2 Nuclear pore complex structure	27
2.3 Components of the nuclear pore complex	29
2.4 The nuclear lamina	29
2.5 Other nuclear processes	30
3 Signals for nuclear targeting	30
3.1 Nuclear localization sequences	33
3.2 Multiple and bipartite nuclear localization sequences	33
3.3 Signals for localization to ‘subnuclear compartments’	36
4 Modulators of NLS function	36
4.1 Protein context and competing signals	37
4.2 ‘Piggy back’ and cell-type-specific effects	38
4.3 Regulated (conditional) nuclear localization	42
5 Cellular components of the nuclear transport system	42
5.1 NLS-binding proteins	43
5.2 Molecular chaperones	44
5.3 Other components	45
6 Export of proteins from the nucleus and shuttling proteins	46
7 Nuclear protein transport kinetics	46
7.1 Systems to analyse protein transport	47
7.2 The kinetics of nuclear protein transport — the CcN motif as a discrete signal element regulating nuclear protein transport	50
8 Summary	51
Acknowledgements	51
References	
 3 Targeting and import of peroxisomal proteins	 63
CHRISTOPHER J. DANPURE	
1 Introduction	63
2 Overview of peroxisome, glyoxysome, and glycosome biogenesis	63

3 Protein targeting	65
3.1 C-terminal targeting sequences	65
3.2 N-terminal targeting sequences	69
3.3 Other ill-defined, ambiguous, and multiple targeting sequences	71
3.4 Evolutionary conservation of peroxisomal, glyoxysomal, and glycosomal protein targeting	74
4 Proteolytic processing	76
5 Import energetics	77
6 Folding, oligomerization, and possible interaction with molecular chaperones	78
7 Import receptors, membrane proteins, and other proteins involved in peroxisome assembly	80
7.1 Proteins involved in yeast peroxisome assembly	81
7.2 Proteins involved in mammalian peroxisome biogenesis	83
7.3 Miscellaneous peroxisomal membrane proteins (PMPs) of uncertain function	85
8 Conclusions	86
References	87
 4 Protein translocation into the endoplasmic reticulum	 101
KARIN RÖMISCH and ANN CORSI	
1 Introduction	101
2 The signal hypothesis	101
3 The signal peptide	102
4 Membrane proteins and topology	103
5 Components involved in translocation into the ER	105
5.1 Co-translational translocation	105
5.2 Post-translational translocation	108
5.3 SRP-independent translocation into the ER	109
5.4 The translocation complex	109
5.5 Definition of a minimal translocation apparatus	111
6 The nature of the translocation site	112
7 Enzymes at the translocation site	113
7.1 Signal peptidase	113
7.2 Oligosaccharyltransferase	113

8 Conclusions	114
Acknowledgements	114
References	115
5 ER-Golgi membrane traffic and protein targeting	123
CAROLYN E. MACHAMER	
1 Introduction	123
2 ER-Golgi and intra-Golgi transport	123
2.1 Vesicular transport	123
2.2 Similarities and differences between ER-Golgi and intra-Golgi transport	129
2.3 Retrograde traffic	130
3 Specific localization of ER- and Golgi-resident proteins	130
3.1 How are these dynamic compartments defined?	132
3.2 ER- and Golgi-resident proteins	133
3.3 General mechanisms for localization: retention vs. retrieval	135
3.4 ER residents	138
3.5 Golgi-resident proteins	142
4 Conclusions	143
References	
6 Biogenesis of constitutive secretory vesicles, secretory granules, and synaptic vesicles -- facts and concepts	152
MASATO OHASHI, RUDOLF BAUERFEIND, and WIELAND B. HUTTNER	
1 Introduction	152
2 Biogenesis of constitutive secretory vesicles	152
2.1 Soluble proteins	154
2.2 Membrane proteins	155
2.3 Molecular machinery	159
2.4 Regulation	159
3 Biogenesis of secretory granules	161
3.1 Immature secretory granules	161
3.2 Granule maturation	165
4 Biogenesis of synaptic vesicles	168

4.1 Synaptic-like microvesicles	168
4.2 Synaptic vesicles	169
4.3 Small dense-core vesicles	169
Acknowledgements	171
References	171
 7 Protein sorting during endocytosis	 176
NICHOLAS T. KTISTAKIS and MICHAEL G. ROTH	
1 Introduction	176
2 Internalization from clathrin-coated pits	176
2.1 Tyrosine-containing signals	177
2.2 Signal transplants	181
2.3 Signal prediction	181
2.4 Signal fine-tuning	183
2.5 Signals that do not contain tyrosine	185
3 Internalization, lysosomal, TGN, and basolateral signals: a common theme for a homotypic membrane system?	185
4 How the signal works	187
4.1 Components which recognize and bind the signal	187
4.2 Formation and invagination of coated pits	189
5 Sorting following internalization	191
5.1 Recycling is by default	193
5.2 Transcytosis requires receptor phosphorylation or occupancy	194
5.3 Sorting in the late endosome: proteins arriving by an intracellular route	195
5.4 Sorting in the late endosome: proteins arriving from the cell surface	197
6 A model for sorting in the endosomal homotypic membrane system	199
References	202
 <i>Index</i>	 213