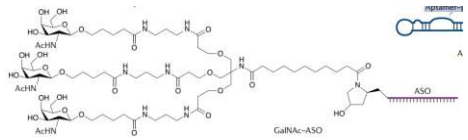
WuXi AppTec

WuXi Biology

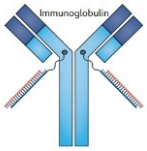
Oligonucleotide Delivery Platform

Overview of Delivery Strategies

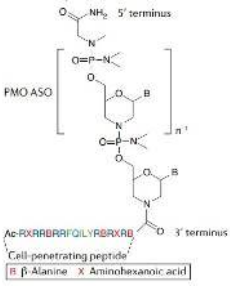
GalNAc or other small molecules



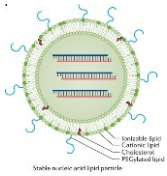
Antibody



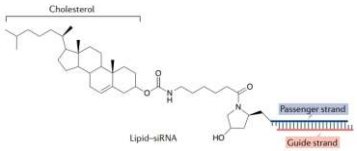
Peptide



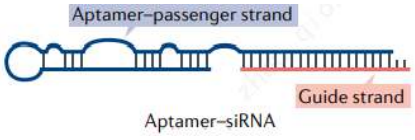
LNPs



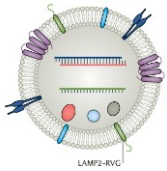
Lipids



Aptamer



Exosomes

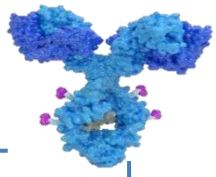


◆ Efficient delivery is a major challenge for oligonucleotide therapeutics, as delivery platforms must protect oligonucleotides from degradation, facilitate cellular uptake, and enable tissue-specific targeting. Various delivery strategies - including ligand, antibody, peptide conjugates and LNPs - have been developed to improve pharmacokinetics, biodistribution, and intracellular delivery to target tissues.

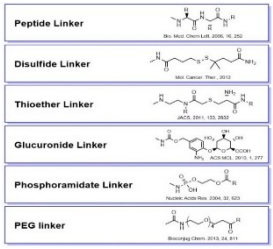
Antibody-Oligonucleotide Conjugate (AOC)

Antibody engineering & expression





Linker/payload synthesis



Conjugation strategy

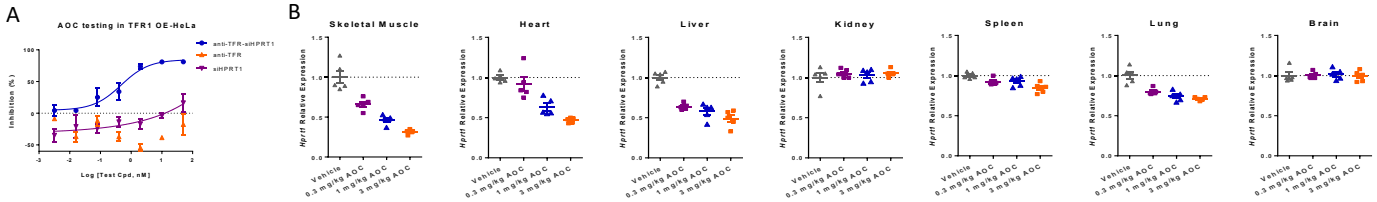
- Lysine-based conjugation
- Cysteine-based conjugation
- Site-specific conjugation by mutagenesis
- Site-specific conjugation by enzyme



AOC characterization

- AOC-specific critical quality attributes
- Physicochemical characterization
- *In vitro* and *in vivo* validation

◆ **Highly diverse** conjugation strategies, **site-specific** chemistries **and customized** linker synthesis.



A. AOC achieves stronger target knockdown in cells with high TFR1 expression. **B.** The target mRNA levels in mouse tissues (PD) after intravenous Cy5-AOC injection. Significant mRNA knockdown occurs in TFR1-rich heart and muscle tissues.

◆ AOCs provide high target specificity, prolonged systemic exposure, and efficient intracellular delivery, making them particularly suitable for receptor-expressing tissues such as **skeletal muscle**, **cardiac muscle**, and potentially the **central nervous system**.

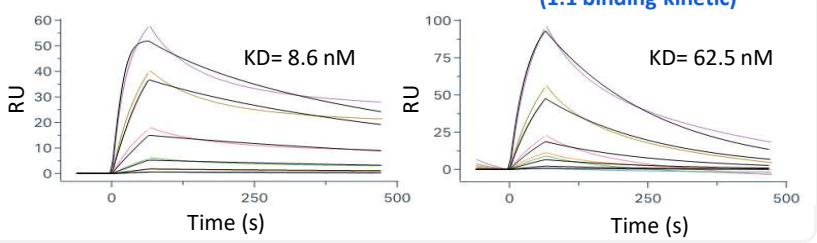
WuXi AppTec

WuXi Biology

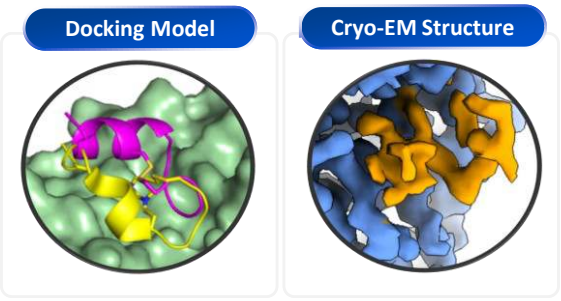
Peptide-Oligonucleotide Conjugates (POC)

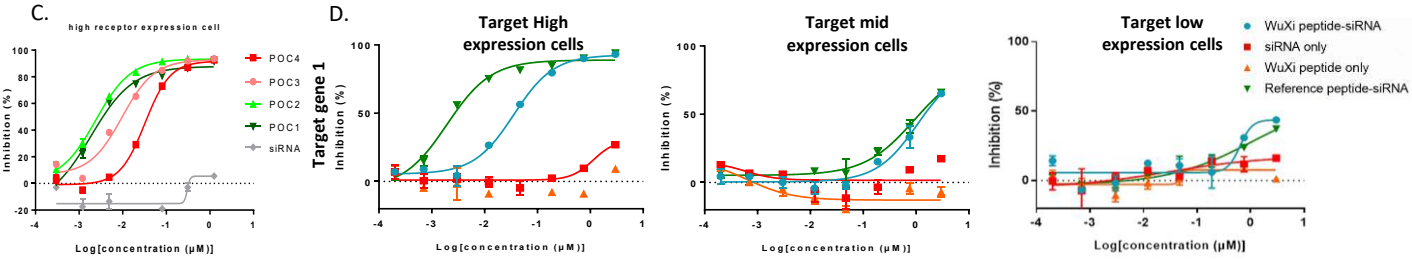
Peptide: Allosteric Binder

A.



B.



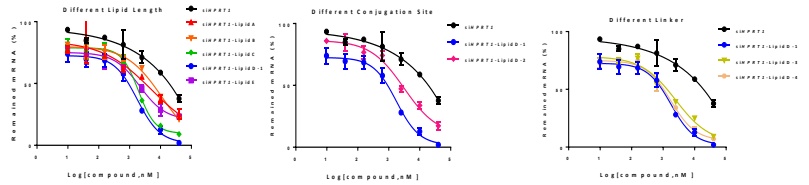


A. mRNA display–based peptide discovery yielded cyclic peptide hits with excellent target-binding kinetics, as confirmed by SPR. **B**. The lead peptide binding pocket was confirmed by cryo-EM and molecular docking simulations. **C**. POC knockdown efficiency was evaluated in high target-expressing cells across peptides with varied Ki values. **D**. The WuXi-POC produces clear, dose-dependent gene knockdown in target-expressing cells, with an IC50 comparable to the reference.

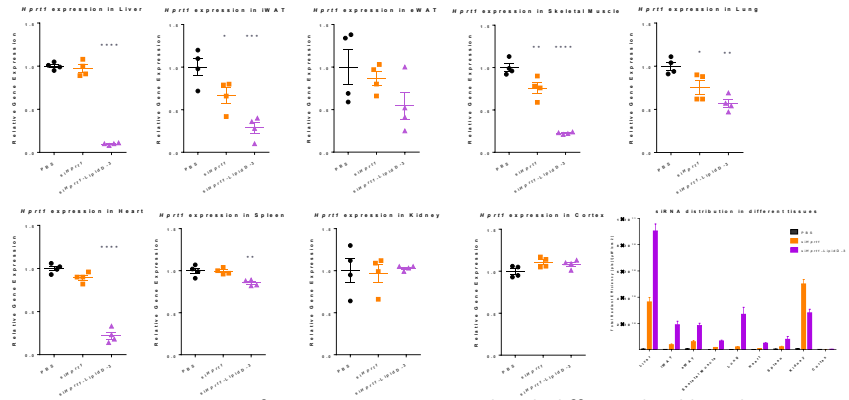
◆ POCs offer a versatile and modular delivery strategy with improved intracellular uptake and broad tissue compatibility, making them well-suited for diverse organs including **skeletal/cardiac muscle, liver, lung**, where peptide-mediated transport substantially augments therapeutic potency.

Lipid-Oligonucleotide Conjugates (LOC)

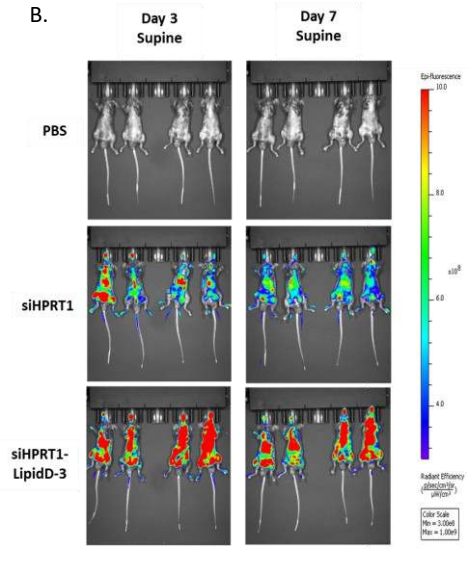
A.



C.



B.



A. Dose-response curves of Cy5-siRNAs conjugated with different lipid lengths, conjugation sites, and linkers in HSKMC. **B.** Live imaging of mice with single s.c. injection of Cy5-siRNA by IVIS. **C.** The remaining target mRNA level in different tissues (PD) after s.c. injection with indicated Cy5-siRNAs.

◆ LOCs deliver robust tissue selectivity, sustained systemic circulation, and potent intracellular uptake, making them well-suited for diverse organs **including liver, skeletal/cardiac muscle, the central nervous system**, where ligand-mediated receptor trafficking substantially boosts therapeutic efficacy.

- Icons by Freepik from Flaticon

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