

Contents

Contents	3
1 Introduction (<i>O. Slabý</i>)	7
2 Mendelian inheritance and monogenic diseases (<i>O. Slabý, K. Slabá</i>)	8
2.1 History	8
2.1.1 Mendel's experiments with plant hybrids	8
2.1.2 The rediscovery of Mendel, the laws of heredity, and the beginnings of genetics	11
2.2 Essential genetic terminology	12
2.3 Mendelian inheritance	13
2.3.1 Monohybridism, Mendel's first and second laws	13
2.3.2 Allelic interactions	15
2.3.3 Dihybridism and Mendel's third law	16
2.4 Deviations from Mendel's laws	18
2.4.1 Sex-linked inheritance	18
2.4.2 Gene interactions	19
2.4.3 Penetrance and expressivity	21
2.4.4 Mitochondrial inheritance	22
2.4.5 Genocopy and phenocopy	22
2.4.6 Other factors	22
2.5 Monogenic hereditary diseases and the use of Mendel's laws in medicine	23
2.5.1 Genealogical analysis	23
2.5.2 Autosomal dominant diseases	26
2.5.3 Autosomal recessive diseases	29
2.5.4 X-linked recessive diseases	33
2.5.5 X-linked dominant diseases	35
3 Multifactorial inheritance – inheritance of complex (quantitative) traits (<i>I. Slaninová</i>)	38
3.1 Heritability	38
3.2 Twin method	40
3.3 Multifactorial inheritance with the threshold model	41
3.4 Genome-wide association studies	41
4 Genetic linkage (<i>I. Slaninová</i>)	43
4.1 Linkage group, linkage phase	43
4.2 Chromosome map	45
4.3 Three-point test cross	46
4.4 Study of gene linkage and chromosome mapping in humans	46
4.5 Gene linkage in medicine	47

5 Population genetics (<i>I. Slaninová, S. Ševčíková</i>)	49
5.1 Hardy-Weinberg equilibrium	49
5.2 Conditions of genetic equilibrium	51
5.3 Factors that disturb genetic equilibrium	52
5.4 Application of Hardy-Weinberg equilibrium	55
6 Epigenetics (<i>S. Uldrijan</i>)	57
6.1 Epigenetic regulation of gene expression	57
6.1.1 DNA methylation	58
6.1.2 Histone modifications	59
6.2 Genomic imprinting and diseases associated with its defects	61
6.3 X chromosome inactivation	65
7 Immunogenetics (<i>O. Slabý</i>)	66
7.1 Introduction to the immune system, basic concepts	66
7.1.1 Cells of the immune system	68
7.1.2 Molecules of the immune system	70
7.1.3 Innate (non-specific) immunity	70
7.1.4 Specific (adaptive) immunity	72
7.2 Genetics of immunoglobulins and antigenic receptors	77
7.2.1 Immunoglobulins	77
7.2.2 B cell receptors (BCR)	80
7.2.3 T cell receptors (TCR)	81
7.3 Genetics of antigens	82
7.3.1 The major histocompatibility complex and presentation of peptide fragments	82
7.3.2 Genetic determination of blood groups of the AB0 system	85
7.3.3 Genetic determination of the Rh system	87
7.4 Immune tolerance and transplantation genetics	88
7.5 Immunopathology genetics	91
8 Cancer biology (<i>O. Slabý</i>)	93
8.1 Carcinogenesis	93
8.2 Genes critical for the development of cancer	95
8.2.1 Oncogenes	96
8.2.2 Tumor suppressors	97
8.3 Types of genetic and epigenetic changes during carcinogenesis	99
8.4 Enabling hallmarks of cancer	100
8.4.1 Genomic instability and mutations	102
8.4.2 Tumor inflammation	103
8.5 Hallmarks of cancer.	104
8.5.1 Self-sufficiency in the production of growth signals	105
8.5.2 Insensitivity to cell cycle regulators	108
8.5.3 Unlimited replication potential	110
8.5.4 Evasion of apoptosis	111
8.5.5 Induction of angiogenesis	112
8.5.6 Invasion and metastasis	114

8.5.7 Deregulation of cellular energetic metabolism	116
8.5.8 Escape from the immune system	117
8.6 Normal and tumor tissue, tumor microenvironment	118
8.7 Personalized treatment and the concept of precision oncology	119

9 Basic techniques of cellular and molecular biology (*J. Šána, O. Slabý*) 126

9.1 Restriction endonucleases and gel electrophoresis	127
9.1.1 Restriction endonucleases	127
9.1.2 Gel electrophoresis of nucleic acids	128
9.1.3 Restriction maps	128
9.1.4 Restriction fragment length polymorphism	130
9.2 Hybridization methods for the study of nucleic acids	132
9.2.1 Southern blotting	132
9.2.2 Fluorescence in situ hybridization	132
9.2.3 Comparative genomic hybridization (CGH) and array-CGH	134
9.3 Polymerase chain reaction	134
9.3.1 Real-time polymerase chain reaction	136
9.3.2 Reverse transcription and the study of gene expression	139
9.4 Determination of the DNA sequence	140
9.4.1 Sanger sequencing	140
9.4.2 Next-generation sequencing	141
9.4.3 Basic applications of next-generation sequencing	143
9.5 Genetic engineering	144
9.5.1 DNA cloning	144
9.5.2 Genome editing – CRISPR/Cas9	146
9.5.3 Transgenic animals	148

10 Gene therapy (*O. Slabý*) 152

10.1 General principles of gene therapy	153
10.2 Non-viral gene therapy	155
10.3 Gene therapy using viral vectors	156
10.3.1 Retroviruses	157
10.3.2 Lentiviruses	160
10.3.3 Adeno-associated viruses (AAV)	161
10.3.4 Adenoviruses	162
10.3.5 Safety of viral gene therapy	163
10.4 Gene silencing using oligonucleotide therapy	164
10.5 Gene editing	164
10.6 Clinical testing of gene therapy medicinal products	165

11 Human microbiome (*D. Šmajš, J. Bosák*) 166

11.1 General functions of the human microbiome	166
11.2 Skin microbiome	167
11.3 Oral microbiome	168
11.4 Gastrointestinal microbiome	169
11.5 Methods for the study of microbiome	172

12 Stem cells and tissue engineering (<i>V. Rotrekl</i>)	174
12.1 Stem cells – general introduction	174
12.1.1 Stem cells: the beginning	175
12.1.2 Definition and basic features of stem cells	176
12.1.3 Proliferation capacity	176
12.1.4 Differentiation ability	177
12.1.5 Progenitors and precursors	178
12.2 Occurrence of stem cells and their differentiation during ontogeny	179
12.2.1 Determinants of the stem cell fate	179
12.2.2 Morphogens in the control of stem cell fate	182
12.2.3 Synthetic matrices and artificial microenvironments	182
12.2.4 Intercellular interactions in the control of stem cell fate	183
12.3 Stem cells in medicine	184
12.3.1 Mesenchymal stem cells in medicine	184
12.3.2 Pluripotent stem cells in medicine	186
12.4 Organoids	190
12.5 From cells and organoids to organs: the journey from 2D to 3D tissue culture	191
12.6 Organ production in chimeric animals	192
13 Introduction to human ontogeny (<i>P. Krejčí, V. Rotrekl</i>)	194
13.1 Introduction to developmental biology	194
13.2 Polarization of the embryo	196
13.2.1 Establishment of the embryo axis	197
13.2.2 Embryo plasticity	198
13.3 Epigenetic mechanisms in early embryonic development	200
13.3.1 Embryonic genome activation	200
13.3.2 X chromosome inactivation	201
13.4 Morphogenesis	202
13.4.1 Cellular mechanisms of morphogenesis	202
13.4.2 Main morphogenetic processes	204
13.4.3 Gastrulation	205
13.4.4 Primordial animal	207
13.4.5 Molecular mechanisms of morphogenesis	207
13.4.6 Limb morphogenesis	211
14 Evolutionary biology (<i>I. Slaninová</i>)	215
14.1 Evolutionary theories	215
14.2 The origin of life on Earth	215
14.3 Charles Darwin – Darwinism	218
14.4 Importance of fossils	220
14.5 Mechanisms of evolution	220
14.6 Molecular evolution	220
14.7 Evolution of human	224
14.8 Evolution of primates	224
14.9 Evolution of <i>Homo sapiens</i>	225