Contents to Volume 1

List of Contributors *xiii*
Foreword *xxiii*
Preface *xxv*

Part I Fundamentals *1*

1 **Introduction to Tissue Engineering** *3*
Rami Mhanna and Anwarul Hasan
1.1 Introduction *3*
1.2 Clinical Need for Tissue Engineering and Regenerative Medicine *4*
1.3 History of Tissue Engineering and Regenerative Medicine *5*
1.4 Fundamentals of Tissue Engineering and Regenerative Medicine *6*
1.4.1 Tissue Engineering versus Regenerative Medicine *6*
1.4.2 The Triad of Tissue Engineering *7*
1.4.3 Approaches in Tissue Engineering *8*
1.4.4 Recent Advances in Tissue Engineering *10*
1.4.4.1 Advances in Cell Sourcing and Cell Manipulation *10*
1.4.4.2 Advances in Biomaterials and Scaffold Production *10*
1.4.4.3 Advances in Cell Signaling Research and Bioreactor Development *11*
1.4.4.4 Engineering Complex Tissues and Organs *13*
1.5 Applications of Tissue Engineering *14*
1.5.1 Implantable Tissues and Organs *15*
1.5.2 *In Vitro* Models for Disease Studies *19*
1.5.3 Smart Diagnosis and Personalized Medicine *20*
1.6 Challenges in Tissue Engineering *21*
1.7 The Future of Tissue Engineering *22*
1.8 Conclusions *23*
References *24*

2 Biomaterials in Tissue Engineering *35*
Samad Ahadian, Rahaf Rahal, Javier Ramón-Azcón, Raquel Obregón, and Anwarul Hasan
2.1 Introduction *35*
2.2 Biomaterial–Tissue Interactions *37*
2.3 Properties of Biomaterials *40*
2.4 Scaffold Requirements for Specific Tissues *44*
2.5 Classification of Biomaterials *45*
2.5.1 Natural Biomaterials *45*
2.5.1.1 Collagen *45*
2.5.1.2 Hyaluronic Acid *47*
2.5.1.3 Alginic Acid (Alginate) *50*
2.5.1.4 Chitosan *51*
2.5.1.5 Gelatin *52*
2.5.1.6 Fibrin *53*
2.5.1.7 Silk *53*
2.5.1.8 Peptides *54*
2.5.1.9 Elastin *55*
2.5.2 Synthetic Biomaterials *55*
2.5.2.1 Poly(*N*-isopropylacrylamide) *55*
2.5.2.2 Poly(lactic acid) *57*
2.5.2.3 Poly(lactic acid-*co*-glycolic acid) *57*
2.5.2.4 Poly(ε-caprolactone) *58*
2.5.2.5 Poly(ethylene glycol) *60*
2.5.2.6 Poly(vinyl alcohol) *61*
2.6 Fabrication Methods of Biomaterials *61*
2.6.1 Conventional Fabrication Methods *61*
2.6.2 Advanced Fabrication Methods *61*
2.6.2.1 Electrospinning *63*
2.6.2.2 Rapid Prototyping *64*
2.7 Testing of Biomaterials *64*
2.8 Challenges for Biomaterials in Tissue Engineering *65*
2.9 Conclusions and Future Directions *67*
Acknowledgment *69*
Abbreviations *69*
References *70*

3 Harnessing the Potential of Stem Cells from Different Sources for Tissue Engineering *85*
Divya Murali, Kunal G. Kshirsagar, Anwarul Hasan, and Arghya Paul
3.1 Introduction *85*
3.2 Stem Cells in Tissue Engineering *86*
3.3 Unique Properties *86*
3.4 Types of Stem Cells *87*
3.4.1 Embryonic Stem Cells *87*
3.4.2 Induced Pluripotent Stem Cells *89*

3.4.3 Adult Stem Cells *90*
3.4.3.1 Mesenchymal Stem Cell *91*
3.4.3.2 Hematopoietic Stem Cells *91*
3.4.3.3 Wharton's Jelly Stem Cells *92*
3.5 Application of Stem Cells in Tissue Engineering *92*
3.5.1 Bone Tissue Engineering *92*
3.5.2 Cartilage Tissue Engineering *96*
3.5.3 Cardiac Tissue Engineering *97*
3.5.4 Neural Tissue Engineering *97*
3.5.5 Tissue Engineering for Other Tissues Including Skin, Liver, Lungs, Bladder, and Pancreas *99*
3.6 Challenges and Future Directions *101*
3.7 Conclusion *102*
Acknowledgments *102*
References *102*

4 Induced Pluripotent Stem Cells in Scaffold-Based Tissue Engineering *111*
Deepti Rana, Minal Thacker, Maria Leena, and Murugan Ramalingam
4.1 Introduction *111*
4.2 Basics of Induced Pluripotent Stem Cells *112*
4.3 Concept of Scaffold-Based Tissue Engineering *116*
4.4 Cell–Scaffold Interactions *118*
4.5 Application of Induced Pluripotent Stem Cells *121*
4.5.1 Bone Tissue Engineering *121*
4.5.2 Cartilage Tissue Engineering *125*
4.5.3 Cardiac Tissue Engineering *127*
4.5.4 Skin Tissue Engineering *131*
4.5.5 Neural Tissue Engineering *132*
4.6 Concluding Remarks *134*
Acknowledgments *134*
References *134*

5 Biosensors for Optimal Tissue Engineering: Recent Developments and Shaping the Future *143*
Jihane Abouzeid, Ghinwa Darwish, and Pierre Karam
5.1 Introduction *143*
5.2 Fundamentals of Biosensors *143*
5.3 Biosensing Techniques *145*
5.3.1 Spectroscopic Tools *145*
5.3.1.1 Colorimetry Using Gold Nanoparticles *145*
5.3.1.2 Fluorescence Spectroscopy *146*
5.3.2 Electrochemical Methods *146*
5.4 Real-Time Sensing in Tissue Engineering and Cell Growth *147*
5.4.1 Metabolites *147*

5.4.2 Oxygen Monitoring During Cell Growth *148*
5.4.3 Reactive Oxygen Species *149*
5.4.4 Cell Adhesion *150*
5.4.5 Nanowire Field-Effect Transistors *150*
5.4.5.1 Introduction to Field-Effect Transistors *150*
5.4.5.2 Field-Effect Transistors for Intracellular Monitoring *151*
5.4.6 Microfluidics-Based Biosensors *153*
5.4.6.1 Microfluidic Chips *154*
5.4.6.2 Microfluidics-Integrated Tissue Scaffold *155*
5.5 *In Vivo* Implementations and the Challenges Faced *155*
5.5.1 Antifouling Coatings *156*
5.5.2 Nitric Oxide *157*
5.5.3 Templated Porous Scaffolds *157*
5.6 Conclusion and Future Directions *158*
References *159*

6 Bioreactors in Tissue Engineering *169*
Raquel Obregón, Javier Ramón-Azcón, and Samad Ahadian
6.1 Introduction *169*
6.2 Bioreactors *170*
6.2.1 Spinner Flasks *171*
6.2.2 Rotating-Wall Vessel Bioreactors *172*
6.2.3 Wave Bioreactors *173*
6.2.4 Perfusion Bioreactors *173*
6.2.4.1 Parallel-Plate Bioreactors *173*
6.2.4.2 Hollow-Fiber Bioreactors *173*
6.2.4.3 Fixed (Packed) and Fluidized-Bed Bioreactors *174*
6.2.5 Microfluidic Bioreactors *174*
6.3 Applications of Bioreactors in Tissue Engineering *175*
6.3.1 Bioreactors for Liver Tissue Engineering *176*
6.3.1.1 Spinner Flasks *176*
6.3.1.2 Rotating-Wall Vessel Bioreactors *176*
6.3.1.3 Perfusion Bioreactors *177*
6.3.2 Bioreactors for Musculoskeletal Tissue Engineering *179*
6.3.2.1 Rotating-Wall Vessel Bioreactors *179*
6.3.2.2 Spinner Flasks *182*
6.3.2.3 Perfusion Bioreactors *183*
6.3.3 Bioreactors for Neural Tissue Engineering *185*
6.3.4 Bioreactors for Cardiovascular Tissue Engineering *187*
6.3.5 Bioreactors for Bladder, Uterine, and Cornea Tissue Engineering *189*
6.4 Summary and Future Perspectives *191*
Acknowledgment *191*
Abbreviations *191*
References *192*

Part II Applications *215*

7 Tissue-Engineered Human Skin Equivalents and Their Applications in Wound Healing *217*
Lara Yildirimer, Divia Hobson, Zhi Yuan (William) Lin, Wenguo Cui, and Xin Zhao
7.1 Introduction *217*
7.2 Development of Tissue-Engineered Human Skin Equivalents *220*
7.2.1 Epidermal Models *220*
7.2.2 Dermal Models *221*
7.2.3 Bilayered Models *221*
7.2.4 Multifunctional Skin Models *223*
7.3 Application of TESs in Wound Healing *226*
7.3.1 Clinical Wound-Healing Applications *226*
7.3.1.1 Epidermal Skin Regeneration *226*
7.3.1.2 Dermal Substitutes *227*
7.3.1.3 Dermo-Epidermal Skin Substitutes *228*
7.3.2 *In vivo* Wound-Healing Applications *230*
7.3.3 *In vitro* Wound-Healing Models *231*
7.4 Conclusions and Future Directions *233*
Acknowledgments *234*
References *234*

8 Articular Cartilage Tissue Engineering *243*
Jiayin Fu, Pengfei He, and Dong-An Wang
8.1 Introduction *243*
8.1.1 Articular Cartilage Composition and Structure *243*
8.1.2 Articular Cartilage Function *244*
8.2 Articular Cartilage Lesions and Repair *245*
8.2.1 Articular Cartilage Lesions *245*
8.2.2 Current Treatments in Articular Cartilage Repair *246*
8.2.2.1 Bone-Marrow-Simulation-Based Techniques *246*
8.2.2.2 Osteochondral Transplantation Techniques *246*
8.2.2.3 Cell-Based Techniques *247*
8.2.2.4 Tissue Engineering *247*
8.3 Basics of Articular Cartilage Tissue Engineering *248*
8.3.1 Cells *248*
8.3.1.1 Chondrocytes *249*
8.3.1.2 Mesenchymal Stem Cells *249*
8.3.1.3 Pluripotent Stem Cells *251*
8.3.2 Scaffold *253*
8.3.2.1 Desired Properties for Scaffolds *253*
8.3.2.2 Classification *254*
8.3.3 Biochemical Stimuli *262*
8.3.3.1 Growth Factors *262*
8.3.3.2 Other Bioactive Reagents *263*
8.3.4 Mechanical Stimuli *264*

8.4 Strategies in Current Cartilage Tissue Engineering *265*
8.4.1 Controlled Delivery of Biochemical Factors *265*
8.4.2 Combination Tissue Engineering with Gene Therapy *266*
8.4.3 Biomimetic Hierarchical Cartilage Tissue Engineering *268*
8.4.4 Application of Cartilage-ECM-Derived Scaffolds *269*
8.4.5 Scaffold-Free Cartilage Tissue Engineering *270*
8.4.6 Homing Endogenous Cells for Cartilage Regeneration *271*
8.5 Conclusions and Future Directions *273*
List of Abbreviations *275*
References *276*

9 Liver Tissue Engineering *297*
Jessica L. Sparks
9.1 Introduction *297*
9.2 Liver Biology *299*
9.2.1 Organ-Scale Anatomy *299*
9.2.2 Histological Structure *300*
9.2.3 Cell Types of the Liver *302*
9.2.4 Liver Extracellular Matrix *303*
9.3 Liver Biomechanics *304*
9.3.1 Liver Biomechanical Properties *304*
9.3.2 Liver Hemodynamics *307*
9.4 Liver Mechanobiology *308*
9.4.1 Cellular-Scale Mechanical Forces *308*
9.4.2 Cellular Mechanotransduction Mechanisms *309*
9.4.3 Mechanosensitivity of Liver Cell Types *310*
9.5 Biophysical Stimuli in Liver Tissue Engineering Scaffolds *313*
9.6 Conclusion and Future Directions *314*
References *314*

10 Development of Tissue-Engineered Blood Vessels *325*
Haiyan Li
10.1 Introduction *325*
10.2 Biology of Blood Vessels *326*
10.2.1 Structure and Component of Native Blood Vessels *326*
10.2.2 Functions of Native Blood Vessels *326*
10.2.3 Vasculogenesis and Angiogenesis *329*
10.3 Tissue Engineering of Blood Vessels *329*
10.3.1 Tissue Engineering of Microvascular Networks *329*
10.3.1.1 Prevascularization-Based Techniques *329*
10.3.1.2 Vasculogenesis- and Angiogenesis-Based Techniques *332*
10.3.2 Strategies for Engineering Vascular Replacement Grafts *340*
10.3.2.1 Material Selection *340*
10.3.2.2 Tubular Scaffold Fabrication *342*
10.4 Conclusion and Perspective *344*
Acknowledgment *345*
References *345*

Contents to Volume 2

Foreword *xv*
Preface *xvii*

11 **Engineering Trachea and Larynx** *363*
Marta B. Evangelista, Sait Ciftci, Peter Milad, Emmanuel Martinod, Agnes Dupret-Bories, Christian Debry, and Nihal E. Vrana

12 **Pulmonary Tissue Engineering** *389*
Patrick A. Link and Rebecca L. Heise

13 **Cardiac Tissue Engineering** *413*
Eun Jung Lee and Pamela Hitscherich

14 **Approaches and Recent Advances in Heart Valve Tissue Engineering** *445*
Anna Mallone, Benedikt Weber, and Simon P. Hoerstrup

15 **Musculoskeletal Tissue Engineering: Tendon, Ligament, and Skeletal Muscle Replacement and Repair** *465*
Jorge A. Uquillas, Settimio Pacelli, Shuichiro Kobayashi, and Sebastián Uquillas

16 **Bone Tissue Engineering: State of the Art, Challenges, and Prospects** *525*
Jan O. Gordeladze, Håvard J. Haugen, Ståle P. Lyngstadaas, and Janne E. Reseland

17 **Tissue Engineering of the Pancreas** *553*
Masayuki Shimoda

18 **Tissue Engineering of Renal Tissue (Kidney)** *575*
Raquel Rodrigues-Díez, Valentina Benedetti, Giuseppe Remuzzi, and Christodoulos Xinaris

19 **Design and Engineering of Neural Tissues** *603*
Muhammad N. Hasan and Umut A. Gurkan

20 **Neural-Tissue Engineering Interventions for Traumatic Brain Injury** *655*
Tala El Tal, Rayan El Sibai, Stefania Mondello, and Firas Kobeissy

21 **Bionics in Tissue Engineering** *677*
Thanh D. Nguyen and Brian P. Timko

Index *701*