MCE

Master of Bioactive Molecules

Dark Quenchers

BHQ1	BHQ2	BHQ3	Dabcyl	Eclipse
MGB				

Degenerate Bases

IUB Base Codes	B=C/G/T	D-A/G/T	H=A/C/T	I=Universal Base
K=G/T	M=AIC	N-A/C/G/T	R=A/G	S=C/G
V=AIC/G	W=AIT	Y=C/T		

Attachment Chemistry / Linkers Modifications

Acrydite	Aldehyde	Alkyne	Amino	Azide
Biotin	Carboxy	COOH	DBCO	Digoxin
Maleimide	Thiol			

Spacers Modifications

C3 Spacer	C6 Spacer	C12 Spacer	dSpacer	PC-linker
Spacer 18	Spacer 9			

Modified Bases

2' Fluoro bases	2-O-Methyl Base	2-Aminopurine	5-Aza-2'-dC	5-Bromo dU
5-Hydroxymethyl dC	5-Methyl dC	5-Nitroindole	8-Oxo deoxyguanosine	deoxyInosine
DeoxyUridine	Dideoxycytidine	Inverted dG	Inverted dT	LNA
N6 Methyl dA	phosphorothioate	Phosphorylation	Pyrrolo-dC	

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Related popular products are listed below

Cat. No.	Drug Name	Description	Type
HY-147080	Avacincaptad pegol sodium	an anti-C5 RNA aptamer that inhibits the cleavage of complement factor 5 (C5) into C5a and C5b.	Aptamer
HY-147081	AS 1411	Targets nucleolin, has anti-tumor activity.	Aptamer
HY-108753	Eteplirsen	Targets to exon 51 in the dystrophin, used for Duchenne muscular dystrophy research (DMD).	ASO
HY-108764	Mipomersen (sodium)	Targets human apoB-100, used for familial hypercholesterolemia research.	ASO
HY-109528	Fomivirsen (sodium)	Inhibits cytomegalovirus proliferation.	ASO
HY-112980	Nusinersen	Modifies pre-mRNA splicing of the SMN2 gene, used for the research of spinal muscular atrophy.	ASO
HY-132579	Tominersen	Targets huntingtin protein (HTT) mRNA, used for the research of Huntington's disease (HD).	ASO
HY-132580	Tofersen	Mediates RNase H-dependent degradation of SOD1 mRNA, used for the research of amyotrophic lateral sclerosis (ALS).	ASO
HY-132584	Casimersen	Targets exon 45 of dystrophin pre-mRNA, used for the research of Duchenne muscular dystrophy.	ASO
HY-132608	Inotersen (sodium)	Targets the splicing of exon 53 in the dystrophin gene, used for the research of the DMD.	ASO
HY-132611	Golodirsen	Targets exon 53 of dystrophin pre-mRNA used for the research of Duchenne muscular dystrophy (DMD).	ASO
HY-139290	RGLS4326	Inhibits miR-17 function，used for the research of autosomal dominant polycystic kidney disease (ADPKD)	ASO
HY-146244	Agatolimod	A TLR-9 agonist, used as vaccine adjuvant.	CpG ODN
HY-146245	ODN 1826	A TLR-9 agonist, used as vaccine adjuvant.	CpG ODN
HY-150724	ODN 1018	A TLR-9 agonist, used as vaccine adjuvant.	CpG ODN

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Cat. No.	Drug Name	Description	Type
HY-150741	ODN 2216	A TLR-9 agonist, used as vaccine adjuvant.	CpG ODN
HY-150751	ODN TTAGGG	A TLR9, AIM2 and cGAS antagonist, used in the study of lupus erythematosus and other related autoimmune diseases.	CpG ODN
HY-132588	Lumasiran	Reduces hepatic oxalate production by targeting glycolate oxidase.	siRNA
HY-132591	Inclisiran	Inhibits the transcription of PCSK-9, used for hyperlipidemia and cardiovascular disease (CVD) research.	siRNA
HY-132609	Patisiran sodium	Targets a sequence within the TTR messenger RNA, used for the research of hereditary TTR amyloidosis.	siRNA
HY-132610	Givosiran	Targets hepatic ALAS1 messenger RNA, used for the research of acute intermittent porphyria.	siRNA
HY-112251	D-Lin-MC3-DMA	An ionizable cationic lipid used as a siRNA delivery vehicle.	Lipid
HY-112758	DLin-KC2-DMA	An ionizable cationic lipid used as a siRNA delivery vehicle.	Lipid
HY-138170	ALC-0315	An ionisable aminolipid that is responsible for mRNA compaction.	Lipid

References:

[1] Front Bioeng Biotechnol. 2021;9:628137.
[2] J Neuromuscul Dis. 2020;7(1):1-13.
[3] Chonnam Med J. 2020;56(2):87-93.
[4] Nat Nanotechnol. 2021;16(6):630-643.
[5] Nat Rev Neurol. 2018;14(1):9-21.
[6] Adv Drug Deliv Rev. 2020;154-155:37-63.
[7] Nat Rev Genet. 2022 May;23(5):265-280.
[8] Mol Cancer. 2021;20(1):54.
[9] Cells. 2020;9(1):137. Published 2020 Jan 7.
[10] Adv Drug Deliv Rev. 2018;134:65-78.

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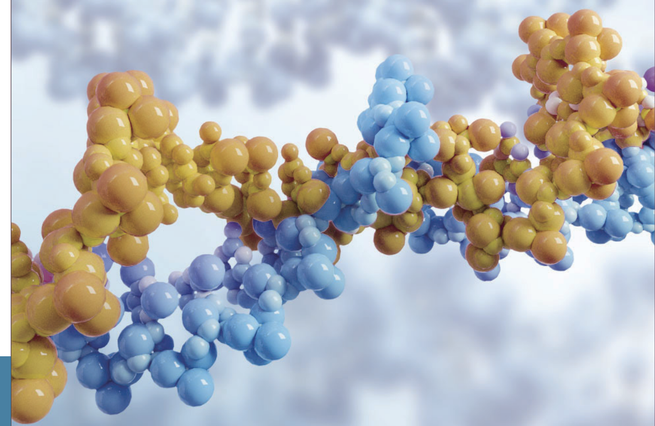
Oligonucleotides

RNA therapy: A Break-through for 'Undruggable-target' Limitations



- Wide range of indications
- Avoid the risk of drug resistance
- Various types
- Rich candidate targets
- Relatively simple production and preparation technology
- Long lasting effect
- Short development cycle

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Oligonucleotides

Conventional drug strategy relies on the ability of small molecule drugs to target active sites of proteins to inhibit or alter their function. However, only **10–14%** of proteins have active binding sites that are druggable targets for small molecules, the vast majority of proteins cannot be targeted for small molecules [1]. There is no cure for some rare diseases, for example, the use of small molecule drugs (such as **Valproic acid**, **Albuterol** and **Riluzol**) to treat spinal muscular atrophy (SMA) is not much effective [2]. This limitation was addressed in part by the revolution of small nucleic acid drugs. **Antisense oligonucleotide**, **Nusinersen** (Spinraza®) is the only approved therapy for SMA in 2016 [2].

The utilization of oligonucleotides as drugs is a relatively novel approach as compared to conventional small molecule inhibitors. The potential of RNA therapies in precision genetics has raised enthusiasm for similar applications in cancer, cardiovascular diseases, and rare diseases therapies. The recent FDA approvals of **Givosiran**, **Lumasiran** and **Viltolarsen** have ushered the wave of RNAi or RNA-based therapies into the mainstream of drug development.

Oligonucleotides are composed of nucleotides with specially designed sequences. Most of the oligonucleotides hybridize with the target gene mRNA or pre-mRNA through complementary base pairing, and can theoretically selectively regulate any target gene and protein expression, including many "undruggable" targets. This means that oligonucleotides have the potential to be used for many rare diseases whose pathogenesis is still unclear. Oligonucleotides also have additional advantages, including relatively simple production and preparation technology, short development cycles, and long-lasting effect.

Currently, common oligonucleotides are **antisense oligonucleotides** (ASOs), **siRNA** (small interfering RNA), **microRNA** and **aptamers**[1][3].

ASOs usually refer to short, synthetic, single-stranded DNA or RNA (13-30 nucleotides)[4]. Following binding to the targeted mRNA or pre-mRNA, ASOs modulate RNA function by several different mechanisms [5][6][7].

1. ASOs can form an RNA–DNA hybrid that becomes a substrate for RNase H, resulting in target mRNA degradation.
2. ASOs can modulate gene expression via steric blocking of the ribosomal machinery, which can lead to reduced expression, modulation of splicing and/or restoration of a functional protein.
3. Binding of ASOs to pre-mRNA can alter splicing factor recruitment and regulate splicing events.

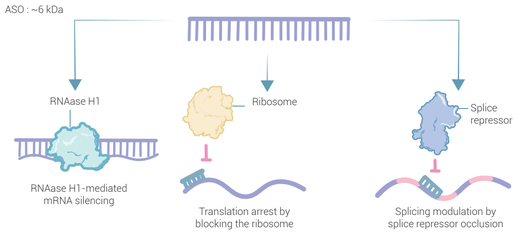


Figure 1. The expanding universe of therapeutic RNA payloads [7].

SiRNAs are small exogenous double-stranded RNA (dsRNA) (20-25 nucleotides), which triggers the RNA interference (RNAi) pathway. The short dsRNA unwinds and the sense strand is degraded. Antisense strand forms **RNA** induced silencing complex (RISC) with various protein components. The antisense strand retained in RISC is specifically complementary to the target gene mRNA. Meanwhile, RISC has nuclease activity, which can cut and degrade the target gene mRNA, and inhibit the expression of target gene. Incomplete complementarity results in mRNA translation inhibition [8].

MicroRNAs (miRNAs) are endogenous non-coding **RNAs** that contain approximately 22 nucleotides, and their primary function is to mediate gene silencing. **MiRNAs** usually bind to 3'-UTR of **mRNA**. For mammals, the base-pairing is always imperfect, resulting in the suppression of **mRNA** translation. In contrast, most plant miRNAs bind with near-perfect complementarity to sites within the coding sequence of their targets, and the **mRNA** of the target gene is sliced and degraded. In addition, miRNAs can have multiple targets, because they act through less complementarity [8][9].

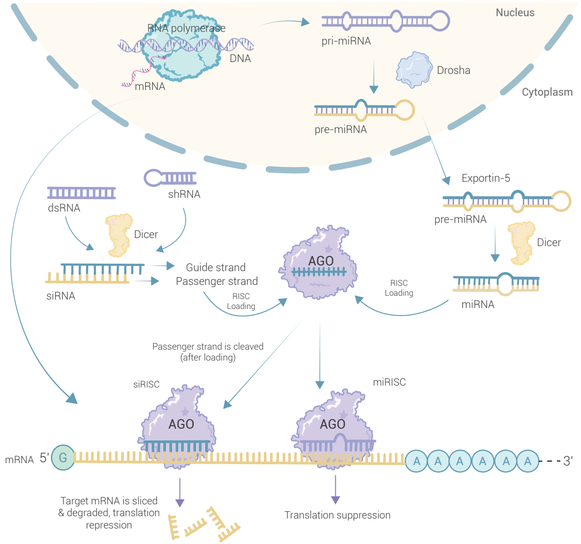
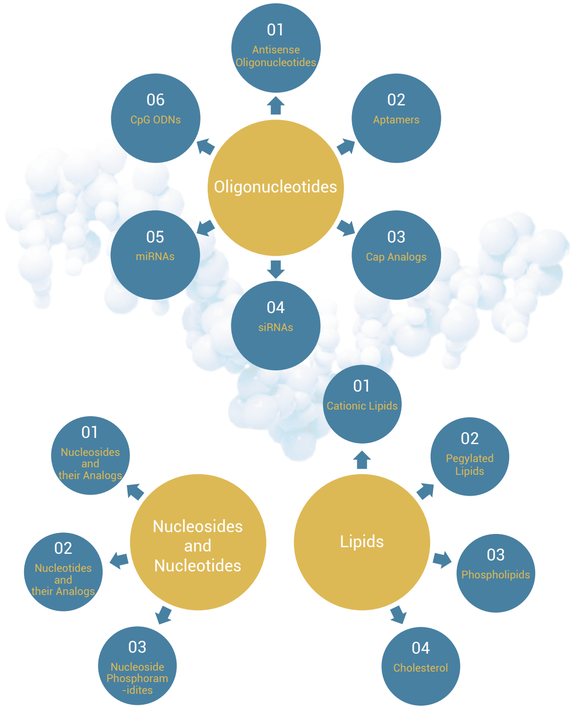


Figure 2. Schematic illustrations for siRNA/miRNA biogenesis and, the mRNA inhibition via siRNA and miRNA-mediated mechanisms [8].

Aptamers are short single-stranded DNA or RNA, which can bind to various targets, such as proteins, peptides, carbohydrates, and other molecules, by virtue of their tertiary structures, rather than their sequences. The aptamers have a high affinity to target proteins similar to antibodies. Compared to antibodies, however, aptamers are small in size and have additional advantages, including improved transport into the cells and lower cost [1][4][10].



Synthesis Services

MCE owns a professional team and state-of-the-art facilities in the production and analysis of oligonucleotides. MCE can synthesize oligonucleotides to suit your specific needs, carry out related testing procedures (purity, structure and stability analysis), and ensure the accuracy and reproducibility of data with high-quality and efficient services.

Advantages

- High purity
- Good stability
- Powerful synthesis ability
- Various chemical modifications

Related Synthesis Services

- **siRNAs:** single gene siRNA set and siRNA libraries.
- **miRNAs:** miRNA libraries (miRNA mimics or miRNA inhibitors).
- **Oligos:** various modifications (Locked Nucleic Acid (LNA), Phosphorothioate, 2' -OMe, 2' -MOE, 2'-Fluoro, CY3, CY5, FAM, etc.)
- **Oligonucleotide-conjugates**: PEGs, lipids, small molecule compounds, polypeptides, etc.
- **Preparation of lipid nanoparticles (LNPs)**.

MCE offers more than 100 modifications (only some commonly used modifications are listed).

Fluorophores

Alexa Fluor 488	AMCA	AquaPhluor 593	Atto 425	Atto 590
BODIPY FL	Cy3	Cy5	Cy5.5	Cy7
FAM	HEX	JOE	NED	Pacific Blue
Quasar 570	Quasar 670	ROX	TAMRA	TET
Texas red	VIC	Yakima Yellow		