ChemComm

## Supporting Information for: Cell-Perm Stereochemist **Cell-Permeable GPNA Containing Appropriate Backbone** Stereochemistry and Spacing Binds Sequence-Specifically to RNA

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Figure S1. UV melting curves for PNA1-RNA and GPNA(6-8)-RNA duplexes. Thermal denaturation studies were performed on a Varian Cary 3 spectrophotometer equipped with thermoelectrically-controlled multicell holder, using 2 µM complementary strands in 100mM NaCl, 10mM sodium phosphate, and 1mM EDTA, pH 7. All samples were annealed before using for melting experiments by heating up to 90 °C and slowly cooling down to room temperature. Thermal denaturation was monitored at 260 nm at a heating rate of 1 °C/min from 20 to 90 °C. The melting transitions were determined from the first derivatives of the UV-melting curves.



**Figure S2.** CD spectra of PNA1-RNA and GPNA(6-7)-RNA duplexes. CD experiments were performed on a Jasco J-715 spectropolarimeter using the same samples used for the melting experiments. Scans were run from 320 to 200 nm taking measurements every 1 nm. All spectra represent an average of at least 15 scans and were recorded at a rate of 100 nm/min. A 1-cm pathlength cuvette was used, and the temperature was maintained at 22 °C.



**Figure S3.** UV melting curves of GPNA8-RNA and PNA1-RNA duplexes for perfectly matched and mismatched sequences. Thermal denaturation studies were performed on a Varian Cary 3 spectrophotometer equipped with thermoelectrically-controlled multicell holder, using 2  $\mu$ M complementary strands in 100 mM NaCl, 10 mM sodium phosphate, and 1 mM EDTA, pH 7. All samples were annealed before using for melting experiments by heating up to 90 °C and slowly cooling down to room temperature. Thermal denaturation was monitored at 260 nm at a heating rate of 1 °C/min from 20 to 90 °C. The melting transitions were determined from the first derivatives of the UV-melting curves.



**Figure S4.** CD melting curves for GPNA8-RNA duplexes containing perfectly matched and mismatched sequences. The CD spectra were recorded at 260 nm as a function of temperature from 20 to 90°C. CD melting experiments were performed on a Jasco J-715 spectropolarimeter using 2  $\mu$ M complementary strands in 100 mM NaCl, 10mM sodium phosphate, and 1mM EDTA, pH 7. All samples were annealed before using for melting experiments by heating up to 90 °C and slowly cooling down to room temperature. The melting transitions were determined from the first derivatives of the UV-melting curves.



**Figure S5.** UV melting curves for antiparallel and parallel GPNA8-RNA and PNA1-RNA duplexes. Thermal denaturation studies were performed on a Varian Cary 3 spectrophotometer equipped with thermoelectrically-controlled multicell holder, using 2  $\mu$ M complementary strands in 100 mM NaCl, 10 mM sodium phosphate, and 1 mM EDTA, pH 7. All samples were annealed before using for melting experiments by heating up to 90 °C and slowly cooling down to room temperature. Thermal denaturation was monitored at 260 nm at a heating rate of 1 °C/min from 20 to 90 °C. The melting transitions were determined from the first derivatives of the UV-melting curves.

	PNA1	GPNA8
	H-GCATGTTTGA- <sup>L</sup> Lys-NH <sub>2</sub>	$H-H-G^{D}CA^{D}TG^{D}TT^{D}TG^{D}A-NH_{2}$
RNA		
5'-UCAAACAUGC-3'	$T_{\rm m} = 53 ^{\circ}{\rm C}$	$T_{\rm m} = 52 \ ^{\rm o}{\rm C}$
RNA-U		
5'- UCA <u>U</u> ACAUGC-3'	$T_{\rm m} = 38 \ ^{\rm o}{\rm C}$	$T_{\rm m} = 31 \ {\rm ^oC}$
RNA-C		
5'- UCA <u>C</u> ACAUGC-3'	$T_{\rm m} = 35 \ ^{\rm o}{\rm C}$	$T_{\rm m} = 38 \ ^{\rm o}{\rm C}$
RNA-G		
5'- UCA <u>G</u> ACAUGC-3'	$T_{\rm m} = 42 \ ^{\rm o}{\rm C}$	$T_{\rm m}$ = 39 °C
RNAp		
3'- UCA <u>G</u> ACAUGC-5'	$T_{\rm m} = 37 ^{\rm o}{\rm C}$	$T_{\rm m} = 31 \ {\rm ^oC}$

**S6**. Tabulation of melting transitions between perfectly matched and mismatched antiparallel GPN8-RNA and PNA1-RNA, and perfectly matched parallel GPNA8-RNAp and PNA1-RNAp duplexes. The indicated  $T_{ms}$  were determined from the data shown in S3, S4, and S6.