

Contents

- 1 Blood** 1
 - 1.1 Blood Functions 2
 - 1.2 Plasma 3
 - 1.3 Plasma Constituents 5
 - 1.3.1 Electrolytes 5
 - 1.3.2 Glucids..... 6
 - 1.3.3 Plasma Proteins 7
 - 1.3.4 Plasma Lipids and Lipoproteins 8
 - 1.3.5 Blood Gas 15
 - 1.4 Blood Disorders 15
 - 1.4.1 Blood Cell Disorders..... 16
 - 1.5 Blood Therapies 17
 - 1.5.1 Blood Substitutes..... 17
 - 1.5.2 Plasmapheresis 18
- 2 Hematopoiesis**..... 19
 - 2.1 Hematopoietic Stem Cells 21
 - 2.1.1 LSK Hematopoietic Stem Cells 23
 - 2.1.2 Hemangioblast..... 24
 - 2.2 Biological Models of Hematopoiesis..... 24
 - 2.2.1 Arborescence Models of Hematopoiesis 25
 - 2.2.2 Lymphoid Progenitors 25
 - 2.3 Stem Cell Niches 27
 - 2.3.1 Types of Bone-Marrow Niches 27
 - 2.3.2 Cells of Bone Marrow Niches 28
 - 2.3.3 Crosstalk between Niche-Resident Cells..... 29
 - 2.4 Regulation of Hematopoiesis 31
 - 2.4.1 Transcription Factors of Hematopoiesis 32
 - 2.4.2 Hormones, Growth Factors, and Morphogens 42
 - 2.4.3 MicroRNAs..... 49
 - 2.4.4 Other Regulators 50

2.5	Mastocyte Formation.....	50
2.6	Hematopoietic Stem Cells in Angiogenesis.....	51
3	Blood Cells	53
3.1	Immunophenotyping of Leukocytes.....	53
3.2	Vasculature as an Immunity Compartment.....	54
3.3	Proliferation and Mobilization of Blood Cells	55
3.3.1	Cytokines	55
3.3.2	Chemokines	57
3.4	Scaffold Proteins in Immunocytes.....	57
3.5	Red Blood Capsules	60
3.5.1	Formation, Maturation, and Clearance	60
3.5.2	Shape.....	62
3.5.3	Plasma Membrane.....	63
3.5.4	Influence of Oxygen Content in the Local Environment	66
3.5.5	Oxygen Sensor	67
3.5.6	Blood Groups of the RBC Plasma Membrane	67
3.5.7	Hemoglobin Solution in Erythrocytic Capsule	71
3.5.8	Iron Acquisition and Storage	81
3.6	Platelets	83
3.6.1	Platelet Cytoskeleton	84
3.6.2	Translational Machinery	84
3.6.3	Platelet Granules	84
3.6.4	Platelet Activation.....	86
3.6.5	Non-Genomic Function of Transcription Factors.....	87
3.6.6	Other Regulators of the Platelet Function	88
3.6.7	Inflammatory Platelet	89
3.7	Granulocytes.....	89
3.7.1	Basophils	89
3.7.2	Eosinophils	92
3.7.3	Neutrophils	93
3.8	Mastocytes	97
3.8.1	Mastocyte Origin and Maturation	98
3.8.2	Mastocyte Functions	99
3.8.3	Mastocyte Production and Types	100
3.9	Lymphocytes	106
3.9.1	Selection between CD4 and CD8 Coreceptors	106
3.9.2	Sensing of Endo- and Exogenous Molecules	107
3.9.3	Resistance to Oxidizing Environment	108
3.9.4	PIP ₃ and IP ₄ Signals in Lymphocytes	109
3.9.5	Immunological Memory	109
3.10	T Lymphocytes	111
3.10.1	T-Lymphocyte Development.....	111
3.10.2	Antigen Presentation	113

3.10.3	T-Lymphocyte Maintenance	116
3.10.4	T-Lymphocyte Subpopulations	117
3.11	Innate Lymphocytes	143
3.11.1	Lymphoid Tissue-Inducer Cells	145
3.11.2	ILC17 Cells	146
3.11.3	NKR+ LTi-like Cells – ILC22 Cells	147
3.11.4	Nuocytes	147
3.11.5	Natural Killer Cells	148
3.12	B Lymphocytes	154
3.12.1	B-Lymphocyte Subpopulations	155
3.12.2	B-Lymphocyte Maturation Stages	155
3.12.3	Antibodies and B-Cell Receptors	156
3.12.4	B-Cell Activation and Signaling	159
3.12.5	Main Regulators of B-Cell Proliferation in Germinal Centers	160
3.12.6	B Cell–T Cell Interactions	160
3.12.7	Plasmocytes	160
3.13	Monocytes and Macrophages	161
3.13.1	Monocytes	162
3.13.2	Macrophages	165
3.14	Dendritic Cells	170
3.14.1	Myeloid and Plasmacytoid Dendritic Cells	172
3.14.2	Thymic Dendritic Cells	173
3.15	Myeloid-Derived Suppressor Cells	174
4	Lymph Drainage	177
4.1	Lymphatics	179
4.2	Lymphoid Tissues	179
4.2.1	Thymus	180
4.2.2	Spleen	180
4.2.3	Other Secondary Lymphoid Tissues	181
4.2.4	Tertiary Lymphoid Tissue – Mucosa- Associated Lymphoid Tissues	182
4.2.5	Lymph Nodes	185
4.3	Lymph	187
5	Cardiomyocytes	189
5.1	External Organization of Cardiomyocytes	189
5.2	Internal Organization of Cardiomyocytes	190
5.2.1	Sarcolemma	190
5.2.2	Sarcoplasmic Reticulum	194
5.2.3	Mitochondria	196
5.2.4	Nuclear GPCRs	204
5.3	Sarcomere	206
5.3.1	Myofibrils	208
5.3.2	Myosin Thick Filaments	209

5.3.3	Actin Thin Filaments.....	210
5.3.4	Z Disc, a Stretch-Sensing Structure	216
5.3.5	Main Sarcomeric Constituents.....	216
5.4	Cardiac Adenylate Cyclases and the cAMP Pathway	226
5.5	Calcium Signals	227
5.5.1	Calcium-Dependent Ion Carriers	227
5.5.2	Inositol Polyphosphate Messengers – Phosphoinositide Sources.....	228
5.5.3	Mitochondrial Calcium Uniporter	229
5.5.4	Mechanotransduction	229
5.5.5	Sodium–Calcium Exchangers and Sodium– Potassium Pumps.....	230
5.5.6	Normal and Impaired Calcium Signaling	230
5.6	Endocrine Function	232
5.6.1	Natriuretic Peptides	233
5.6.2	Hemojuvelin–Hepcidin Regulation.....	240
5.7	Energy Supply and Reserve.....	240
5.8	Cardiomyocyte Adaptive Growth	242
5.8.1	Mechanotransduction in CMC Hypertrophy	243
5.8.2	Chemical Regulators of CMC Hypertrophy	244
5.9	Cardiomyocyte Orientation	252
5.10	Ion Carriers	254
5.10.1	Voltage-Gated Sodium Channels	256
5.10.2	Sodium–Calcium Exchangers	257
5.10.3	Myocardial Calcium Channels	258
5.10.4	Myocardial Potassium Channels	262
5.10.5	Calcium-Activated Chloride Channels	268
6	Heart Wall.....	271
6.1	Cardiogenesis and Cardiac Remodeling	272
6.1.1	First and Second Heart Fields	274
6.1.2	Heart Growth Patterns	276
6.1.3	Epithelial–Mesenchymal Transition.....	276
6.1.4	Vasculo- and Angiogenesis	277
6.1.5	Neurogenesis	278
6.1.6	Valvulogenesis.....	279
6.1.7	Postnatal Growth	281
6.1.8	Regulators	282
6.1.9	Cardiac Progenitor Cells and Precursors	294
6.2	Wall Structure	299
6.2.1	Cardiofibroblasts	300
6.2.2	Telocytes.....	303
6.2.3	Epicardial Adipose Tissue and Adipokines	303
6.2.4	Heart Valves	306
6.2.5	Conduction Paths of the Depolarization Wave.....	308

6.3	Cardiac Regulation of Energy Homeostasis	313
6.4	Main Ion Currents	314
6.4.1	Pacemaker Cells	315
6.4.2	Ventriculomyocytes	322
6.5	Action Potential	324
6.5.1	Sinoatrial Node Action Potential	325
6.5.2	Ventricular Action Potential	328
6.5.3	Electrophysiological Myocyte Types.....	329
6.5.4	Repolarization	331
6.5.5	Electrophysiology and Contraction Kinetics.....	331
6.6	Excitation–Contraction Coupling	332
6.6.1	Intercellular and Cell-Matrix Adhesions	334
6.6.2	Troponins and Tropomyosin	334
6.6.3	Calcium Ion and Its Partners	334
6.6.4	Zinc Ion and Its Partners	337
6.6.5	Cyclic Adenosine Monophosphate	338
6.6.6	S100 Protein	339
6.6.7	Nervous Influences	339
6.6.8	Cell Excitability Adjustment	342
6.6.9	Electromechanical Modeling	343
6.7	Nervous Inputs	344
7	Vessel Wall.....	349
7.1	Physical Environment	349
7.2	Vasculature Development	350
7.3	Wall Structure	351
7.3.1	Large Vessels	353
7.3.2	Small Vessels	359
7.4	Blood–Brain Barrier.....	361
7.4.1	BBB Restricted Permeability	362
7.4.2	Neurovascular Units.....	364
7.4.3	Functional Hyperemia	366
7.4.4	Drug Delivery	367
7.4.5	BBB Formation.....	368
7.5	Other Cerebral Epithelial Barriers – Choroid Plexi.....	368
7.6	Perivascular Nerves	369
7.7	Pericytes	369
7.8	Nervous Inputs	371
7.9	ATP Signaling in Blood Vessel Walls	373
7.9.1	Extracellular ATP Processing.....	374
7.9.2	Nucleotide Receptors	375
7.9.3	ATP Release	375
7.10	Vascular Oxygen Sensing	378
7.11	Wall Adaptability.....	379

8	Smooth Myocytes	381
8.1	Markers of Smooth Myocytes	382
8.1.1	Actin	383
8.1.2	Tropomyosin	383
8.1.3	Myosin	383
8.1.4	Calmodulin	384
8.1.5	Caldesmon	386
8.1.6	Calponin	386
8.2	Glycocalyx	386
8.3	Intrinsic Regulators of Smooth Myocyte Tone	387
8.3.1	Caldesmon and Calmodulin	387
8.3.2	Arachidonic Acid	388
8.3.3	G-Protein-Coupled Receptors	388
8.3.4	Guanylate Cyclases, Nitric Oxide, and Natriuretic Peptides	388
8.3.5	Inositol Trisphosphate Receptors and Calcium Release	389
8.4	Airway Smooth Myocytes	393
8.4.1	Mechanical Loading-Induced Cytoskeleton Remodeling	393
8.4.2	Contractile and Proliferative Phenotype	393
8.4.3	Calcium Influx	393
8.4.4	Airway Smooth Myocyte Products	394
8.4.5	Hyperresponsiveness and Hypersensitivity	402
8.4.6	Deep Inspiration as Bronchodilation Inducer	402
8.5	Vascular Smooth Myocytes	405
8.5.1	Vascular Smooth Myocyte Subtypes	407
8.5.2	Mesangial and Juxtaglomerular Cells	407
8.5.3	Vascular Smooth Myocyte Phenotypes	408
8.5.4	Vascular Smooth Myocyte Uptake	417
8.5.5	Vascular Smooth Myocyte Activity	417
8.5.6	Vascular Smooth Myocyte Production	423
8.5.7	Vascular Smooth Myocyte Migration	425
8.5.8	Vasomotor Tone	429
9	Vascular Endothelium	453
9.1	Endothelial Cell	454
9.1.1	Glycocalyx	456
9.1.2	Endothelial Cell Adhesions	457
9.1.3	Vascular Permeability	467
9.2	Endothelium Types	468
9.2.1	High Endothelial Venules	468
9.2.2	Lymphatic Endothelium	469
9.2.3	Endothelial Fenestrae	469

9.3	Endothelial Progenitor Cells	469
9.3.1	Hemangioblast.....	470
9.3.2	Endothelial Progenitor Cell – Circulating Angiogenic Cell	472
9.4	Endothelial Cell Migration	474
9.5	Molecular Expression in the Vascular Endothelium	474
9.5.1	Caveolae	477
9.5.2	Nuclear Receptors.....	479
9.5.3	Examples of Endothelial Receptors	479
9.5.4	Ion Carriers of Endothelial Cell	485
9.5.5	Hormones and Vasoactive Substances	492
9.5.6	Adhesion Molecules	498
9.5.7	Miscellaneous	499
9.5.8	Vessel Wall Homeostasis	499
9.5.9	Growth Factors and Regulators of Growth Factor Signaling	504
9.5.10	MicroRNAs.....	507
9.5.11	Angiogenesis Guidance Molecules.....	510
9.5.12	Blood Group Antigens	512
9.6	Transendothelial Mass Transfer	512
9.6.1	Flow-Dependent Transendothelial Transport	513
9.6.2	Transport Mechanisms	514
9.6.3	Endothelial Permeability and Vascular Compartments ..	522
9.6.4	Endothelial Permeability Regulation	522
9.7	Extravasation	535
9.7.1	Flowing Cell Adhesion to Endothelium.....	536
9.7.2	Cell Movement over the Wetted Endothelial Surface ...	537
9.7.3	Integrin-Based Cell Adhesion	538
9.7.4	Intracellular Signaling in Endothelial Cells.....	538
9.7.5	Intracellular Signaling in Leukocytes	539
9.7.6	Extravasation Steps	540
9.7.7	Extravasation Modes	543
9.7.8	Migration across Pericyte Sheath and Basement Membrane	544
9.7.9	Migration through Subendothelial Layer and Interstitium.....	545
9.7.10	Regulation of Inflammation.....	546
9.8	Hemostasis.....	548
9.8.1	Blood Coagulation	553
9.8.2	Fibrinolysis	561
9.8.3	Embolus Extravasation.....	562
9.8.4	Thrombosis	562
9.8.5	Mathematical Modeling and Numerical Simulations....	564
9.9	Effects of High-Density Lipoproteins on Endothelium	565

9.10	Chemical and Mechanical Regulation of the Vasomotor Tone	566
9.10.1	Transducers of Mechanical Stresses	570
9.10.2	Flow Chambers	575
9.10.3	Nitric Oxide	578
9.10.4	Endothelin	582
9.10.5	Calcium Signaling in Vasomotor Tone Regulation	583
9.10.6	Other Mechanotransduction Effects	585
9.10.7	Other Aspects of the Regulation of the Vasomotor Tone	588
9.10.8	Hypoxic Vasoconstriction of Pulmonary Arteries	594
9.10.9	Hypoxic Vasodilation of Cerebral Arterioles	594
9.10.10	Vasomotor Tone during Pregnancy	596
9.10.11	Modeling of Mechanotransduction in Arteries	596
10	Vasculature Growth	605
10.1	Vasculogenesis	606
10.2	Angiogenesis	606
10.2.1	Stem, Progenitor, and Precursor Cells in Angiogenesis and Neovascularization	607
10.2.2	Involved Factors in Angiogenesis	609
10.2.3	Endothelial Sprouting: Tip and Stalk Cells	609
10.2.4	Other Modes of Vessel Formation and Remodeling	613
10.2.5	Lumenogenesis	614
10.3	Arteriogenesis	615
10.4	Vasculature Compartments	616
10.4.1	Lumen Size and Vessel Architecture	616
10.4.2	Cost Functions	616
10.4.3	Arteriovenous Differentiation	616
10.5	Extracellular Matrix in Vessel Formation	618
10.5.1	Growth Factors	618
10.5.2	Protein Fragments and Peptidases of the Extracellular Matrix	620
10.5.3	Cell Adhesion Molecules	622
10.5.4	Fibulins	624
10.5.5	Thrombospondins	625
10.5.6	Matrix Metallopeptidases	625
10.5.7	Transglutaminase and Carboxypeptidases	625
10.5.8	Collagen Prolyl 4-Hydroxylase	626
10.6	Mediators of Vascular Formation	626
10.6.1	Navigation Signals	626
10.6.2	Transcriptional Regulators	630
10.6.3	MicroRNAs	634
10.6.4	Morphogens	636
10.6.5	Growth Factors	639
10.6.6	Hormones and Cytokines	647

10.6.7	G-Protein-Coupled Receptors	653
10.6.8	Regulators of Small GTPases	654
10.6.9	Phosphoinositide 3-Kinase and Phospholipase-C	654
10.6.10	Protein Kinase-B	655
10.6.11	Cyclooxygenases and Prostaglandins	656
10.6.12	Tissue Factor	657
10.6.13	Tissue Kallikrein and Kininogen	657
10.6.14	Gasotransmitters Hydrogen Sulfide and Nitric Oxide ...	658
10.6.15	Oxidative Stress and Inflammation	660
10.6.16	Mechanical Signals	661
10.7	Angiogenesis-Targeted Therapies	662
10.7.1	Angiogenesis Promotion	662
10.7.2	Angiogenesis Inhibition	664
10.8	Lymphangiogenesis	668
10.8.1	Transcription Factors in Lymphangiogenesis	669
10.8.2	Growth Factors and Guidance Molecules	670
10.8.3	Other Mediators	671
10.9	Modeling of Angiogenesis	671
11	Tissue Development, Repair, and Remodeling	675
11.1	Organogenesis	676
11.1.1	Ecto-, Endo-, and Mesoderm	676
11.1.2	Precursor Cells	678
11.1.3	Organogenesis, Vascularization, and Innervation	679
11.1.4	Regulation of Organogenesis	680
11.2	Cell Differentiation	682
11.3	Branching Morphogenesis	682
11.3.1	Airway Morphogenesis	683
11.3.2	Airway Morphogenesis Mediators	684
11.3.3	Mechanical Basis of Branching	688
11.3.4	Molecular Basis of Branching	688
11.4	Therapeutic Repair	692
11.4.1	Stem Cells and Regenerative Therapy	692
11.4.2	Gene Therapy	697
11.4.3	Tissue Engineering	699
11.5	Inflammation	703
11.5.1	Extravasation	703
11.5.2	Molecular Basis of Extravasation	704
11.5.3	Crossing of the Vascular Basement Membrane	713
11.5.4	Interstitial Migration of Leukocytes	713
11.5.5	Molecular Mechanisms of Leukocyte Chemotaxis	713
11.5.6	Inflammatory Mediators	715
11.5.7	Angiogenesis and Inflammation	728
11.5.8	Inflammatory Diseases	730

11.6	Healing.....	731
11.6.1	Plasma Enzymatic Systems	732
11.6.2	Involved Cells	732
11.6.3	Myofibroblasts	733
11.6.4	Healing Phases	735
11.6.5	Modeling of Healing	737
11.7	Respiratory Epithelium Repair	739
11.8	Vascular Tissue Remodeling	740
11.8.1	Myocardium Remodeling	741
11.8.2	Vessel Wall Remodeling	742
11.9	Growth Modeling	745
12	Airway Surface Liquid and Respiratory Mucus	749
12.1	Double-Layered Airway Surface Fluid.....	751
12.1.1	Control of the Quantity and Composition of the Airway Surface Fluid	752
12.2	Mucociliary Clearance	754
12.2.1	Factors of the Mucociliary Clearance	755
12.2.2	Cough Clearance	755
12.2.3	Mucociliary Clearance and Infection.....	756
12.2.4	Alterations in Mucociliary Clearance	756
12.3	Mucus Delivery.....	758
12.3.1	Secretory Cells	758
12.3.2	Mucus Release	766
12.3.3	Regulation of Mucus Secretion	767
12.4	Mucus Composition	769
12.4.1	Mucin	770
12.4.2	Other Proteic Constituents of Mucus.....	772
12.4.3	Lipids	773
12.4.4	Surfactant	773
12.4.5	Minerals	773
12.5	Mucus Properties	774
12.5.1	Mucus Permeability	774
12.5.2	Mucus Contact Properties.....	775
12.5.3	Mucus Rheology	775
12.6	Mucus Motility	778
12.6.1	Respiratory Cilium	778
12.6.2	Cilium Beats	780
12.6.3	Ciliogenesis.....	785
12.7	Mucus Transport Modeling	786
12.7.1	Governing Equations	787
13	Surfactant	789
13.1	Surface Tension	789
13.2	Alveolar Surfactant.....	794
13.2.1	Formation of the Alveolar Surface Film	794

13.2.2	Alveolar Liquid Film Homeostasis	795
13.2.3	Secretion and Role of Alveolar Surfactant	796
13.3	Surfactant Composition	797
13.3.1	Surfactant Proteins	797
13.3.2	Surfactant Lipids	799
13.3.3	Calcium	800
13.4	Immune Function of Surfactant	800
13.5	Governing Equations and Surfactant Transport Modeling	800
13.5.1	Interfacial Tension and Marangoni Stress	801
13.5.2	Dimensionless Governing Parameters	801
13.5.3	Surfactant and Marangoni Flows	802
14	Conclusion	805
	References	813
	Notation Rules: Aliases and Symbols	903
	List of Currently Used Prefixes and Suffixes	909
	List of Aliases	913
	Complementary Lists of Notations	943
	Index	949

Tissue Functioning and Remodeling in the Circulatory
and Ventilatory Systems

Thiriet, M.

2013, XXI, 962 p., Hardcover

ISBN: 978-1-4614-5965-1