Heteroduplex Oligonucleotide **(HDO)**

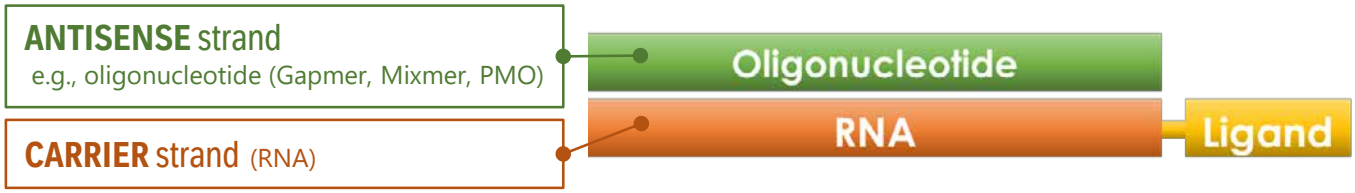
Trial service

We launches a service that allows customers to try **HDO** widely.

Both of pharmaceutical companies and academies can try this trial service.

About Technology

- **HDO** is an artificial functional nucleic acid consisting of an **ANTISENSE** strand and a **CARRIER** strand.
- A variety of **LIGAND**s can be bound to the **CARRIER** stand.
- **HDO with LIGAND** have significantly better **knockdown activity** than ASO.



Service Contents

We offer HDO with ligand* in your specified sequence and ligand.

Synthesis	A variety of modified oligonucleotides and ligands available
Purification	LC (RP, IEX)
Double-Stranded Formation	Annealing
Drying	Lyophilization
Standard Test Items	RP-UHPLC and MS (single strand) / Native PAGE (double strand)

Cautions

- Maximum sample volume is 30 mg.
- For experiment and research purposes only (not for human studies).
- We may refuse sequences targeting fatty acid synthase genes.

* HDO with ligand is provided by Nippon Shokubai Co., Ltd. under license from Rena Therapeutics Inc.

Business Flow

STEP 01 **Contact** → STEP 02 **Quote** → STEP 03 **Synthesis / Analysis**

Contact Information

Trial Service NIPPON SHOKUBAI

Health & Medical Business Office
Email : health_medical@shokubai.co.jp

HDO Technology Rena Therapeutics

Business Development Division, Ryohei Shimizu
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Heteroduplex oligonucleotide (HDO)

a nucleic acid pharmaceutical platform technology

Rena Therapeutics Inc. | https://www.renatherapeutics.com/?lang=en / | info@renatherapeutics.com

■HDO structure

HDO is composed as follows.

Antisense strands

Has a medicinal effect

Carrier strand（RNA）

Deliver antisense strand (medicinal effect) to disease site.

Ligand

By binding a substance that specifically binds to a specific receptor to the carrier strand, it delivers the antisense strand to a targeted disease site.

■HDO's mechanism of action

The mechanism of action of the RNaseH-dependent antisense effect is as follows :

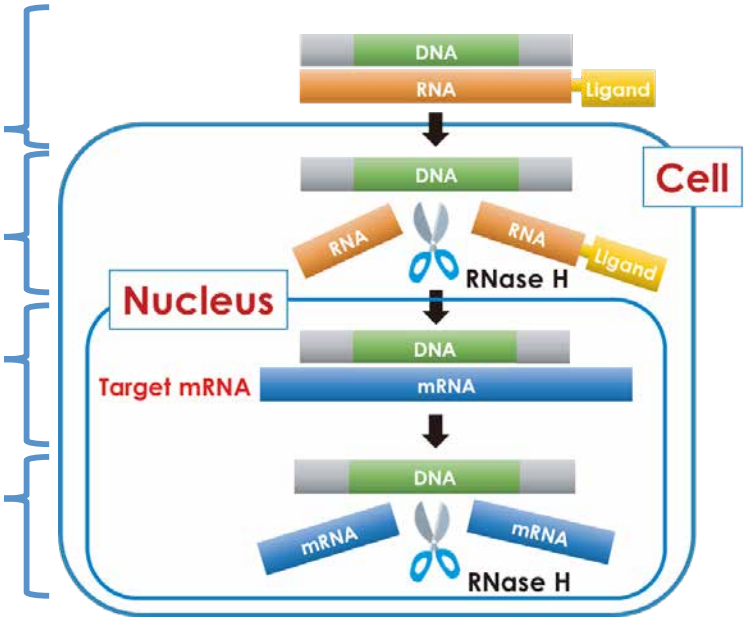
Step 1: HDO enters into the cell.

Step 2: Intracellular ribonuclease RNase H is cleaves the HDO carrier strand (RNA).

Step 3: The active strand (DNA) forms a double strand with the target mRNA in the cell nucleus, etc..

Step 4: As the target mRNA is cleaved by Rnase H, mRNA expression is suppressed, and drug efficacy is demonstrated.

※RNase H has the property of cleaving RNA among double strands composed of DNA / RNA.



■Strengths of HDO technology

Knockdown activity

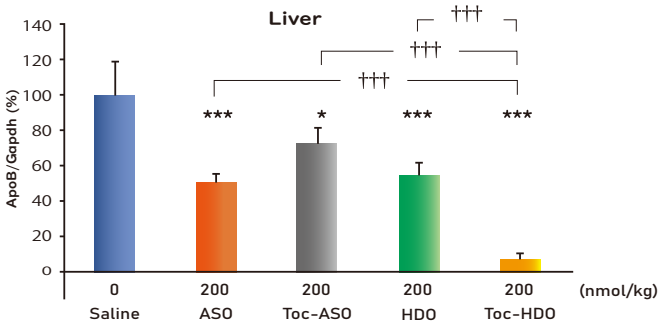
Ligand-bound HDO has much better knockdown activity than ASO.

When the knockdown activity was compared in an in vivo study, Toc-HDO knocked down 95% of the target mRNA, showing a much stronger knockdown activity than ASO and Toc-ASO.

Reagent : Saline, ASO, Toc-ASO, HDO, Toc-HDO ※Toc=Tocopherol
Target : ApoB mRNA
Subject : c57BL/6J (n=5)
Dose : 200 nmol/kg (0.87 mg/kg as antisense strand for all reagents)
Administration : Single bolus iv
Time : 3 days after dosing

* : Compared to Saline p<0.05
*** : Compared to Saline p<0.001
††† : p<0.001

Comparison of knockdown activity of HDO & ASO in mouse liver



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