Electronic Supplementary Material (ESI) for Biomaterials Science.

Supporting Information

Hydrogel based lipid-oligonucleotides: a new route to self-delivery of therapeutic sequences

*Sébastien Benizri[§], Alexandra Gaubert[§], Charlotte Soulard, Étienne Gontier, Isabelle Svahn, Palma Rocchi, Gaëlle Vacher, and Philippe Barthélémy**

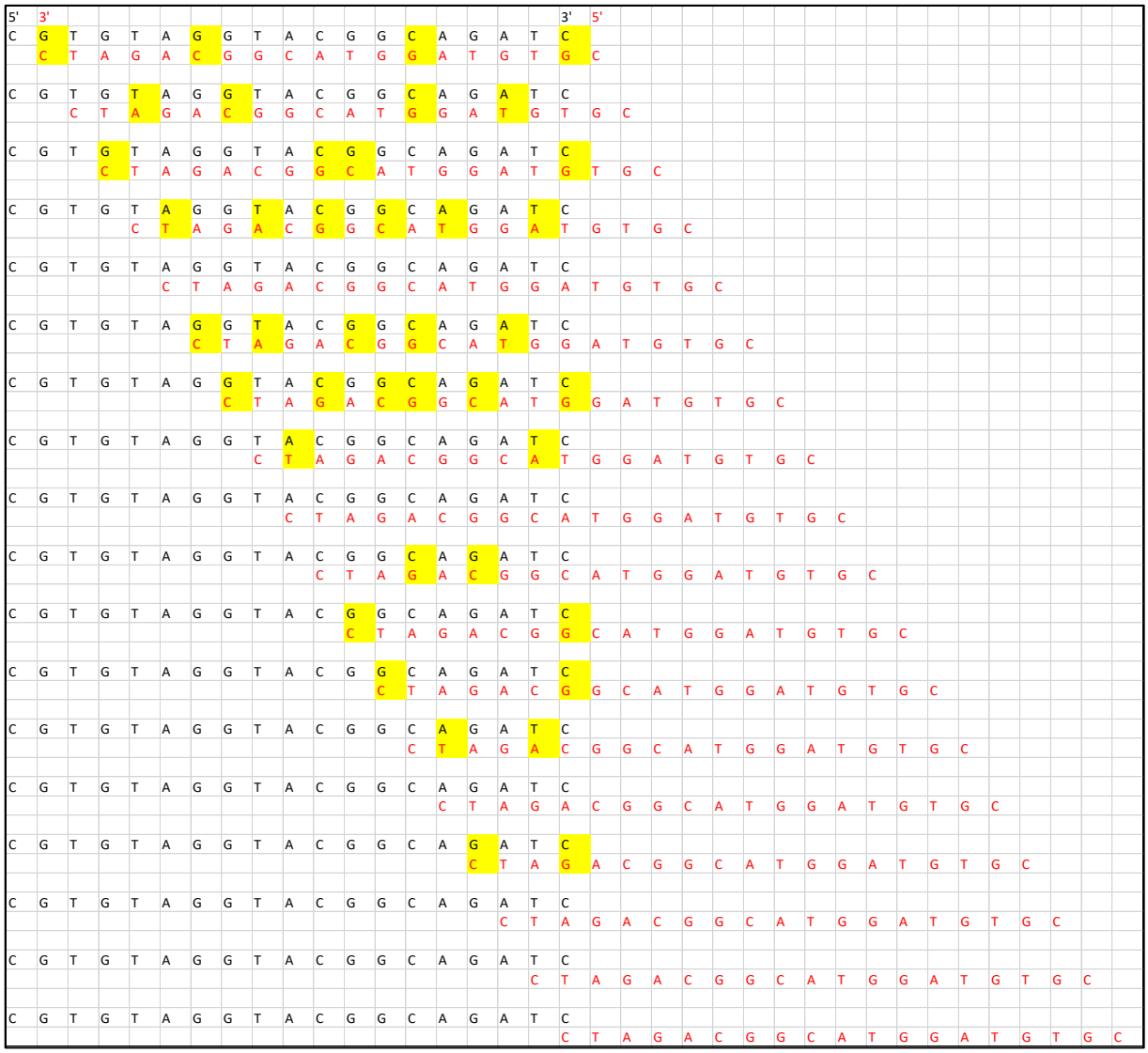
Supplementary Table 1. Mass spectrometry

Name of oligonucleotide sequence	M calculated	M experimental
ASO_{TCTP}	**6428.2**	**6433.5**
$LASO_{TCTP}$	**7183.2**	**7187.5**
ASO_{α}	**8091.8**	**8091.8**
$LASO_{\alpha}$	**8846.2**	**8847.1**
ON_{Ctrl}	**6157.9**	**6161.9**
LON_{Ctrl}	**6912.9**	**6915.8**

Supplementary Table 1. Mass spectrometry data (calculated and experimental) obtained by mass spectrometry in electrospray ionization (ESI) mode.

Supplementary Figure 1. Sequence overlap

A) LON_{Ctrl}



B) LASO$_{TCTP}$

5'	3'																	3'	5'																		
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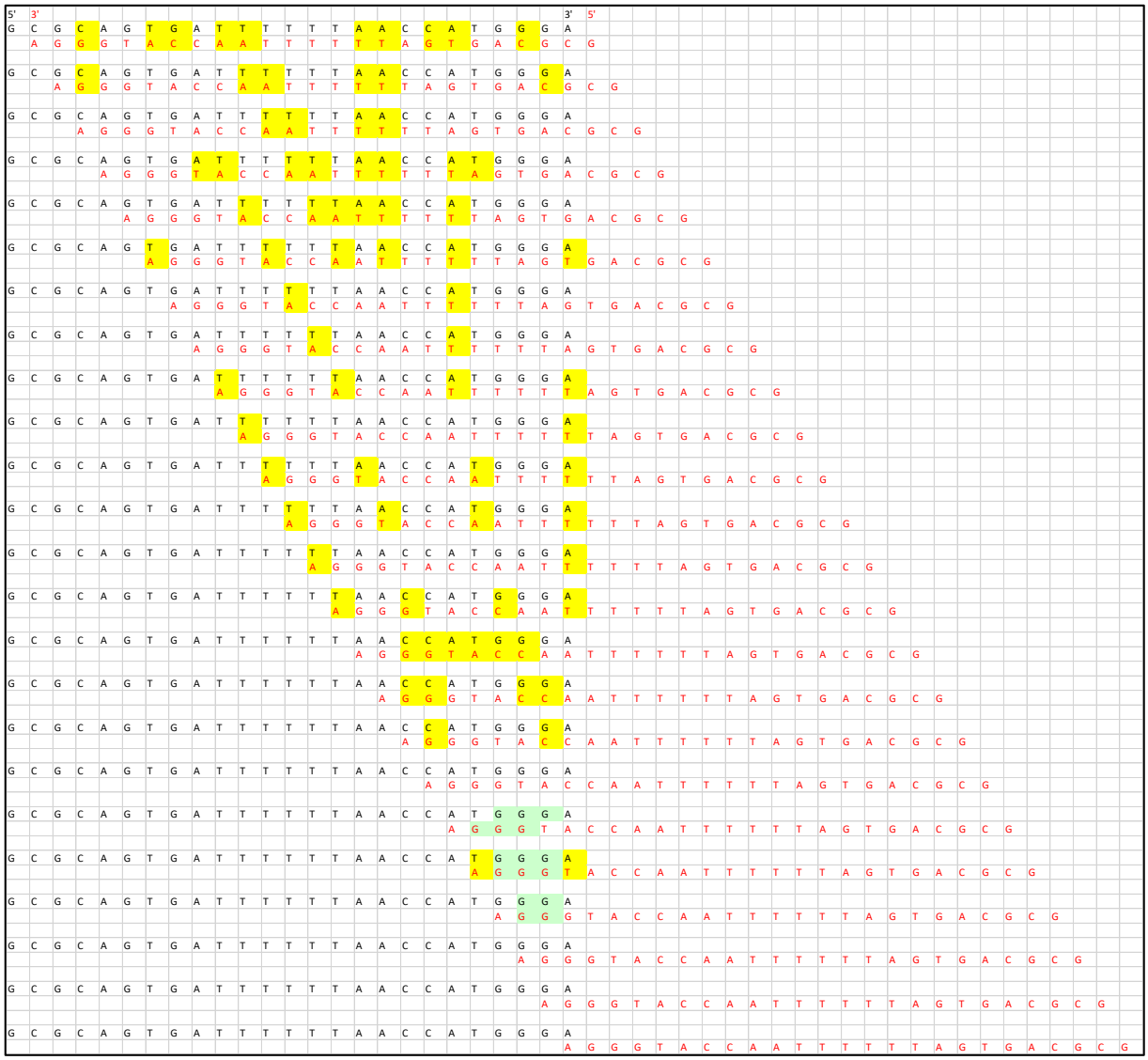
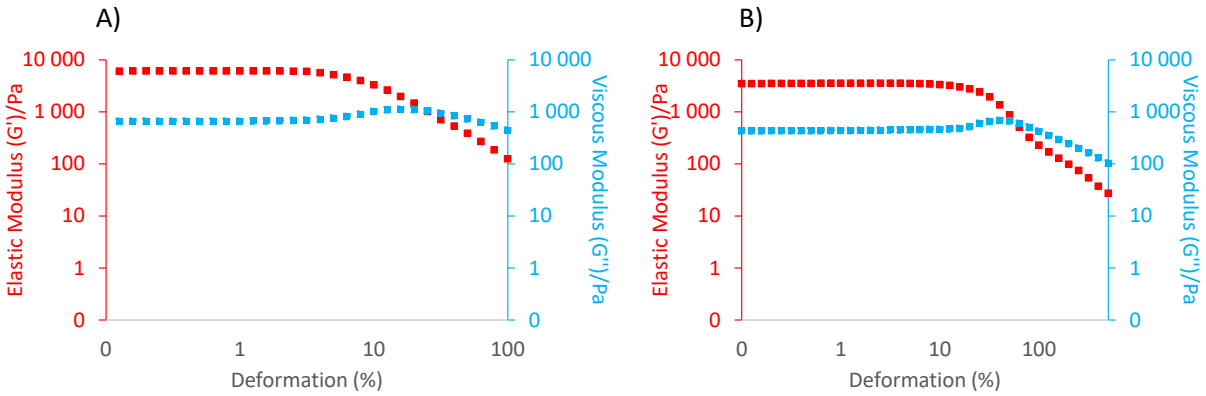
C) LASO$_{\alpha}$



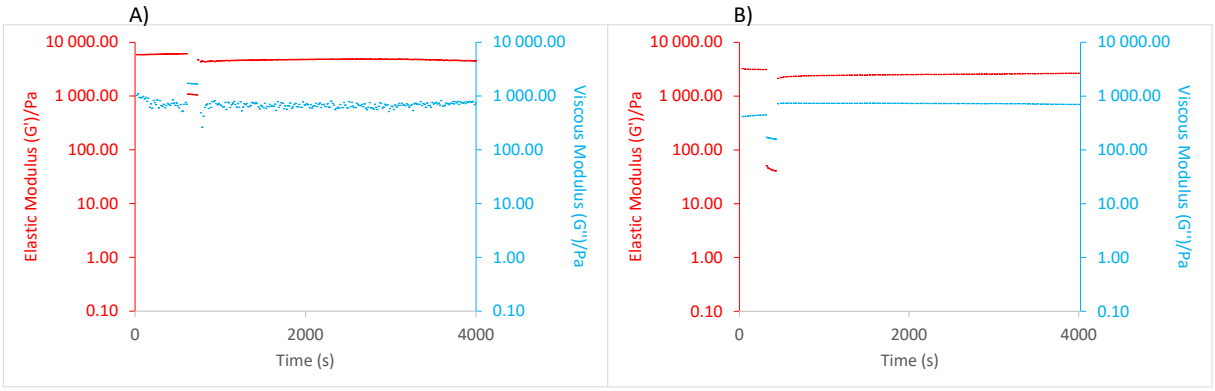
Supplementary Figure 1. Self-complementarity sequences. A) LON$_{Ctrl}$, B) LASO$_{TCTP,}$ C) LASO$_{\alpha}$. Complementarity are shown in yellow.

Supplementary Figure 2. Amplitude sweep experiments



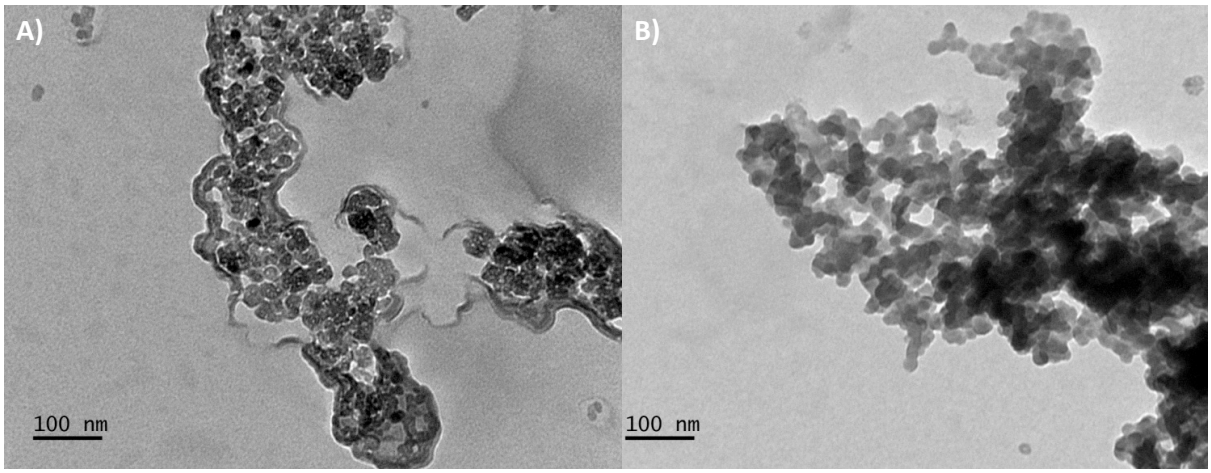
Supplementary Figure 2. Amplitude sweep experiments of A) $LASO_{TCTP}$ and B) $LASO_{\alpha}$ hydrogels at 13.9 mM (T° 37°C, 1 Hz, shear strain 0.01% to 100%). In the case of $LASO_{TCTP}$ hydrogel, the Linear Viscoelastic Region (LVR) was found up to 3.16% with a breaking point (corresponding to the transition from a gel state to a sol state (moduli inversion (G" > G'))) at 26%, whereas $LASO_{\alpha}$ hydrogel exhibited a LVR up to 7.94% and a breaking point at 63%, highlighting a tougher material.

Supplementary Fig. 3. Step-strain measurements



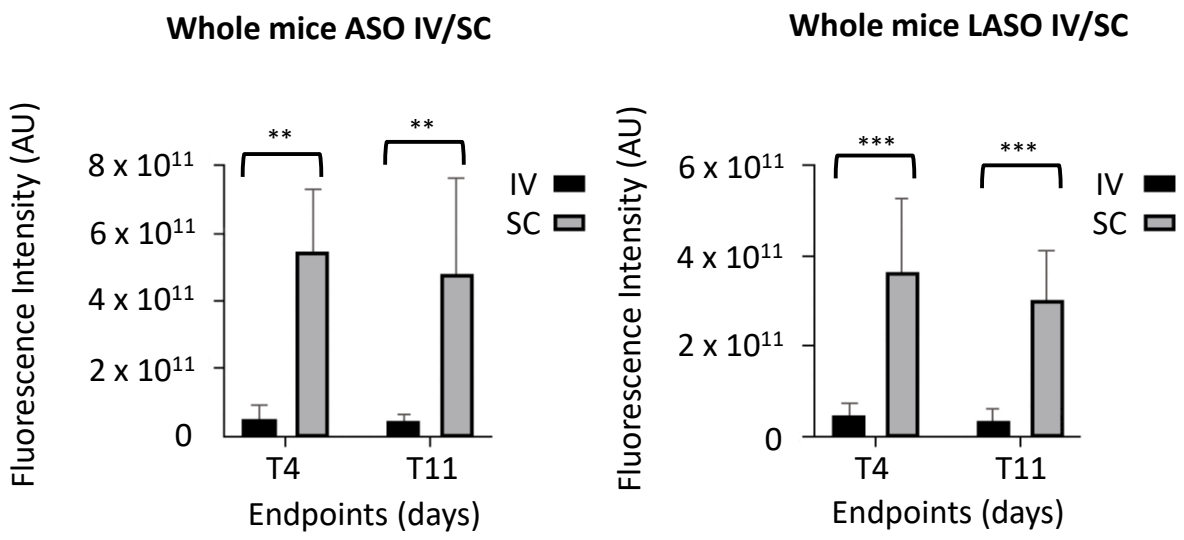
Supplementary Figure 3. Step-strain experiments of A) $LASO_{TCTP}$ and B) $LASO_{\alpha}$ hydrogels (13.9 mM) at 37°C and with a fixed angular frequency of 1 Hz. The gels were swept from 0.03% (structuration step) to 30% (destructuration step) shear strain and then back to 0.03% (structuration step) shear strain. Both biomaterials are thixotropic.

Supplementary Figure 4. Transmission Electronic Microscopy



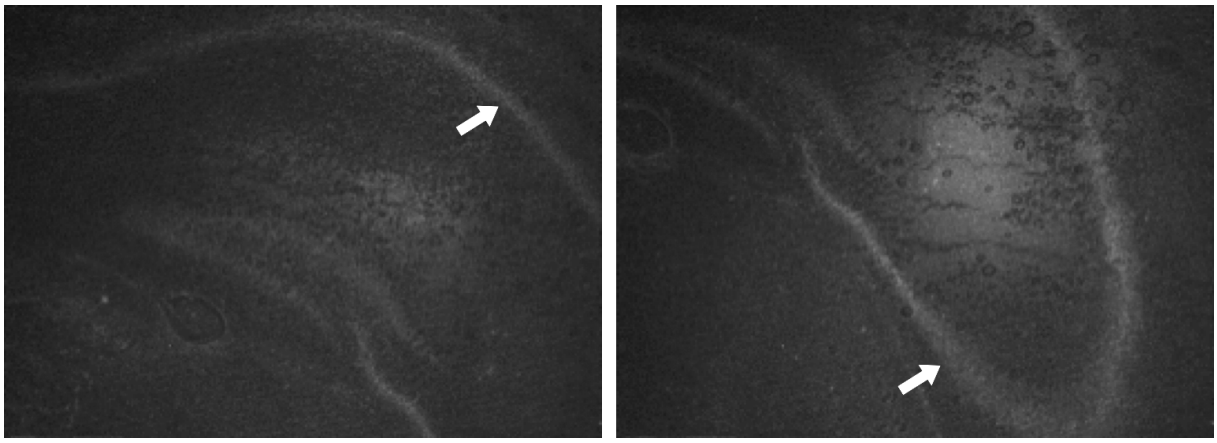
Supplementary Fig. 4. Transmission Electron Microscopic images of A) $LASO_{\alpha}$ and B) $LASO_{TCTP}$ hydrogels in PBS (13.9 mM) (Scale bar: 100 nm).

Supplementary Figure 5. Fluorescence intensity in mouse body after ASO_{TCTP} and $LASO_{TCTP}$ injection



Supplementary Figure 5. Fluorescence intensity measured on the whole mouse 4 days (T4) and 11 days (T11) post-injection either intravenously (black) or subcutaneously (grey) of ASO_{TCTP} (a) and $LASO_{TCTP}$ (b) (n =5 mice).

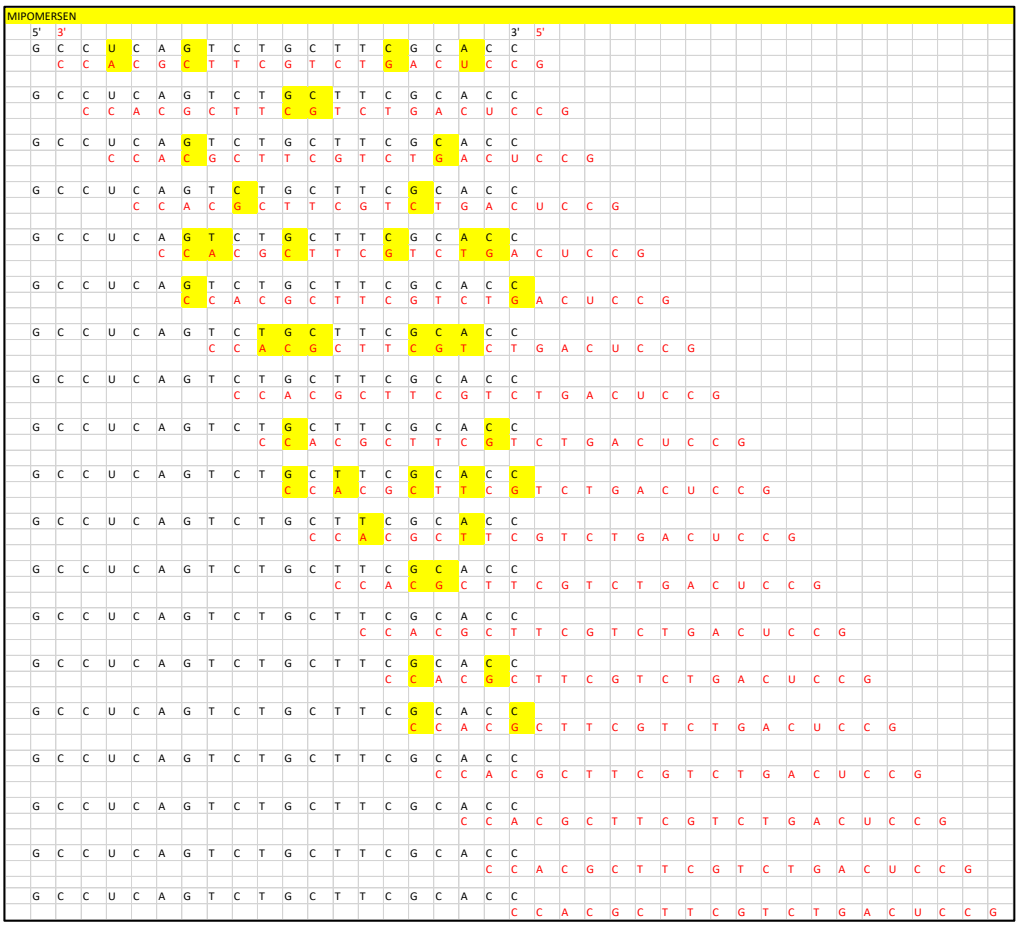
Supplementary Figure 6. Fluorescence confocal microscopy



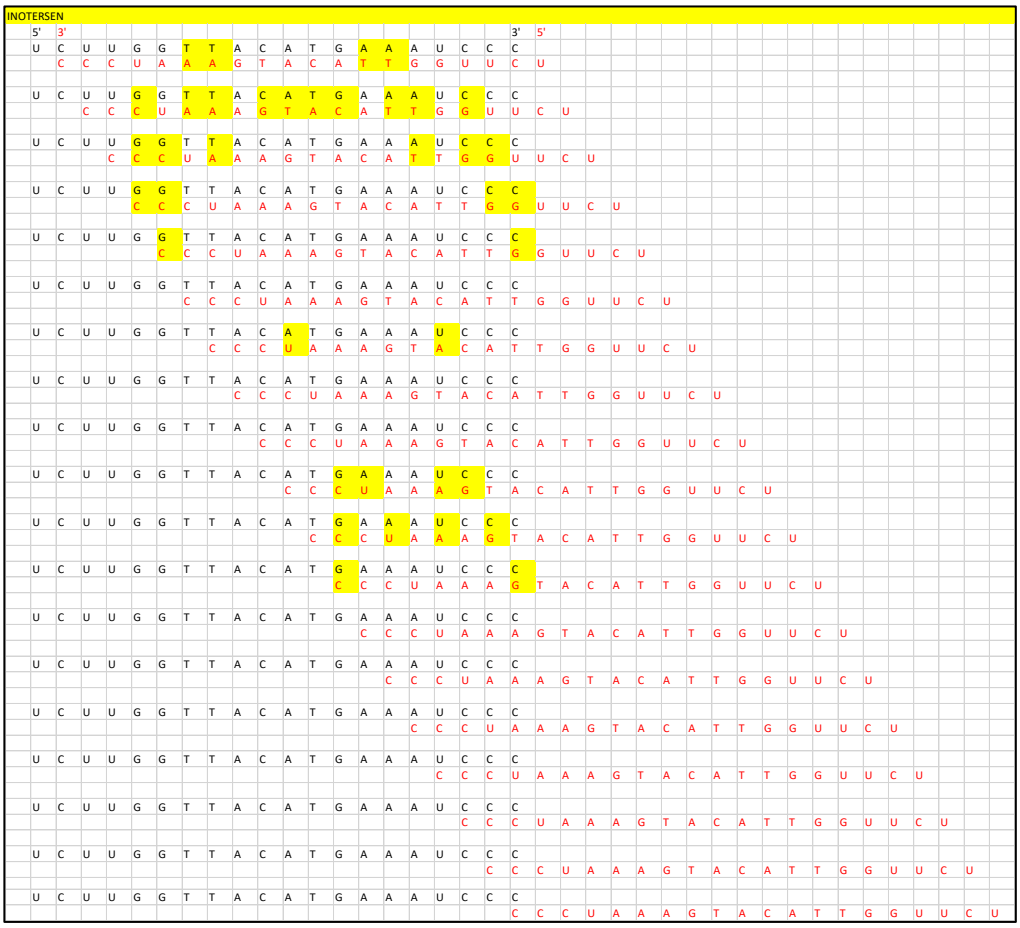
Supplementary Figure 6. Fluorescence confocal microscopy pictures of a brain cross section (90 µm) of a mouse 30 minutes after IV injection of $LASO_{TCTP}$ solution (1mg.ml^{-1}). The white arrow indicates Cy5 covalently linked to $LASO_{TCTP}$ highlighting an accumulation in the hippocampus.

Supplementary Figure 7 Sequence overlap of therapeutic oligonucleotide sequences

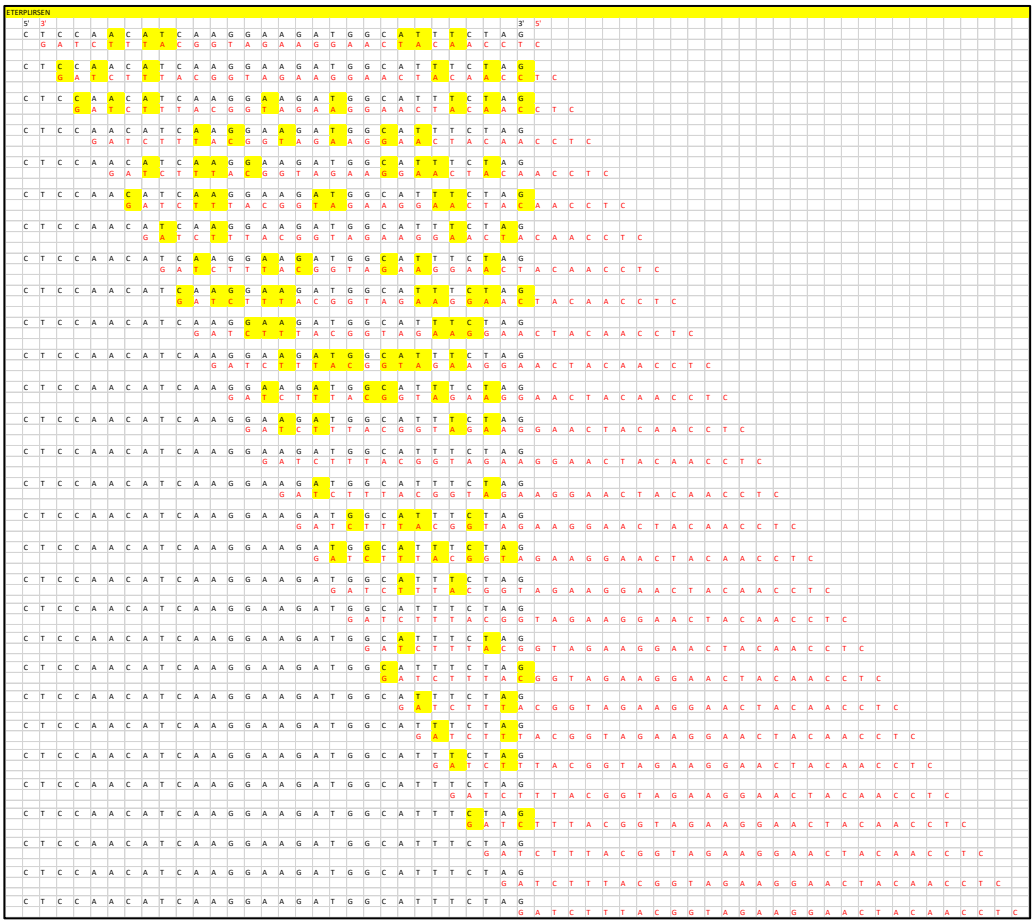
A) Mipomersen



B) Inotersen



C) Eterplirsen



D) Golodirsen

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GOLODIRSEN
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          C T T G T G G A A G T C T T G G C C T C C G T T G

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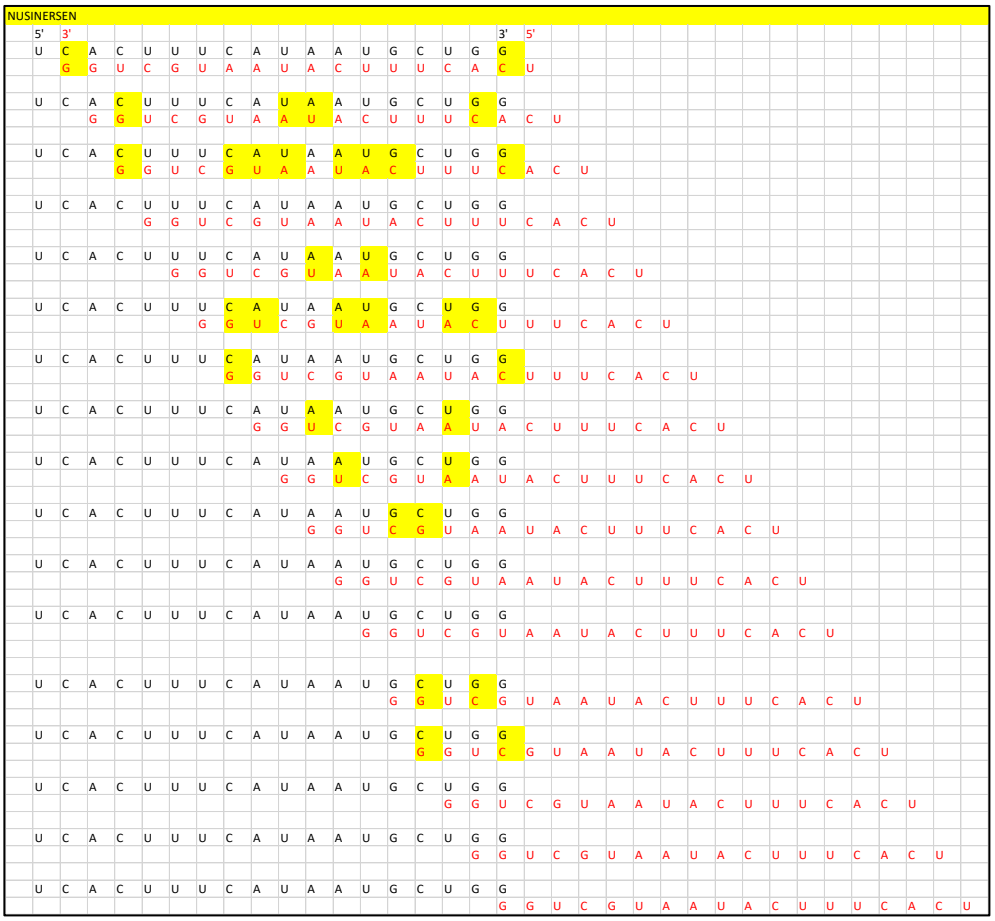
E) Nusinersen



Supplementary Figure 7. Self-complementarity sequences of FDA approved therapeutic oligonucleotides. A) Mipomersen, B) Inotersen, C) Eterplirsen, D) Golodirsen, E) Nusinersen. Complementarity are shown in yellow.