Contents

Preface xv

1	State of the Art in Nanomedicine 1
	Yujun Song and Wei Hou
1.1	Intractable Diseases and Development of the Related Novel Therapy and
	Medicines 1
1.2	Key Features of Nanomedicines 4
1.3	Nanotechnology Translational Nanomedicine: Emergence and
	Progress 6
1.4	Interdisciplinary Features of Nanomedicines: Multi-mode and
	Multi-function Features Promoting Nanomedicine-mediated
	Immunotherapy and/or Physical Field Ablation Therapy for Subversive
	Therapy 12
1.5	Future Development of Nanomedicines by Coupling Advanced
	Biomedicines (Including Biochemistry and Biophysics), Modern
	Physicochemical Technologies, and Artificial Intelligence
	Technology 27
	References 29
2	Fundamentals in Nanomedicine 49
	Xiangrong Song, Mengran Guo, Zhongshan He, Xing Duan, and Wen Xiao
2.1	Design Theory of Nanomedicines 49
2.1.1	Passive Targeting Function Design of Nanomedicines 49
2.1.1.1	Size-dependent Biological Functions for Nanomedicine Design 50
2.1.1.2	Surface Charge and PEGylation of Nanoparticles for Nanomedicine
	Design 50
2.1.1.3	Shape-dependent Biological Effect of Nanoparticles for Nanomedicine
	Design 50
2.1.2	Active Targeting Function Design of Nanoparticles for
	Nanomedicine 51
2.1.2.1	Small Molecule and Aptamer-directed Active Targeting Function
	Design 51
2.1.2.2	Protein and Peptide-directed Active Targeting Function Design 52
2.1.2.3	Antibody-directed Active Targeting Design 52



Contents	
2.1.3	Auto-targeting Design 53
2.1.3.1	Platelets Targeting Function Design 53
2.1.3.2	RBC Targeting Function Design 53
2.1.3.3	Macrophage Targeting Function Design 53
2.1.3.4	Exosomes and Supramolecular Cell Membrane Vesicle Targeting
	Design 54
2.1.4	In Vitro or In Vivo 3D Traceable Function 54
2.1.4.1	Gold Nanoparticles for Bioimaging 54
2.1.4.2	Quantum Dots for Bioimaging 54
2.2	Progress in the Controlled Synthesis of Nanomaterials 55
2.2.1	Ball Milling Through the Mechanical Method 55
2.2.2	Nanoprecipitation 56
2.2.3	Microfluidic Synthesis 56
2.2.4	Personalized Protein Nanoparticles 58
2.2.5	Biological Entities as Chemical Reactors 58
2.3	Progress in the Surface Modification and Functionalization of
	Nanomaterials for Nanomedicines 60
2.3.1	How Surface Modification Can Improve the Stability of
	Nanomedicine 60
2.3.1.1	Modification of Charged Materials 60
2.3.1.2	Increase the Steric Resistance Between Nanoparticles to Improve the
	Stability of Nanomedicine 62
2.3.1.3	Conformation Change of the Surface Polymer of Nanomaterials
	Improves the Stability of Nanomaterials 62
2.3.2	Surface Modification of Bioactive Groups Can Improve the Efficacy of
	Nanopreparations 63
2.3.2.1	Nanodrugs Modified by Single Targeting Ligand 63
2.3.2.2	Multiligand Modified Nanopreparations 66
	References 67
3	Nanomedicine for Antitumors 73
	Qiong Wu, Xinzhu Yang, Ruixue Zhu, and Yujun Song
3.1	Introduction 73
3.2	Liposomal Nanoparticles 75
3.2.1	Synthesis Methods 76
3.2.1.1	Extrusion Technique 76
3.2.1.2	Sonication 76
3.2.1.3	Microfluidization 76
3.2.1.4	Heating Method 77
3.2.2	Application of Liposomes in Drug Delivery 77
3.3	Polymeric Nanoparticles 78
3.3.1	Techniques for Creating Polymeric Nanoparticles 79
3.3.1.1	Method of Evaporating Solvents 79

Method of Spontaneous Emulsification and Solvent Diffusion 79

3.3.1.2

3.3.1.3

Salting Out Method 79

3.3.1.4	Method of Solvent Displacement/Nanoprecipitation 80
3.3.1.5	Polymerization Methods 81
3.3.1.6	Nanoparticles Developed from Hydrophilic Polymers 81
3.3.2	Controlled Drug Release by Polymeric Nanoparticles 81
3.4	Inorganic Nanoparticles 82
3.4.1	Synthesis and Application of Colloidal Gold Nanoparticles 83
3.4.2	Synthesis and Application of Mesoporous Silica Nanoparticles 84
3.4.3	Synthesis and Application of Graphene 85
3.4.4	Synthesis and Application of Magnetic Nanoparticles 86
3.4.5	Quantum Dot Synthesis and Applications 88
3.4.6	Creation and Use of Stratified Double Hydroxides 89
3.4.7	Nanoparticles with Multifunctional Composite 90
3.5	Mixture (Hybrid) Nanoparticles 90
3.6	Cell Membrane Coating Nanotechnology 93
3.6.1	Synthesis of Cell Membrane-Nanoparticle Structures 93
3.6.1.1	Extrusion 93
3.6.1.2	Sonication 93
3.6.1.3	Electroporation 94
3.6.1.4	Graphene Nanoplatform-mediated Cell Membrane Coating 94
3.6.1.5	Encapsulation of In Situ Using Cell-derived Vesicles 94
3.7	Challenges and Current Limitations 94
3.7.1	Nanomaterials' Physicochemical Characterization 95
3.7.2	Safety Concerns 95
3.7.3	Regulatory Issues 95
3.7.4	Manufacturing Issues 96
3.8	Conclusions 96
	References 97
4	Nanomedicine for the Treatment of Nervous System
	Diseases 113
	Xiaojian Cui and Yujun Song
4.1	Concepts and Types of Nanomedicines for Nervous System
	Diseases 113
4.2	Therapeutical Methods for Nervous System Diseases and Features of
	Current Nanomedicines 114
4.3	Synthesis Methods and Typical Examples (Including Clinical Trial) of
	Polymer-based Nanomedicines for Nervous System Diseases 116
4.3.1	Synthesis Methods of Polymer-based Nanomedicine 116
4.3.1.1	Solvent Evaporation 116
4.3.1.2	Emulsification Process 116
4.3.1.3	Reductive Reaction Reduction Method 116
4.3.2	Polymer-based Nanomedicine: Typical Application 116
4.3.2.1	Targeted Drug Delivery 116
4.3.2.2	Tissue Repair and Regenerative Medicine 117
4.3.2.3	Vaccines and Immunotherapy 117

viii	Contents	
	4.3.2.4	Inclusion of Nanomaterials 117
	4.4	Inorganic-based Nanomedicines: Synthesis Methods and Typical
		Application (Including Clinical) 117
	4.4.1	Quantum Dots 117
	4.4.2	Nanogold 119
	4.4.3	Nanocarbon 120
	4.4.4	Magnetic Nanoparticles 120
	4.4.5	Nanomesoporous Silicon 122
	4.4.6	Nanocalcium 122
	4.5	Metallic-based Nanomedicines: Synthesis Methods and Typical
		Application (Including Clinical) 122
	4.5.1	Preparation and Characterization of Metal-organic Frame
		Materials 123
	4.5.2	Application of Functionalized Metal-organic Framework Materials in
		Tumor Therapy 123
	4.6	Multifunctional Nanomedicines for Nervous System Diseases 125
	4.6.1	Nanomedicine Therapy Strategy Combined with Chemotherapy 125
	4.6.2	Nanomedicine Therapy Strategy Combined with Immunotherapy 126
	4.6.3	Combination Treatment Strategy 127
	4.6.4	Perspectives of Nanomedicines for Nervous System Diseases 127
		References 128
	5	Nanomaterial Translational Nanomedicine for Anti-HIV and
		Anti-bacterial 131
		Hao Luo and Yujun Song
	5.1	Concepts, Anti-HIV Theory, and Types and Features of Current
		Nanomedicines 132
	5.1.1	Anti-HIV Reverse Transcriptase Inhibitors 133
	5.1.2	Anti-HIV Protease Inhibitors 133
	5.1.3	Characteristics of Polymer Nanocarriers 141
	5.2	Polymer-based Nanomedicines: Synthesis Methods and Typical
		Application 142
	5.3	Inorganic-based Nanomedicines: Synthesis Methods and Typical
		Application 146
	5.4	Metallic-based Nanomedicines: Synthesis Methods and Typical
		Application 148
	5.5	Multi-functional (Target) Nanomedicines 150
	5.6	Future Development 152
		References 153
	6	Nanomedicine for Next-generation Dermal Management 157
		Haibin Wu, Qian Chen, and Shen Hu
	6.1	Introduction 157
	6.2	Nano-biomaterials-based Therapeutics for Wound Healing 159
	6.2.1	Nano-biomaterials for Effective Hemostasis 160

6.2.2	Antibacterial Nano-biomaterials 164
6.2.2.1	Inorganic Antibacterial Nano-biomaterials 164
6.2.2.2	Organic Antibacterial Nano-biomaterials 165
6.2.3	Engineering of the Wound Microenvironment 166
6.2.3.1	Redox Modulation of the Wound Microenvironment 167
6.2.3.2	Regulation of Microenvironmental MMP Activity 167
6.2.3.3	Targeting the Pro-inflammatory Mediators 169
6.2.4	Nano-biomaterials-enabled Biophysical Regulation of Wound
	Healing 169
6.2.4.1	Surface Nanotopographical Features 171
6.2.4.2	Mechanical Cues 171
6.2.4.3	Bio-electrical Stimulation 173
6.2.5	Angiogenic Nano-biomaterials 175
6.2.5.1	Nano-biomaterials as Delivery Vehicles for Angiogenic
	Therapeutics 175
6.2.5.2	Nano-biomaterials as Intrinsic Angiogenic Agents 176
6.3	Nano-biomaterials for Imaging and Monitoring of Cutaneous
	Wounds 176
6.3.1	Wound Infection Monitoring 177
6.3.1.1	Nanoprobes for Wound Infection Monitoring 177
6.3.1.2	Theranostic Nano-biomaterials for Wound Infection Control 177
6.3.2	Imaging of Wound Parameters and Markers 179
6.3.2.1	Imaging of Physiological and Pathological Wound Parameters 179
6.3.2.2	Imaging of Stem Cell-based Wound Therapy 180
6.3.2.3	Imaging of Wound Scarring Markers 180
6.4	Conclusion and Future Outlook 181
6.4.1	Standardization of the Preparation and Functionalization of
	Nano-biomaterials 182
6.4.2	Bio-safety of Nano-biomaterials 182
6.4.3	Computational Simulation and Machine Learning 183
	Acknowledgments 183
	References 184
7	Nanomedicine for Targeting Delivery of Gene and Other
	DNA/RNA Therapies Based Viruses Engineering 197
	Xiangrong Song, Mengran Guo, Zhongshan He, Xing Duan, and Wen Xiao
7.1	Targeting Delivery of Gene Therapies to the Tumors 198
7.1.1	Passive Targeting 198
7.1.2	Active Targeting 199
7.2	Targeting Delivery of Gene-based Nanovaccines to the Spleen 199
7.3	Targeting Delivery of Gene-based Nanovaccines to the LNs 200
7.4	Targeting Delivery of Gene-based Nanomedicines to the Liver 200
7.5	Targeting Delivery of Gene-based Nanomedicines to the Lung 200
7.6	Targeting Delivery of Gene-based Nanomedicines to the Brain 202 References 203

×	Contents	
---	----------	--

8	Nanomedicine for Bio-imaging and Disease Diagnosis 207
	Ziqi Wang and Yujun Song
8.1	Concepts, Types, and Features of Current Nanoprobes 207
8.1.1	Optical Nanoprobe 208
8.1.2	Magnetic Nanoprobe 210
8.1.3	Photoacoustic Imaging Nanoprobe 212
8.1.4	CT Nanoprobe 213
8.1.5	Nuclide Imaging Nanoprobe 213
8.1.6	Multifunctional/Multimodal Nanoprobes 214
8.2	Synthesis Methods 214
8.2.1	Preparation and Synthesis of Noble Metal Nanoprobes 216
8.2.1.1	Chemical Synthesis Method 216
8.2.1.2	Photochemical Method 217
8.2.1.3	Template-based Method 217
8.2.1.4	Electrochemical Process 218
8.2.2	Preparation and Synthesis Method of Magnetic Nanoprobe 218
8.2.2.1	Coprecipitation Method 218
8.2.2.2	Thermal Decomposition Method 219
8.2.2.3	Hydrothermal Synthesis Method 219
8.3	Typical Application Examples in the Disease Diagnosis and Study of
	Biological Events 219
8.3.1	Application of Optical Nanoprobes 219
8.3.2	Application of Magnetic Nanoprobes 222
8.3.3	Application of Photoacoustic Imaging Nanoprobes 222
8.3.4	Application of CT Nanoprobe 223
8.4	Future Development 224
	References 225
9	Magnetic Nanoparticles and Their Applications 227
7	Magnetic Nanoparticles and Their Applications 227 Xiuyu Wang and Yuting Tang
9.1	Introduction 227
9.1	Classification of Magnetic Nanoparticles 228
9.2.1	Magnetic Regulation 230
9.2.1.1	Size 230
9.2.1.1	Shape 232
9.2.1.2	Composition 233
9.2.1.3	Exchange-Coupling Interaction 235
9.2.2	Biomedical Applications 236
9.3.1	Magnetic Resonance Imaging 236
9.3.1	Magnetic Resonance imaging 230 Magnetic Hyperthermia 238
9.3.2	Targeted Drug Delivery 239
9.3.4	Neuromodulation 240
9.3.4	Conclusion and Outlook 242
7. T	References 242
	11-41-41-41-41-41-41-41-41-41-41-41-41-4

10	Nanomedicine-mediated Immunotherapy 245
	Wei Hou and Yujun Song
10.1	Immune System and Immune Response 245
10.2	Mechanism of Tumor Immunotherapy 247
10.3	Mechanism of Nanomedicine-enhancing Immunotherapy 248
10.4	Immunological Applications of Nanomedicines 252
10.4.1	Artificial Antibody 252
10.4.2	Reprogrammed Immunity 253
10.4.3	Nanomedicines as Agonists 255
10.4.4	Nanomedicine-combined CAR-T Therapy 257
10.4.5	Nanovaccines 258
10.4.6	Nanomedicines Affect Cytokines 261
10.5	Summary and Outlook 263
	References 264
11	Nanomodicine modicted Illancound Thomas, 260
11	Nanomedicine-mediated Ultrasound Therapy 269 Oingwei Lieo Vacygo Lieo and Wei Si
11.1	Qingwei Liao, Yaoyao Liao, and Wei Si
11.1.1	Concept, Therapy Theory, and Devices 269 The Concept of Ultrasound Thorapy and Its Thorapy Theory 260
	The Concept of Ultrasound Therapy and Its Therapy Theory 269 Thermal Effect 270
11.1.1.2 11.1.1.3	Mechanical Effects 270 Cavitation Effect 270
11.1.1.3	
11.1.1.4	Thixotropic Effect 271 Acoustic Impulse and Acoustic Chemical Effects 271
11.1.2	Concepts and Therapy Theory of Nanomedicines 272
11.1.2.1	Concept of Nanomedicine 272
11.1.2.1	Therapy Theory of Nanomedicine 272
11.1.2.2	Equipment for Nanomedicine-mediated Ultrasound Therapy 273
11.1.3	Nanomedicine Synthesis with Ultrasound Field Response 274
11.2.1	Ultrasound Chemical Precipitation 274
11.2.1	Ultrasonic Atomization Pyrolysis 274
11.2.2	Ultrasonic Electrochemical Method 274
11.2.3	Ultrasonic Reduction Method 275
11.2.4	Application Examples 275
11.5	References 276
	References 270
12	Nanomedicine-mediated Photodynamic and/or Photothermal
	Therapy 279
	Shangqing Jing and Yujun Song
12.1	Photodynamic and Photothermal Mechanism for Anti-cancer 281
12.2	Nanomaterial-based PSs (Nano-PSs) for PDT 283
12.2.1	Metal-based Nanomaterials 283
12.2.1.1	Au NPs 283
12.2.1.2	
12.2.1.3	

13 Nanomedicine-mediated Pulsed Electric Field Ablation Therapy 299 Xinzhu Yang, Qiong Wu, Ruixue Zhu, and Yujun Song 13.1 Introduction 299

- Concept, Therapy Theory, and Devices 13.2
- Concept, Therapy Theory 302 13.2.1
- 13.2.1.1 Enhanced Therapeutic Effects 303
- 13.2.1.2 Overcoming Drug Resistance 303
- 13.2.1.3 Reduce Side Effects 303
- 13.2.1.4 Promote Personalized Treatment 303
- 13.2.1.5 Pulse Generator *304*
- 13.2.1.6 Electrode System *305*
- 13.2.1.7 Pulse Parameter Adjustment 305
- 13.2.2 Devices 306
- Synthesis of Nanomedicine with Electric Field Response 312 13.3
- Synergistic Anticancer Research of Multimodal Iron-based Nanodrugs 13.3.1 and Nanosecond Pulse Technology 312
- Design and Synthesis of Multimodal Iron-based Nanodrugs 313 13.3.1.1
- Characterization of Physical Properties and Structural Analysis 315 13.3.1.2
- Research on Multimodal Physical Imaging Applications 318 13.3.1.3
- Study on In Situ Anticancer Effects in Liver Cancer 320 13.3.1.4
- Progresses of Innovative Combination Therapy 321 13.3.2
- Application Examples 322 13.4

13.4.1	Cancer Treatment 322		
13.4.2	Treatment of Neurological Diseases 323		
13.4.3			
13.5	Conclusion 323		
	References 324		
14	Nanomedicine-mediated Magneto-dynamic and/or		
	Magneto-thermal Therapy 329		
	Yangfei Wang and Yujun Song		
14.1	Concepts, Treatment Theories, and Methods 329		
14.1.1	Overview of Magnetic Hyperthermia Therapy 329		
14.2	Treatment Theories and Methods 330		
14.2.1	Magneto-thermal Conversion Mechanism 330		
14.2.2	The Killing Effect of Magnetic Hyperthermia on Tumor Cells 331		
14.2.3	Cytotoxicity 332		
14.3	Magnetic Field-responsive Nanomedicine Synthesis 333		
14.3.1	Fe ₃ O ₄ Materials 333		
14.3.2	Ferrite Materials 334		
14.3.3	Alloy Materials 335		
14.3.4	Composite Materials 335		
14.3.5	Other Materials 336		
14.4	Applications 337		
14.4.1	Instance 1 337		
14.4.2	Instance 2 337		
14.4.3	Instance 3 338		
	References 339		
15	Nanomedicine-mediated Radiotherapy for Cancer		
	Treatment 341		
	Ruixue Zhu and Yujun Song		
15.1	Concept, Therapy Theory, and Devices 341		
15.2	Nanomaterials as Radiosensitizers for Radiation Therapy 347		
15.3	Nanomaterials Delivering Radioisotope for Internal Radioisotope		
	Therapy 358		
15.4	Nanomedicine Synthesis with Radio/Nuclear Radiation Response 362		
15.5	Conclusion and Prospects 364		
	References 365		
16	Nanomedicine Conjugating with AI Technology and Genomics		
	for Precise and Personalized Therapy 371		
	Lin Liu, Siyu Chen, and Sen Zhang		
16.1	Concept 371		
16.2	Genomics of Nanomedicine 374		
16.2.1	Genomic Modifications in Nanomedicine 376		
16.2.2	Genomic Toxicity of Nanomedicines 376		

xiv	Contents	
	16.2.3 Genomic Responses to Nanomedicines 377	
	16.3	Artificial Intelligence Technology in Nanomedicine Development 377
	16.3.1	Machine Learning Techniques 378
	16.3.2	Computer Vision Technology 378
	16.3.3	Natural Language Processing Technology 378
	16.4	Artificial Intelligence Facilitates Precise and Personalized Nanomedicine Based on Genomics 379
	16.4.1	Cell Replacement Therapy for Diabetes 380
	16.4.2	Precision Medicine in Cancer Treatment 380
		References 382
	17 Microfluidic Conjugating AI Platform for High-throughput	
		Nanomedicine Screening 385
		Xing Huang, Wenya Liao, Zhongbin Xu, and Yujun Song
	17.1	Introduction 385
	17.2	Microfluidic Technologies for Medicine Development 386
	17.2.1	Basics of Microfluidics 386
	17.2.2	Fabrication of Microfluidic Chips 387
	17.2.3	Representative Microfluidic Units 390
	17.3	Microfluidic Preparation of Nanomedicines 391
	17.3.1	Drug Nanoparticle Preparation 392
	17.3.2	Nanocarrier Preparation 393
	17.3.2.1	Polymer Nanoparticles 393
	17.3.2.2	Liposomes 394
	17.3.2.3	Inorganic Nanoparticles 395
	17.4	Microfluidic High-throughput Drug Screening 396
	17.4.1	Microfluidic Drug Screening Based on Cell Assays 396
	17.4.2	Microfluidic Drug Screening Based on Organ-on-a-Chip 398
	17.5	AI-assisted Microfluidic Development of Nanomedicine 400
	17.6	Conclusions and Perspectives 402
		References 404

Index 413