Supplementary Information for

Synthetic Ligands Discovered by In Vitro Selection

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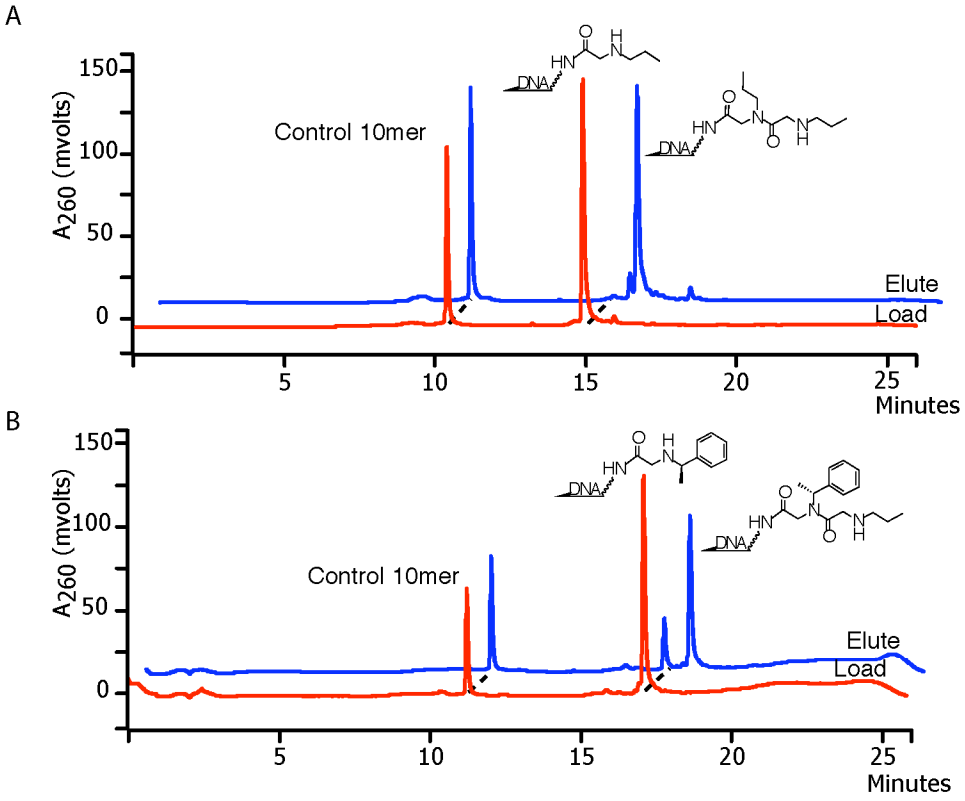
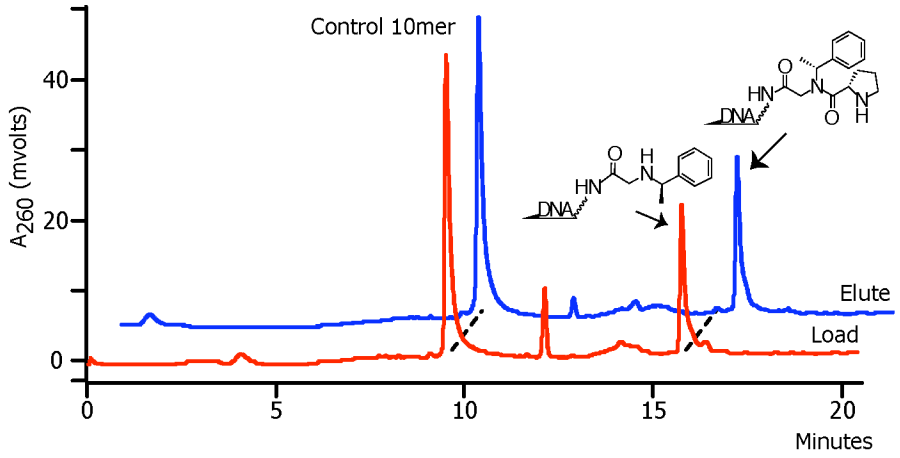
This file contains: Supplementary Figures S1 and S2 with legends
Supplementary Table 1 with legend

Supplementary Fig. 1



Supplementary Fig. 1. HPLC analysis of peptoid coupling on DNA. An unmodified 10mer and a 20mer bearing a 5' secondary amine (red trace) were loaded onto a DEAE Sepharose chemistry column, subjected to peptoid coupling (chloroacetylation and nucleophilic displacement), eluted, and analyzed by HPLC (blue trace). Shown are coupling results with **(A)** relatively unhindered (propyl) and **(B)** hindered (phenethyl) secondary amine substrates. Product masses were determined by MALDI-MS.

Supplementary Fig. 2



Supplementary Fig. 2. HPLC analysis of proline coupling on DNA. An unmodified 10mer and a 20mer bearing a hindered 5' secondary amine (red trace) were loaded onto a DEAE Sepharose chemistry column, subjected to Fmoc-proline coupling and Fmoc deprotection, eluted, and analyzed by HPLC (blue trace). Product mass was determined by MALDI-MS.

Supplementary Table 1. Coupling conditions and product verification for all monomers

Amine side chain	Letter Code	Alkylation Conc.	Alkylation Product MALDI-MS	Alkylation Product Expected	Acylation Product MALDI-MS	Acylation Product Expected	Efficiency
methylamine	B	40%	6488	6486	6556	6563	>95%
cyclopropylamine	C	2.5 M	6519	6512	6592	6589	90%
isobutylamine	D	2.5 M	6529	6528	6609	6605	95%
ethanolamine	E	1.5 M	6516	6519	6588	6596	>95%
trans-4-aminocyclohexanol	F	1.5 M	6570	6572	6656	6649	85-90%
S-(+)-1-cyclohexylethylamine	G	2.5M	6588	6582	6657	6659	75-80%
benzylamine	H	2 M	6565	6562	6643	6639	95%
S-(-)-α-methylbenzylamine	I	3.5 M	6584	6576	6653	6653	75-80%
4-(2-aminoethyl)-morpholine	J	2 M	6586	6585	N/A	N/A	N/A
ethylamine	K	35%	6500	6500	6574	6577	>95%
propylamine	L	1.5 M	6518	6514	6593	6591	>95%
isopropylamine	M	2.5 M	6516	6514	6595	6591	90-95%
3-azidopropylamine	N	40%	6554	6555	6636	6632	>95%
4-(aminomethyl)-pyridine	O	2 M	6561	6563	N/A	N/A	N/A
agmatine	P	1 M	6595	6585	6669	6662	95%
ethylenediamine	Q	1.5 M	6511	6515	N/A	N/A	N/A
1,3-diaminopropane	R	2 M	6528	6529	N/A	N/A	N/A
1,4-diaminobutane	S	2 M	6543	6543	N/A	N/A	N/A
tryptamine	T	1 M	6623	6615	6697	6692	95%
3,3'-diamino-*N*-methyl-dipropylamine	V	2 M	6603	6600	N/A	N/A	N/A
tris-(2-aminoethyl)-amine	W	2 M	6602	6601	N/A	N/A	N/A
piperazine	X	1 M	6549	6541	N/A	N/A	N/A
4-azidobutylamine	Y	40%	6573	6569	6650	6646	>95%
3-(dimethylamino)-propylamine	Z	2 M	6557	6557	N/A	N/A	N/A
β-alanine *tert*-butyl ester		2 M	6602	6600	6684	6677	90-95%
thiophene-2-methylamine		2.5 M	6576	6568	6648	6645	95%
Proline	A	MALDI-MS: 6670		Expected: 6673			
control oligo		MALDI-MS: 6420		Expected: 6415			

[a]Alkylations performed in DMSO unless noted
[b]Reaction performed in water.
[c]Reaction performed in DMSO:water (5:1)

Supplementary Table 1. An unmodified 10mer and a chloroacetylated 20mer oligonucleotide were used to assess peptoid coupling for various amine side chains. For each amine, two chemistry columns were loaded with these oligonucleotides. One column was subjected to nucleophilic displacement (alkylation). The other was subjected to alkylation followed by chloroacetylation (acylation). The eluents from both columns were analyzed by HPLC. The masses of product peaks were determined by MALDI-MS. The observed and calculated masses are shown. Amine concentrations were adjusted such that quantitative alkylation was observed for each amine. Acylation efficiencies are reported to the nearest 5%. Acylation was not assessed for side chains bearing additional free amines in the side chain. The MALDI-MS results for proline coupling to a hindered amine and for a MALDI-MS control oligonucleotide are also shown (Supplementary Fig. 2).