Contents

Preface xi
Acknowledgments xiii
Introduction xv
Contributors xvii

PART I Concepts and Definitions in RNA Nanotechnology

Chapter 1 RNA Structure and Folding 3
Xin Li and Peixuan Guo

Chapter 2 RNA Regulation and Function in Nature 5
Zhefeng Li, Daniel W. Binzel, and Peixuan Guo

Chapter 3 Principles and Fundamentals of RNA Nanotechnology 9
Long Zhang and Peixuan Guo

Chapter 4 Computation and Folding Predictions 15
Lili Du and Peixuan Guo

Chapter 5 Enzymatic Synthesis and Modification of RNA Nanoparticles 19
Daniel W. Binzel and Peixuan Guo

Chapter 6 Synthetic and Enzymatic Methods for RNA Labeling and Modifications 25
Satheesh Ellipilli and Peixuan Guo

Chapter 7 Methods and Assembly of RNA Nanotechnology 33
Hongzhi Wang, Chenxi Liang, and Peixuan Guo

Chapter 8 Purification, Characterization, and Structure Determination of RNA Nanoparticles 37
Satheesh Ellipilli, Nicolas D. Burns, and Peixuan Guo

Chapter 9 SELEX 41
Chenxi Liang and Peixuan Guo

Chapter 10 Uniqueness, Advantages, Challenges, Solutions, and Perspectives in Therapeutics Applying RNA Nanotechnology 43
Peixuan Guo, Farzin Haque, Brent Hallahan, Randall Reif, and Hui Li

PART II Design, Synthesis, and Characterization Methods in RNA Nanotechnology

Chapter 11 The Natural Versatility of RNA 73
Lewis A. Rolband, Oleg A. Shevchenko, Caroline M. West, Ciara E. Conway, Caryn D. Striplin, and Kirill A. Afonin

Chapter 12 Nucleic Acids as a Building Material in Nanotechnology 83
Justin Halman and Kirill A. Afonin

Chapter 13 Multiple Functionalities for RNA Nanoparticles 89
Yelixza I. Avila and Martin Panigaj

Chapter 14 From Computational RNA Structure Prediction to the Design of Biologically Active RNA-Based Nanostructures 95
W.K. Kasprzak and Bruce A. Shapiro

Chapter 15 Application of RNA Tertiary Structure Prediction Tool iFoldRNA in RNA Nanotechnology 101
Jian Wang and Nikolay V. Dokholyan

Chapter 16 HyperFold: A Web Server for Predicting Nucleic Acid Complexes 111
Eckart Bindewald and Bruce A. Shapiro

Chapter 17 RNA Switches: Towards Conditional Dynamic RNA-Based Constructs for Therapeutics and Bioassays 121
Paul Zakrevsky and Bruce A. Shapiro

Chapter 18 RNA Multiway Junction Motifs as Lego for the Construction of Multifunctional RNA Nanoparticles 125
Farzin Haque, Xin Li, and Peixuan Guo

Chapter 19 Fabrication Methods for RNA Nanoparticle Assembly Based on Bacteriophage Phi29 PRNA Structural Features 141
Yi Shu, Hongzhi Wang, Bahar Seremi, and Peixuan Guo

Chapter 20 Purification of RNA, Modified Oligos, and RNA Nanoparticles 159
Jordan Hill, Mario Vieweger, Fengmei Pi, and Peixuan Guo

Chapter 21 Physicochemical Characterization of Nucleic Acid Nanoparticles 173
Daniel Miller and Emil Khisamutdinov

Chapter 22 Light Scattering Techniques for Characterization of NANPs and Their Formulations 181
Lewis A. Rolband and Joanna K. Krueger

Chapter 23 Electron Microscopy of Nucleic Acid Nanoparticles 187
Damian Beasock and Kirill A. Afonin

Chapter 24 A Single-Molecule FRET Approach for Investigating the Binding Mechanisms of Anti-Viral Aptamers 193
Saptaswa Sen and Erik D. Holmstrom

Chapter 25 Entropy and Enthalpy in RNA Nanoparticle Assembly and Thermodynamic Stability for Medical Application Using RNA Nanotechnology 211
Daniel W. Binzel, Xin Li, and Peixuan Guo

PART III Immunorecognition of RNA Nanoparticles

Chapter 26 Immunorecognition of Nucleic Acid Nanoparticles 231
Jessica McMillan and M. Brittany Johnson

Chapter 27 Viral Noncoding RNAs in Modulating Cellular Defense and Their Potential for RNA Nanotechnology 239
Martin Panigaj, Marina A. Dobrovolskaia, and Kirill A. Afonin

Chapter 28 RIG-I as a Therapeutic Target for Nucleic Acid Nanoparticles (NANPs) 251
M. Brittany Johnson

Chapter 29 Driving Dynamic Functions with Programmable RNA Nanostructures 259
Morgan Chandler, Dana Elasmar, Sam Eisen, Luke Schmedake, and Kirill A. Afonin

Chapter 30 Defining Immunological Properties of Nucleic Acid Nanoparticles Using Human Peripheral Blood Mononuclear Cells 267
Marina A. Dobrovolskaia and Kirill A. Afonin

PART IV Delivery of Functional RNA Nanoparticles

Chapter 31 The Emerging Field of RNA Nanotechnology 293
Peixuan Guo

Chapter 32 Thermodynamically Stable RNA Three-Way Junction for Constructing Multifunctional Nanoparticles for Delivery of Therapeutics 309
Dan Shu, Yi Shu, Farzin Haque, Sherine Abdelmawla, and Peixuan Guo

Chapter 33 RNAi Nanotherapeutics for Localized Cancer Therapy 333
Anu Puri and Bruce A. Shapiro

Chapter 34 Delivery of RNA Nanoparticles 337
Weina Ke, Seraphim S. Kozlov, and Kirill A. Afonin

Chapter 35 Recommendations for Planning In Vivo Studies for RNAi Therapeutics 341
Lorena Parlea and Bruce A. Shapiro

Chapter 36 Mesoporous Silica Nanoparticles for Efficient siRNA Delivery 347
Mubin Tarannum and Juan L. Vivero-Escoto

Chapter 37 Method of Large-Scale Exosome Purification and Its Use for Pharmaceutical Applications 355
Fengmei Pi, Yangwu Fang, Dongsheng Li, and Peixuan Guo

Chapter 38 Engineered Extracellular Vesicle-Based Therapeutics for Liver Cancer 365
Kaori Ishiguro and Tushar Patel

Chapter 39 Extracellular Vesicles (EVs): An Innovative Approach to Engineering Nucleic Acid Delivery 377
Senny Nordmeier, Frank Hsiung, and Victoria Portnoy

Chapter 40 Extracellular Vesicles (EVs): Naturally Occurring Vehicles for RNA Nanotherapeutics 383
Alice Braga, Giulia Manferrari, Jayden A. Smith, and Stefano Pluchino

Chapter 41 Harnessing Exosomes and Bioinspired Exosome-Like Nanoparticles for siRNA Delivery 429
Mei Lu, Haonan Xing, and Yuanyu Huang

PART V Application and Exploitation in RNA Nanotechnology

Chapter 42 RNA Structural Modeling for Therapeutic Applications 447
Yi Cheng, Dong Zhang, Travis Hurst, Xiaoqin Zou, Paloma H Giangrande, and Shi-Jie Chen

Chapter 43 RNA Micelles for Therapeutics Delivery and Cancer Therapy 463
Hongran Yin, Yi Shu, and Peixuan Guo

Chapter 44 Bacteriophage RNA Leading the Way in RNA Nanotechnology for Targeted Cancer Therapy 473
Farzin Haque, Haibo Hu, and Peixuan Guo

Chapter 45 Current State in the Development of RNAi Self-Assembled Nanostructures 485
Marwa Ben Haj Salah and John J. Rossi

Chapter 46 RNA-Based Devices for Diagnostic and Biosensing 499
Morgan Chandler and Kirill A. Afonin

Chapter 47 MicroRNAs: Biology and Role in RNA Nanotechnology 507
Bin Guo, Jingwen Liu, and Daniel W. Binzel

Chapter 48 Conjugation of RNA Aptamer to RNA Nanoparticles for Targeted Drug Delivery 517
Marissa Leonard, Fengmei Pi, Peixuan Guo, and Xiaoting Zhang

Chapter 49 MicroRNAs in Human Cancers and Therapeutic Applications 529
Ji Young Yoo, Balveen Kaur, Tae Jin Lee, and Peixuan Guo

Chapter 50 Tuning the Size, Shape, and Structure of RNA Nanoparticles for Favorable Cancer Targeting and Immunostimulation 543
Sijin Guo, Congcong Xu, Hongran Yin, Jordan Hill, Fengmei Pi, and Peixuan Guo

Chapter 51 RNA Nanotechnology and Extracellular Vesicles (EVs) for Gene Therapy 563
Zhefeng Li, Fengmei Pi, and Peixuan Guo

Chapter 52 Application of RNA Aptamers in Nanotechnology and Therapeutics 589
Hua Shi

Index 609