

Contents

Preface *xi*

1	Introductions of Nucleic Acid-Based Nanomaterials	1
	<i>Shaoping Gao and Yunfeng Lin</i>	
1.1	History of DNA-Based Nanomaterials – Design and Construction	3
1.1.1	DNAzymes	4
1.1.2	Aptamers	5
1.1.3	Triplex DNA	5
1.1.4	DNA Origami and DNA Tiles	6
	References	9
2	The Methods to Improve the Stability of Nucleic Acid-Based Nanomaterials	15
	<i>Xueping Xie</i>	
2.1	Introduction	15
2.2	Methods to Improve Stability	16
2.2.1	Artificial Nucleic Acids	17
2.2.2	Backbone Modification of Nucleic Acids	18
2.2.2.1	Phosphate Group Modifications	18
2.2.2.2	Nucleobase or Ribose Modifications	19
2.2.3	Coating with Protective Structures	20
2.2.4	Covalent Crosslinking	22
2.2.5	Tuning Buffer Conditions	23
2.2.6	Construction of Novel NAN	26
2.3	Conclusion and Recommendations	26
	References	27
3	Framework Nucleic Acid-Based Nanomaterials: A Promising Vehicle for Small Molecular Cargos	37
	<i>Yanjing Li</i>	
3.1	Basis of FNAs as Potential Drug Carriers	38
3.1.1	Classification and Construction of FNAs	38
3.1.2	Physical and Chemical Properties	40

3.1.3	Biological Properties	40
3.2	Small-molecule Cargos	41
3.2.1	Antitumor Agents	42
3.2.1.1	Chemotherapeutic Drugs	42
3.2.1.2	Phototherapeutic Agents	43
3.2.2	Antibiotic Agents	44
3.2.3	Phytochemicals	45
3.3	Merits of FNA Delivery Systems in Biomedical Application	46
3.3.1	Efficient Drug Delivery	46
3.3.2	Targeted Drug Delivery	46
3.3.3	Controlled Drug Release	49
3.3.4	Overcoming Drug Resistance	51
3.4	Conclusions and Prospects	52
	References	54
4	The Application of Framework Nucleic Acid-Based Nanomaterials in the Treatment of Mitochondrial Dysfunction	61
	<i>Lan Yao and Tao Zhang</i>	
4.1	Introduction	61
4.2	Treatment Mechanisms in Mitochondrial Dysfunction	61
4.2.1	Treating in mtDNA	62
4.2.1.1	Clearing Mutations	62
4.2.1.2	Inhibiting Replication	64
4.2.2	Treating in mRNA, tRNA, and rRNA	64
4.2.2.1	Increase Normal RNA	64
4.2.2.2	Silencing Abnormal RNA	64
4.2.2.3	Treating in Noncoding RNA	65
4.3	Nucleic Acid Nanomaterial-Based Delivery System in Mitochondrial Treatment	65
4.3.1	Cell and Mitochondria Targeting	66
4.3.1.1	Cell Targeting	66
4.3.1.2	Mitochondria Targeting	66
4.3.2	Framework Nucleic Acid-Based Delivery System in Mitochondria Treatment	68
4.4	Challenges and Prospectives	71
	Funding	72
	References	72
5	Regeneration of Bone-Related Diseases by Nucleic Acid-Based Nanomaterials: Perspectives from Tissue Regeneration and Molecular Medicine	81
	<i>Xiaoru Shao</i>	
5.1	Introduction	81
5.2	The Development Process of Functional Nucleic Acid	82
5.2.1	DNA Tile	83

5.2.2	DNA Origami	83
5.2.3	Three-dimensional DNA Self-assembly	83
5.2.4	DNA Nanobots and DNA Microchips	84
5.3	Nucleic Acid-Based Functional Nanomaterials	84
5.3.1	Nanomaterials That Can Bind to Functional Nucleic Acids	84
5.3.1.1	Metal-Based Nanomaterials	84
5.3.1.2	Carbon-Based Nanomaterials	85
5.3.1.3	Bionanomaterials	86
5.3.1.4	Quantum Dots	86
5.3.1.5	Magnetic Nanomaterials	86
5.3.1.6	Composite Nanomaterials	87
5.3.2	Combination of Functional Nucleic Acids and Nanomaterials	87
5.4	Multiple Roles of Nucleic Acid-Based Functional Nanomaterials in Bone Tissue Repair and Regeneration	89
5.4.1	Sustained Release	89
5.4.2	Bone Targeting	91
5.4.3	Scaffold Material for Bone Regeneration	92
5.4.4	Bioimaging of Bone Tissue Regeneration	93
5.5	Conclusion and Perspectives	94
	References	94

6 ***In Situ* Fluorescence Imaging and Biotherapy of Tumor Based on Hybridization Chain Reaction**

Ye Chen, Songhang Li, and Taoran Tian

6.1	Hybridization Chain Reaction	102
6.2	Nucleic Acid Detection	102
6.2.1	miRNA Detection	103
6.2.1.1	Autocatalytic HCR Biocircuit	103
6.2.1.2	Nonlinear HCR System	104
6.2.2	Single-Nucleotide Variants Detection	105
6.3	Protein Detection	107
6.3.1	Antibody-Based HCR System	107
6.3.2	Aptamer-Based HCR System	108
6.4	Multiple Target Detection	109
6.4.1	Combined HCR-Based Probe	109
6.4.2	HCR-Based Logic Gate	110
6.5	HCR-Based Assembly Nanoplatfoms	113
6.6	HCR-Based Tumor Biotherapy	115
6.6.1	Chemotherapy	115
6.6.2	Photodynamic Therapy	115
6.6.3	RNA Interfering Therapy	116
6.7	Conclusion	116
	References	116

7	Application and Prospects of Framework Nucleic Acid-Based Nanomaterials in Tumor Therapy	123
	<i>Tianyu Chen and Xiaoxiao Cai</i>	
7.1	Development of Nucleic Acid Nanomaterials	124
7.2	Properties and Applications of Nucleic Acid Nanomaterials	125
7.2.1	tFNAs	125
7.2.2	DNA Origami	127
7.2.3	Dynamic DNA Nanostructure	130
7.3	Conclusion	133
	References	133
8	Application of Framework Nucleic Acid-Based Nanomaterials in the Treatment of Endocrine and Metabolic Diseases	139
	<i>Jingang Xiao</i>	
8.1	Endocrine and Metabolic Diseases	139
8.2	Nucleic Acid Nanomaterials	141
8.3	Nucleic Acid and Drugs	141
8.4	Nucleic Acid Nanomaterials for Endocrine and Metabolic Diseases	144
8.4.1	Diabetes Mellitus	144
8.4.2	Osteoporosis	146
8.4.3	Obesity	147
8.4.4	Nonalcoholic Fatty Liver Disease	148
8.5	Conclusion and Outlook	149
	References	151
9	The Antibacterial Applications of Framework Nucleic Acid-Based Nanomaterials: Current Progress and Further Perspectives	161
	<i>Zhiqiang Liu and Yue Sun</i>	
9.1	Some Advantages of DNA Nanostructures in the Antibacterial Field	163
9.1.1	Compatibility of DNA Nanostructures	163
9.1.2	Stability of DNA Nanostructures	163
9.1.3	Editability of DNA Nanostructures	163
9.1.4	Drug-loading Performance of DNA Nanostructures	164
9.2	Application of 2D Nanostructures in the Antibacterial Field	164
9.2.1	Five “Holes” DNA Nanostructure	164
9.2.2	Super Silver Nanoclusters Based on Branched DNA	164
9.2.3	Melamine-DNA-AgNC Complex	165
9.2.4	NET-like Nanogel Based on 2D DNA Networks	166
9.2.5	ϵ -poly-L-lysine-DNA Nanocomplex	166
9.3	Application of 3D DNA Nanostructures in the Antibacterial Field	166
9.3.1	Tetrahedral Framework DNA	166
9.3.1.1	Delivery of Traditional Antibiotics Based on Tetrahedral Framework DNA	168
9.3.1.2	Delivery of Nucleic Acid Antibiotics Based on Tetrahedral Framework DNA	168

9.3.1.3	Delivery of Polypeptide Antibiotics Based on Tetrahedral Framework DNA	169
9.3.2	DNA Six-Helix Bundle	169
9.3.3	DNA Nanoribbon	170
9.3.4	DNA Pom-Pom Nanostructure	170
9.4	Application of DNA Hydrogel Nanostructures in the Antibacterial Field	170
9.5	Challenges and Further Perspectives	172
	References	174
10	Framework Nucleic Acid Nanomaterial-Based Therapy for Osteoarthritis: Progress and Prospects	181
	<i>Yangxue Yao, Hongxiao Huang, and Sirong Shi</i>	
10.1	Introduction	181
10.2	Pathology of OA	181
10.3	Risk Factors of OA	183
10.4	Challenges for OA Therapy	183
10.5	Nucleic Acid Nanomaterial-Based Therapy for OA	184
10.5.1	Vector-Independent Nucleic Acid Nanomaterials for OA Therapy	184
10.5.1.1	Tetrahedral Framework Nucleic Acids (tFNAs)	184
10.5.1.2	Antisense Oligonucleotides (ASOs)	187
10.5.1.3	Aptamers	187
10.5.2	Vector-Dependent Nucleic Acid Nanomaterials for OA Therapy	188
10.5.2.1	MicroRNA (miRNA) Mimics	188
10.5.2.2	Small Interfering RNA (siRNA)	188
10.5.2.3	cDNA	192
10.5.2.4	mRNA	192
10.5.2.5	Circular RNA (CircRNA)	192
10.5.3	Nucleic Acid Nanomaterials as Carriers for OA Therapy	194
10.6	Conclusion and Prospects	194
	References	195