

Supplementary Information

Peptide-LNA Oligonucleotide Conjugates

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Table S1. IE HPLC retention times and MALDI-MS of purified oligonucleotides.

#	Sequence, 5'→3'	Ret. time, min	MALDI-MS	
			Found m/z [M-H] ⁻	Calc. m/z [M-H] ⁻
ON1	TGC ACT CTA TGM ¹ CTG TAT CAT	24.04	6467	6468
ON2	TGC ACT CTA M ¹ GT CM ¹ G TAT CAT	22.14	6575	6575
ON3	TGC ACM ¹ CTA TGT CTG TAM ¹ CAT	24.18	6572	6575

Table S2. IE HPLC retention times and MALDI-MS of **POC1–POC6**.

#	Sequence, 5'→3'	Ret. time, min	MALDI-MS	
			Found m/z [M-H] ⁻	Calc. m/z [M-H] ⁻
POC1	TGC ACT CTA TGM ² CTG TAT CAT	22.91	7550	7551
POC2	TGC ACT CTA M ² GT CM ² G TAT CAT	21.13	8748	8741
POC3	TGC ACM ² CTA TGT CTG TAM ² CAT	21.19	8745	8741
POC4	TGC ACT CTA TGM ³ CTG TAT CAT	23.54	7533	7533
POC5	TGC ACT CTA M ³ GT CM ³ G TAT CAT	21.25	8708	8705
POC6	TGC ACM ³ CTA TGT CTG TAM ³ CAT	23.24	8706	8705

Figure S1. Representative IE HPLC traces of modified oligonucleotides prepared in this study.

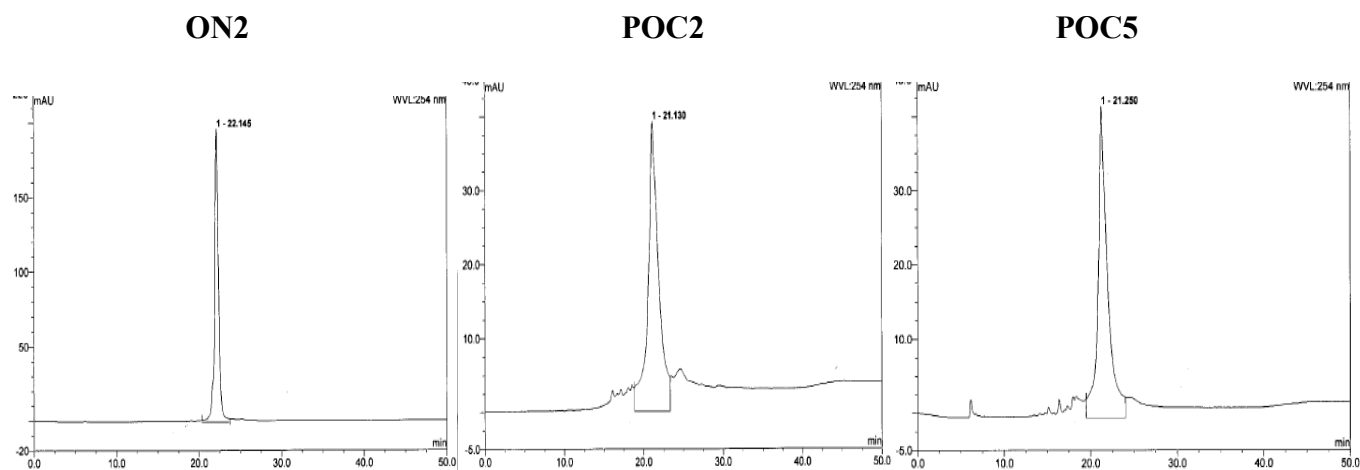


Figure S2. Representative MALDI-MS spectrum of peptide-oligonucleotide conjugate **POC2**.

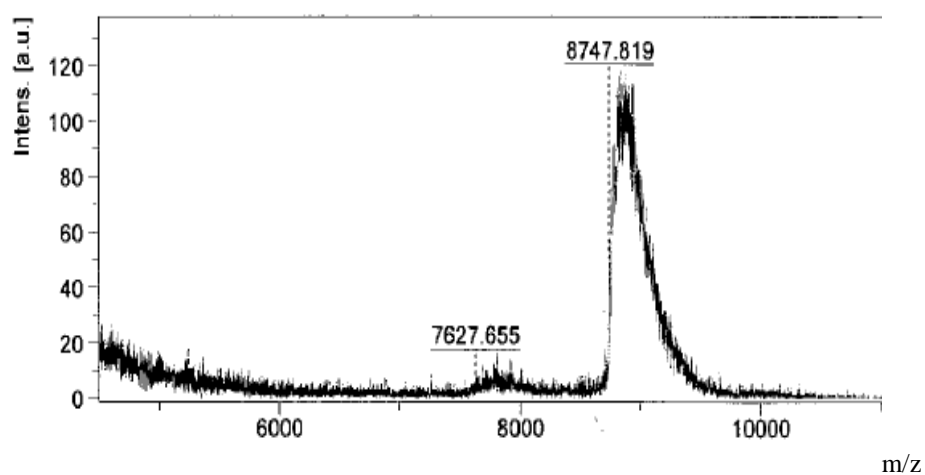
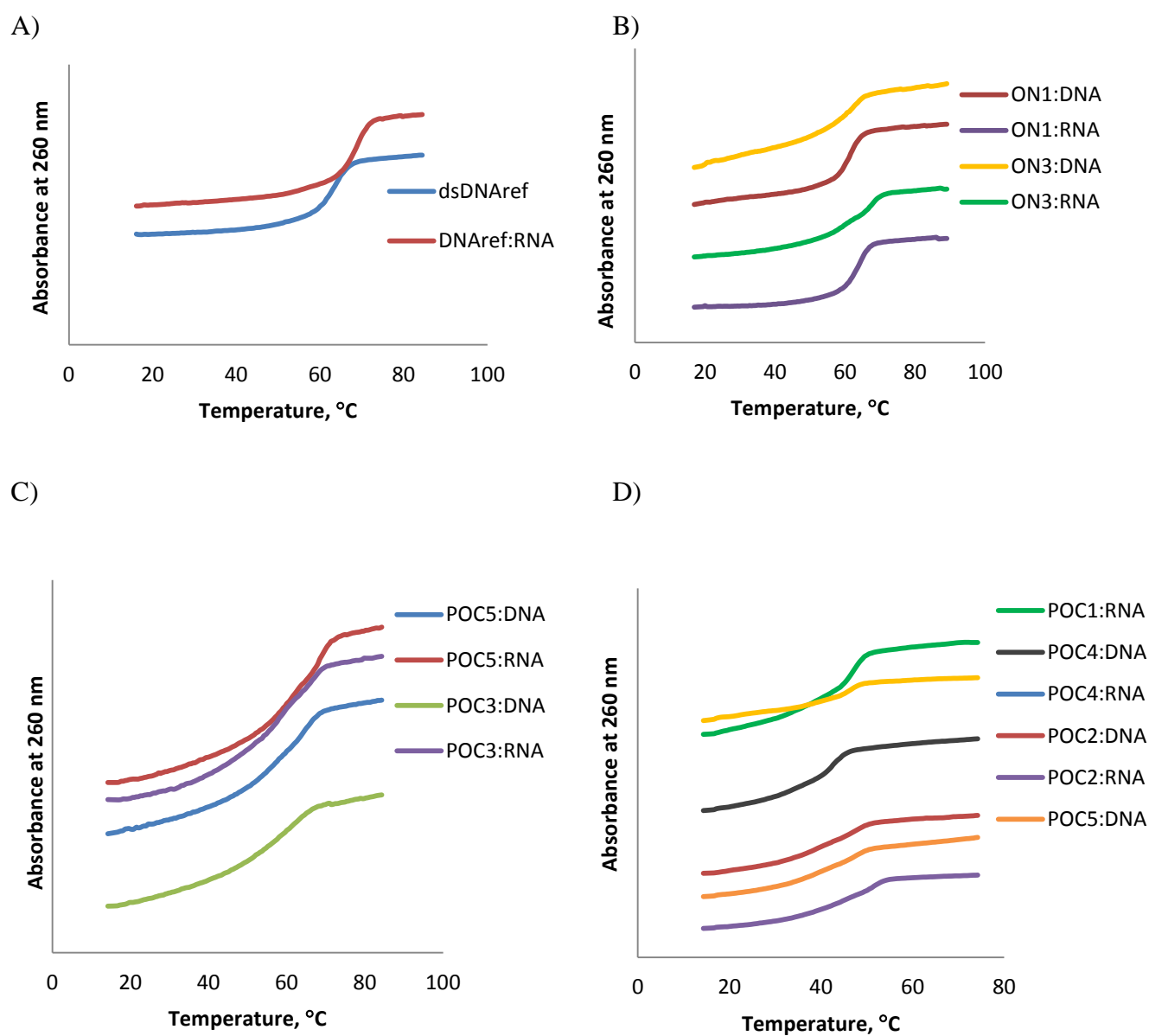


Figure S3. Representative T_m curves.



The melting curves were recorded in a medium salt (A–C) and low salt (D) phosphate buffer using 0.5 μM concentration of complementary strands.

Table S3. Effect of single mismatches on binding affinities of single-labeled **ON1**, **POC1** and **POC2** to DNA/RNA targets in a medium salt phosphate buffer.^a

Conjugate:Target	T_m (°C)									
	X=	DNA target				RNA target				
		A	C	T	G	A	C	U	G	
(ON1) 5' - TGC ACT CTA TGM ¹ CTG TAT CAT 3' - ACG TGA GAT AXA GAC ATA GTA		50.5	62.0 ^{cc}	53.5	53.0	54.5	65.0 ^{cc}	56.0	57.0	
(ON1) 5' - TGC ACT CTA TGM ¹ CTG TAT CAT 3' - ACG TGA GAT ACX GAC ATA GTA		62.0 ^{cc}	53.0	54.0	54.0	65.0 ^{cc}	54.5	55.0	58.0	
(ON1) 5' - TGC ACT CTA TGM ¹ CTG TAT CAT 3' - ACG TGA GAT ACA XAC ATA GTA		49.0	49.0	49.0	62.0 ^{cc}	54.0	50.0	50.0	65.0 ^{cc}	
(POC1) 5' - TGC ACT CTA TGM ² CTG TAT CAT 3' - ACG TGA GAT AXA GAC ATA GTA		51.0	60.0 ^{cc}	55.0	53.0	53.0	63.5 ^{cc}	56.0	55.0	
(POC1) 5' - TGC ACT CTA TGM ² CTG TAT CAT 3' - ACG TGA GAT ACX GAC ATA GTA		60.0 ^{cc}	52.0	52.0	53.0	63.5 ^{cc}	54.0	55.0	57.0	
(POC1) 5' - TGC ACT CTA TGM ² CTG TAT CAT 3' - ACG TGA GAT ACA XAC ATA GTA		50.0	50.0	51.0	60.0 ^{cc}	52.5	49.0	49.5	63.5 ^{cc}	
(POC2) 5' - TGC ACT CTA TGM ³ CTG TAT CAT 3' - ACG TGA GAT AXA GAC ATA GTA		45.0	62.0 ^{cc}	43.0	40.0	53.0	64.5 ^{cc}	55.0	55.5	
(POC2) 5' - TGC ACT CTA TGM ³ CTG TAT CAT 3' - ACG TGA GAT ACX GAC ATA GTA		62.0 ^{cc}	55.0	50.0	52.0	64.5 ^{cc}	55.0	55.0	57.5	
(POC2) 5' - TGC ACT CTA TGM ³ CTG TAT CAT 3' - ACG TGA GAT ACA XAC ATA GTA		52.5	51.0	53.0	62.0 ^{cc}	52.0	50.0	50.5	64.5 ^{cc}	

^a Sequences of DNA target variants are presented; *cc* = complementary complex.

Table S4. Effect of single-base mismatch on binding affinity of **ON2–ON3** to DNA/RNA targets in a medium salt phosphate buffer.^a

ON:TARGET	T_m (°C)									
	X=	DNA target			RNA target					
		A	C	T	G	A	C	U	G	
5' - TGC ACT CTA M ¹ GT CM ¹ G TAT CAT 3' - ACG TGA GAT ACA GAX ATA GTA		54.0	63.5 ^{cc}	57.0	54.0	57.0	69.0 ^{cc}	61.0	59.0	
5' - TGC ACT CTA M ¹ GT CM ¹ G TAT CAT 3' - ACG TGA GAT ACA GXC ATA GTA		63.5 ^{cc}	50.0	57.0	57.0	69.0 ^{cc}	61.0	60.0	64.0	
5' - TGC ACT CTA M ¹ GT CM ¹ G TAT CAT 3' - ACG TGA GAT XCA GAC ATA GTA		63.5 ^{cc}	55.0	56.0	57.0	69.0 ^{cc}	62.0	62.0	65.0	
5' - TGC ACT CTA M ¹ GT CM ¹ G TAT CAT 3' - ACG TGA GAX ACA GAC ATA GTA		55.5	55.0	63.5 ^{cc}	59.5	62.0	60.0	69.0 ^{cc}	65.0	
5' - TGC ACM ¹ CTA TGT CTG TAM ¹ CAT 3' - ACG TGA GAT ACA GA ATA XTA		54.0	53.0	55.0	63.0 ^{cc}	59.0	55.0	60.0	68.0 ^{cc}	
5' - TGC ACM ¹ CTA TGT CTG TAM ¹ CAT 3' - ACG TGA GAT ACA GA ATX GTA		63.0 ^{cc}	53.0	54.0	55.0	68.0 ^{cc}	60.0	60.0	62.0	
5' - TGC ACM ¹ CTA TGT CTG TAM ¹ CAT 3' - ACG TGA GAT ACX GA ATA BTA		63.0 ^{cc}	52.0	53.0	55.0	68.0 ^{cc}	58.8	58.8	63.0	
5' - TGC ACM ¹ CTA TGT CTG TAM ¹ CAT 3' - ACG TGA XAT ACA GA ATA BTA		50.0	52.0	50.0	63.0 ^{cc}	55.0	53.0	56.0	68.0 ^{cc}	

^a Sequences of DNA target variants are presented; *cc* = complementary complex.

Figure S4. Representative CD spectra of single-stranded (ss) POCs and their duplexes with complementary DNA/RNA.

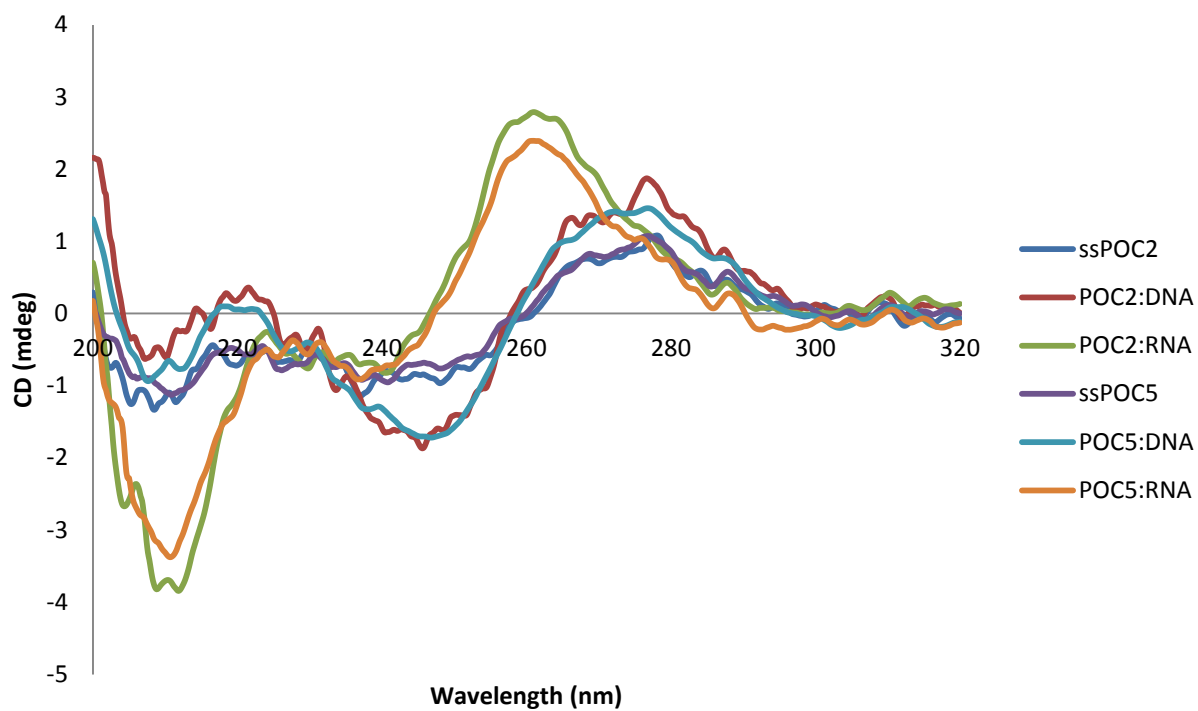
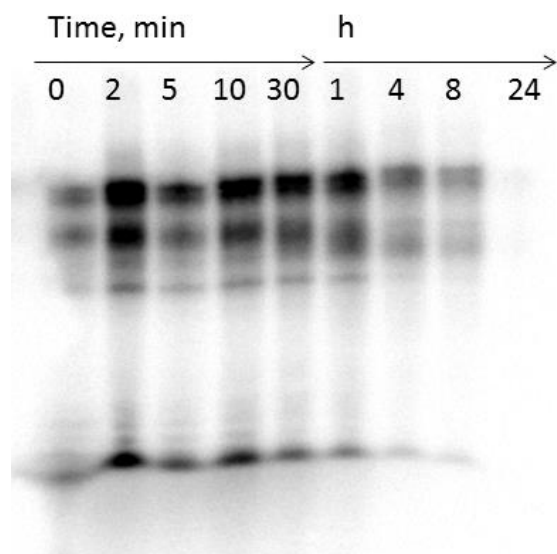
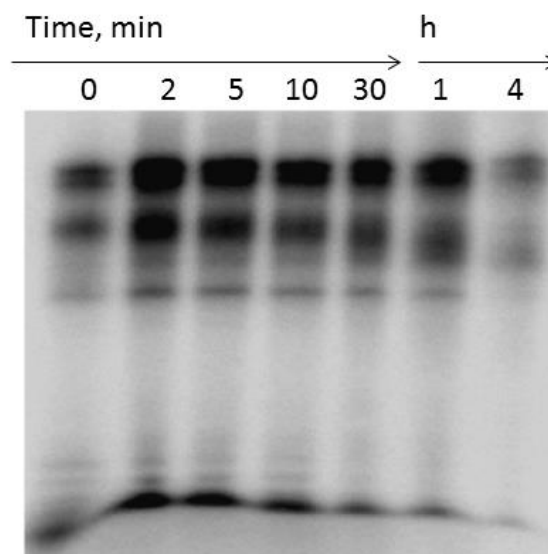


Figure S5. Gel electrophoresis of 5'-³²P-labeled oligonucleotides incubated with HS.

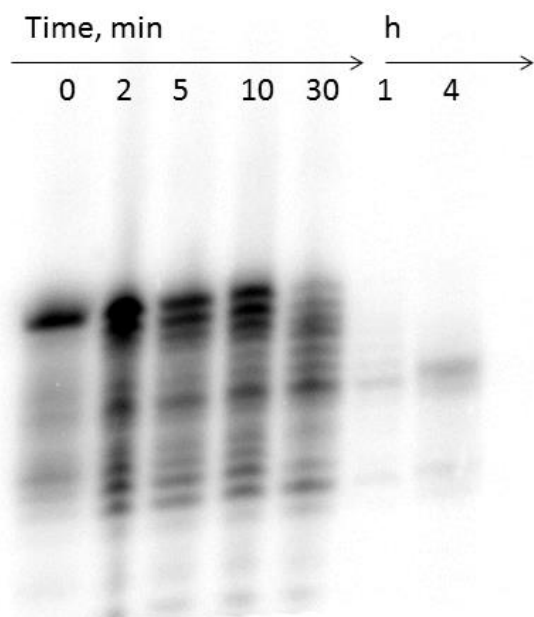
A) POC3



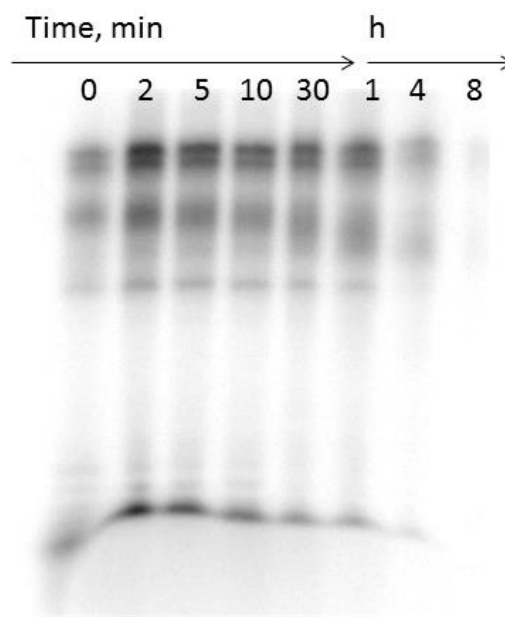
B) POC4



C) ON2

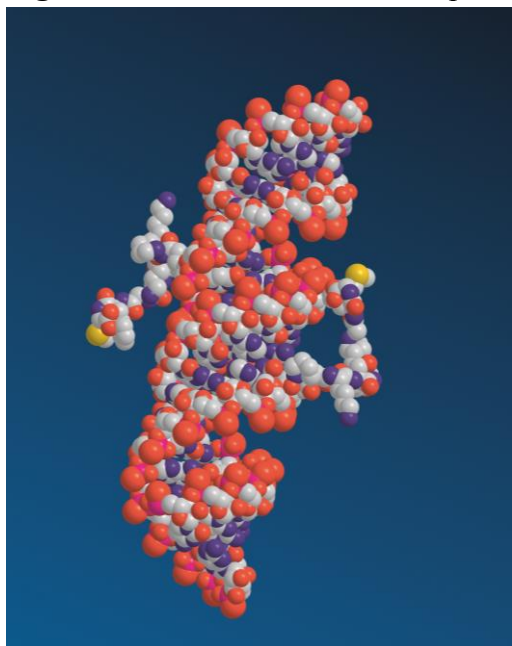


D) POC5



Assay conditions: (A–B) 90% HS in HBSS buffer; (C–D) 90% HS pre-treated with 1 mM paraoxon-ethyl, HBSS buffer.

Figure S6. Molecular model of duplex **POC2:DNA**.



White, red, pink, blue and yellow balls represent carbon, oxygen, phosphorus, nitrogen and sulphur atoms, respectively; hydrogen atoms are not shown.