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 TG**M**^{1} CTG TAT CAT	24.04	6467	6468
ON2	TGC ACT CTA **M**^{1}GT C**M**^{1}G TAT CAT	22.14	6575	6575
ON3	TGC AC**M**^{1} CTA TGT CTG TA**M**^{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 TG**M**^{2} CTG TAT CAT	22.91	7550	7551
POC2	TGC ACT CTA **M**^{2}GT C**M**^{2}G TAT CAT	21.13	8748	8741
POC3	TGC AC**M**^{2} CTA TGT CTG TA**M**^{2} CAT	21.19	8745	8741
POC4	TGC ACT CTA TG**M**^{3} CTG TAT CAT	23.54	7533	7533
POC5	TGC ACT CTA **M**^{3}GT C**M**^{3}G TAT CAT	21.25	8708	8705
POC6	TGC AC**M**^{3} CTA TGT CTG TA**M**^{3} CAT	23.24	8706	8705

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

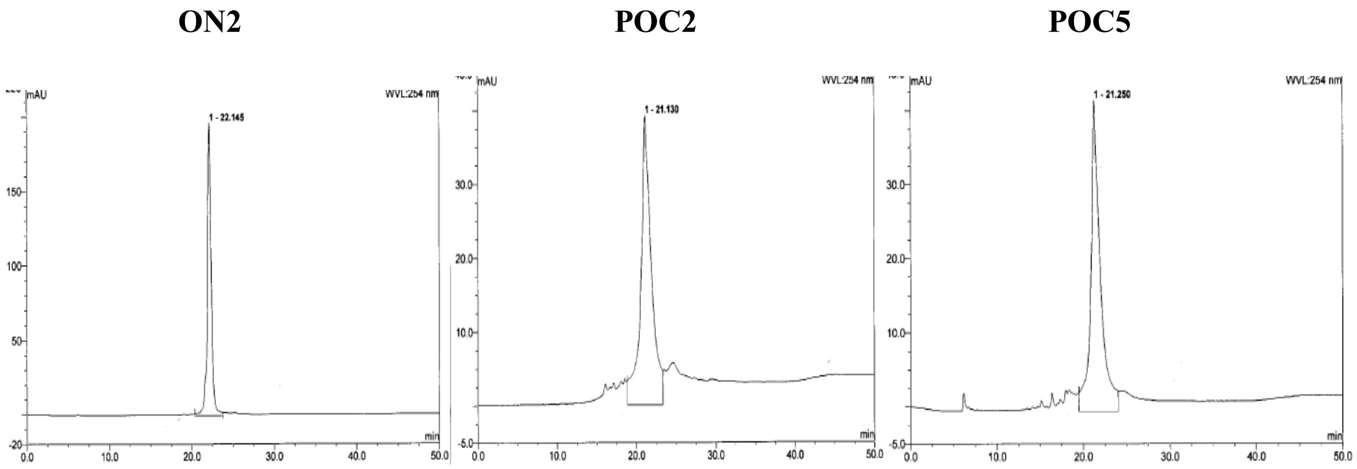

ON2 **POC2** **POC5**

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

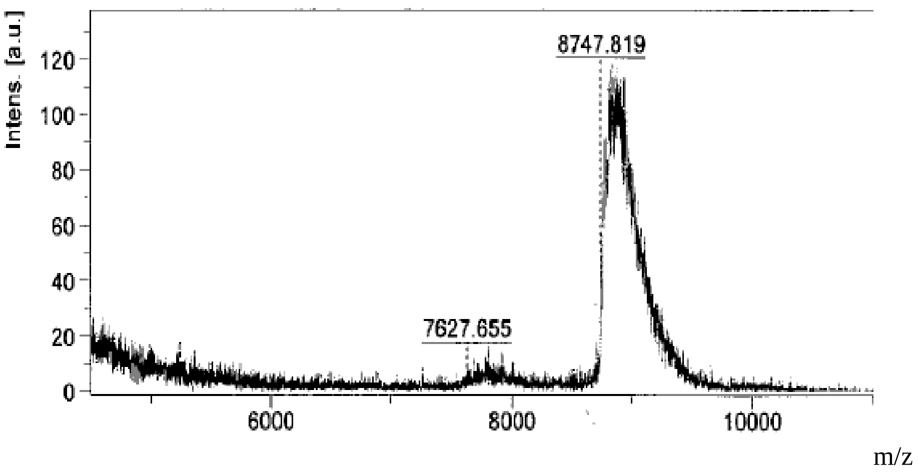
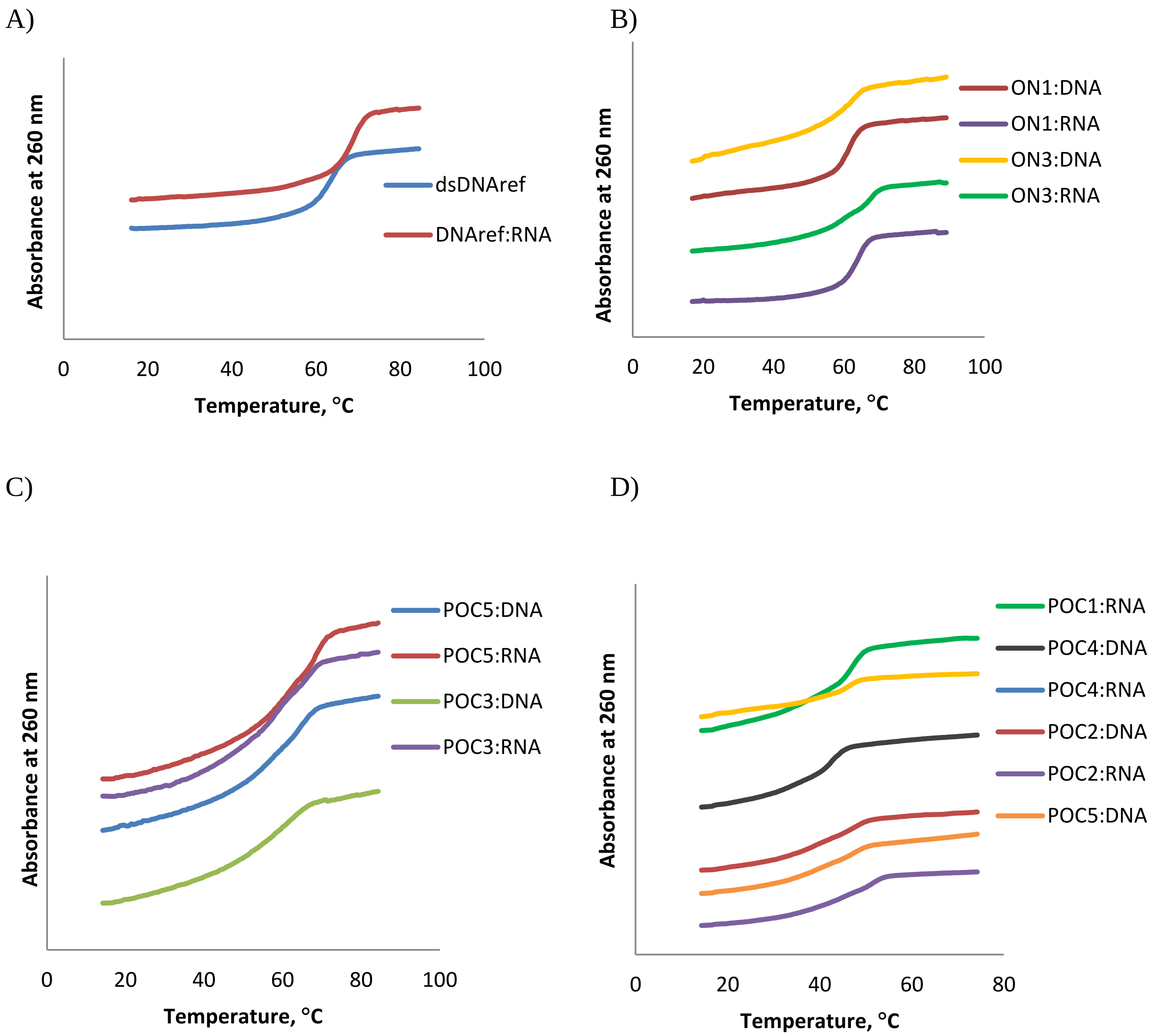


Figure S3. Representative T_m curves.



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)							
		DNA target				RNA target			
	X=	A	C	T	G	A	C	U	G
(ON1) 5´ - TGC ACT CTA TG**M**^{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 TG**M**^{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 TG**M**^{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 TG**M**^{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 TG**M**^{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 TG**M**^{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 TG**M**^{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 TG**M**^{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 TG**M**^{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]

		T_m (°C)							
ON:TARGET		DNA target				RNA target			
	X=	A	C	T	G	A	C	U	G
5´ - TGC ACT CTA **M**^{1}GT C**M**^{1}G TAT CAT 3´ - ACG TGA GAT ACA GA**X** 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 C**M**^{1}G TAT CAT 3´ - ACG TGA GAT ACA G**X**C 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 C**M**^{1}G TAT CAT 3´ - ACG TGA GAT **X**CA 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 C**M**^{1}G TAT CAT 3´ - ACG TGA GA**X** ACA GAC ATA GTA		55.5	55.0	63.5^{cc}	59.5	62.0	60.0	69.0^{cc}	65.0
5´ - TGC AC**M**^{1} CTA TGT CTG TA**M**^{1} CAT 3´ - ACG TGA GAT ACA GA ATA **X**TA		54.0	53.0	55.0	63.0^{cc}	59.0	55.0	60.0	68.0^{cc}
5´ - TGC AC**M**^{1} CTA TGT CTG TA**M**^{1} CAT 3´ - ACG TGA GAT ACA GA AT**X** GTA		63.0^{cc}	53.0	54.0	55.0	68.0^{cc}	60.0	60.0	62.0
5´ - TGC AC**M**^{1} CTA TGT CTG TA**M**^{1} CAT 3´ - ACG TGA GAT AC**X** GA ATA BTA		63.0^{cc}	52.0	53.0	55.0	68.0^{cc}	58.8	58.8	63.0
5´ - TGC AC**M**^{1} CTA TGT CTG TA**M**^{1} CAT 3´ - ACG TGA **X**AT 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.

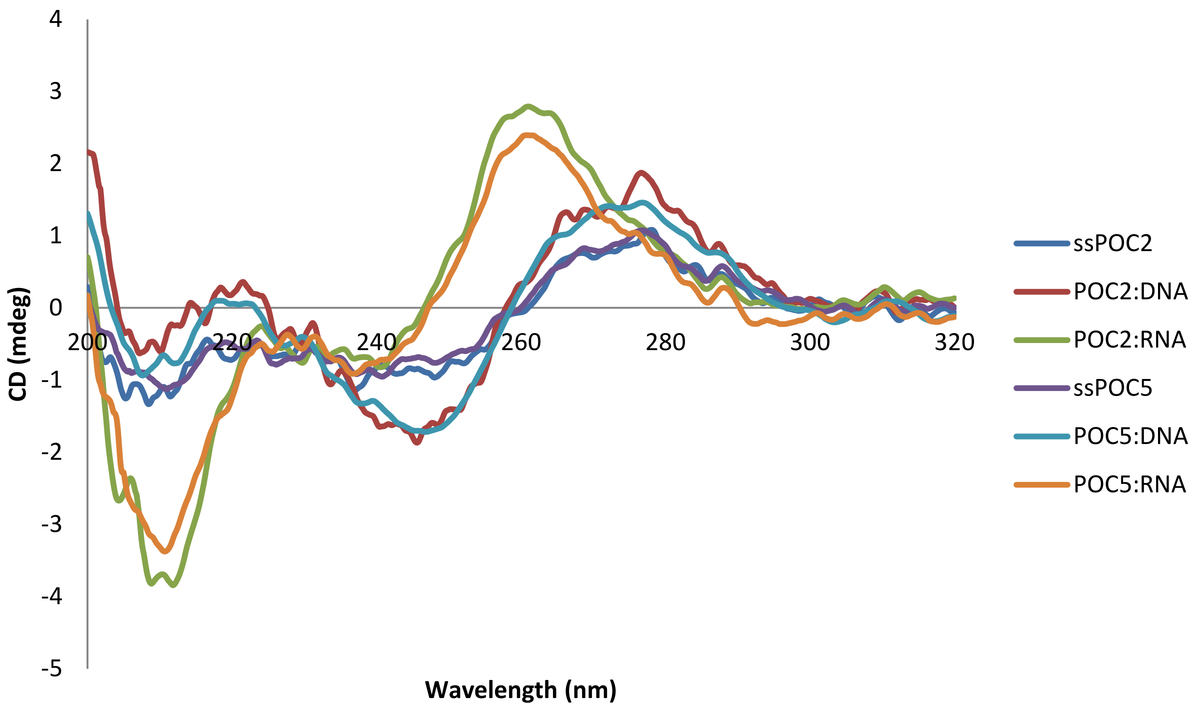
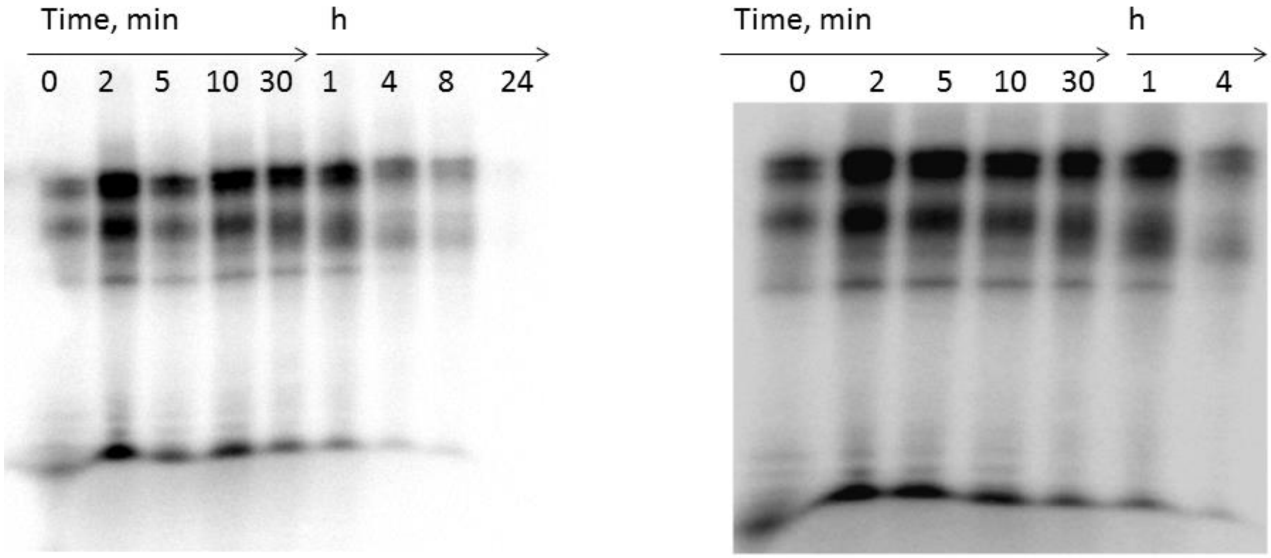
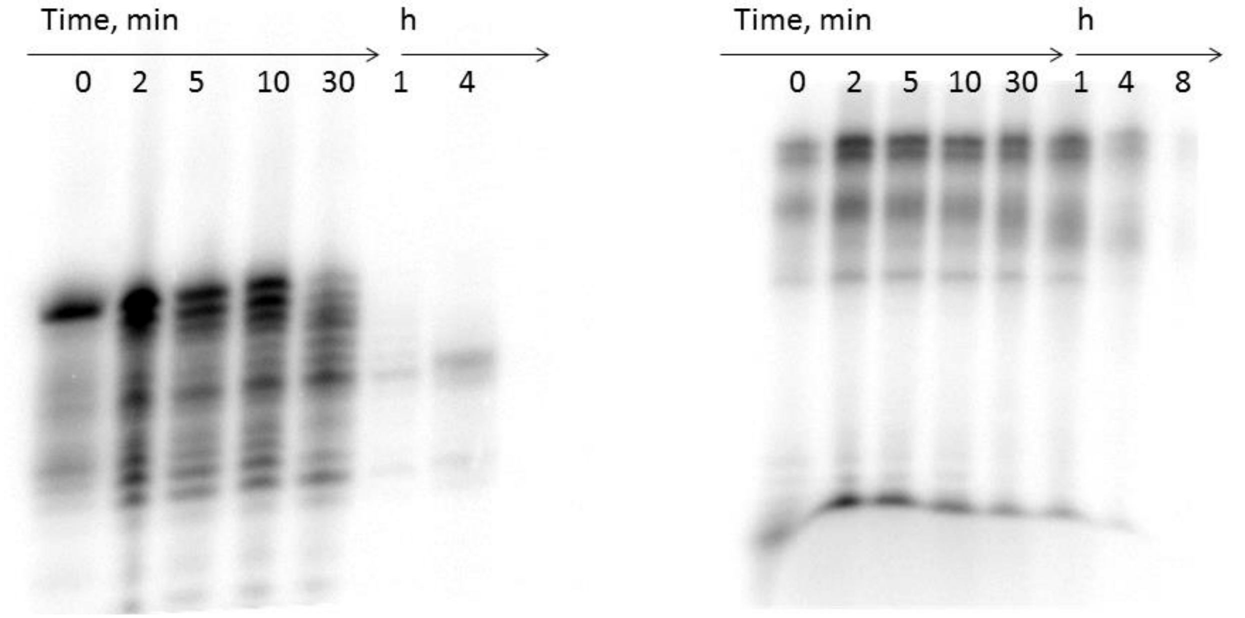


Figure S5. Gel electrophoresis of 5′-^{32}P-labeled oligonucleotides incubated with HS.


A) **POC3**

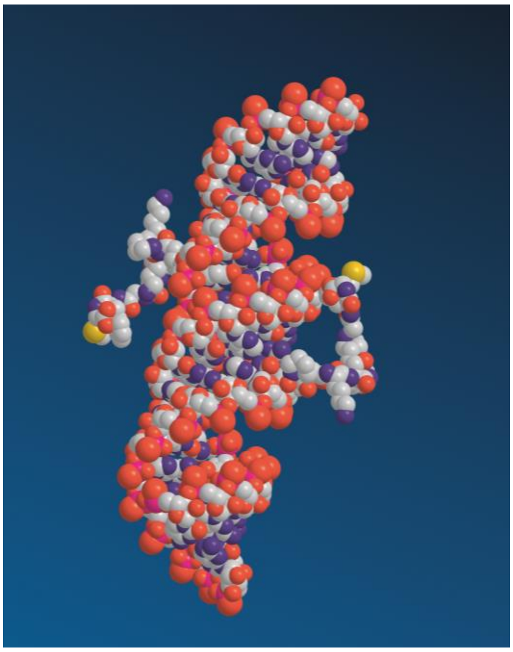
B) **POC4**


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.