Supporting Information

Structural Basis for Cyclic Py-Im Polyamide Allosteric Inhibition of Nuclear Receptor Binding

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SUPPORTING INFORMATION FIGURES:

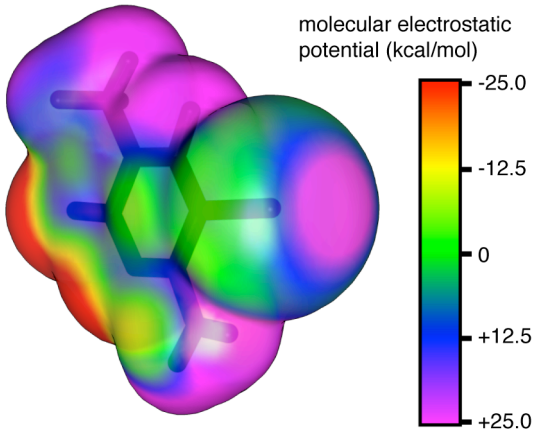

Figure S1. Molecular electrostatic potential map for 5-iodocytosine (C_I) showing the electropositive crown of the highly polarizable iodine atom involved in halogen bonding interactions. The electrostatic potential surface was generated by mapping the electrostatic potential onto the molecular electron density surface (0.002 electron/Å^3). The molecular electrostatic potential energy values range from -25 kcal/mol for values of negative potential (red) to +25 kcal/mol for values of positive potential (purple).

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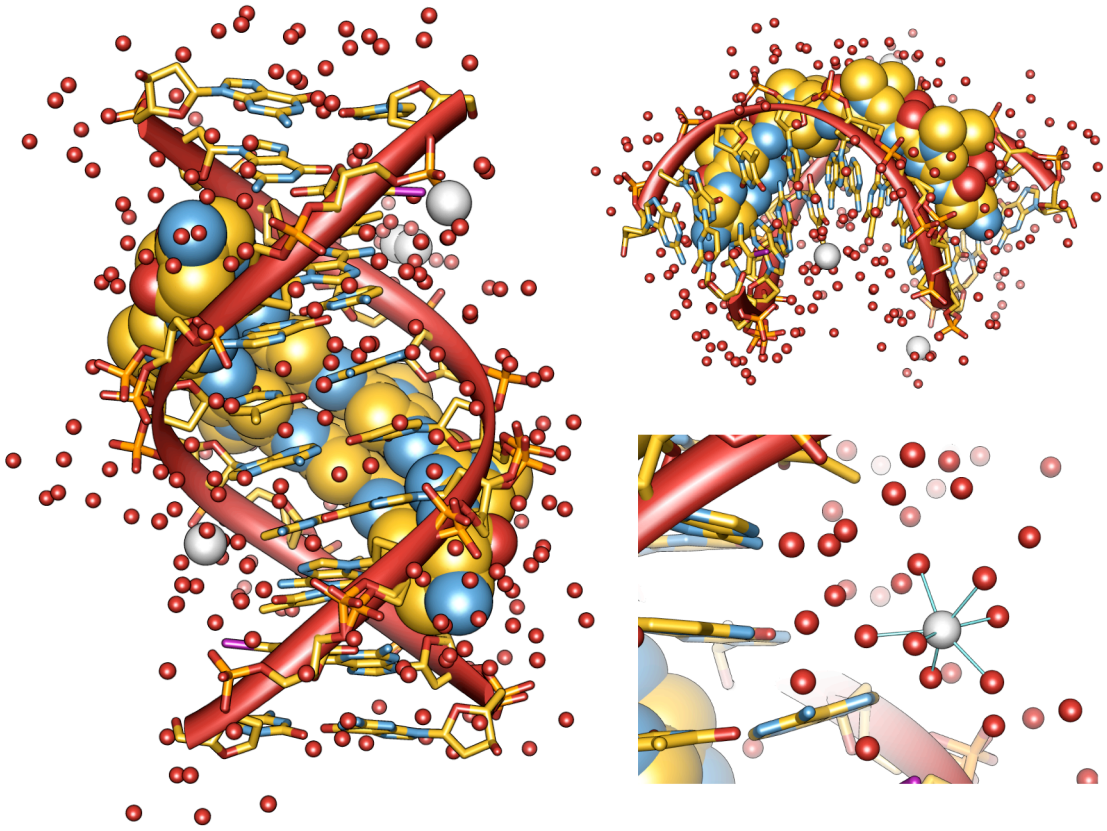

Figure S2. Hydration of the polyamide-DNA complex.

Local base-pair step parameters

Parameter*	CC/GG	CA/TG	AG/CT	GT/AC	TA/TA	AC/GT	CT/AG	TG/CA	GG/CC
Shift, Å									
DNA	-0.58	0.23	0.58	-0.73	0.00	0.73	-0.58	-0.23	0.58
PA/DNA	-0.07	0.45	-1.72	-0.74	-0.04	0.78	1.75	-0.80	0.34
Slide, Å									
DNA	0.78	2.87	0.80	0.29	-0.10	0.29	0.80	2.87	0.78
PA/DNA	-0.12	0.86	0.26	-0.15	0.90	-0.21	0.28	1.29	0.13
Rise, Å									
DNA	3.28	3.29	3.10	3.29	3.66	3.29	3.10	3.29	3.28
PA/DNA	3.28	3.16	3.39	3.20	3.28	3.24	3.33	3.06	3.19
Tilt, °									
DNA	3.32	-1.37	-3.91	2.23	0.00	-2.22	3.90	1.37	-3.33
PA/DNA	5.81	0.74	-8.44	0.18	-0.16	0.40	7.94	0.64	-5.68
Roll, °									
DNA	9.03	-7.95	9.87	-0.74	3.26	-0.74	9.89	-7.96	9.03
PA/DNA	7.70	8.79	11.19	2.85	7.23	2.47	10.59	9.57	3.58
Twist, °									
DNA	28.26	50.50	21.04	35.80	48.48	35.80	21.04	50.49	28.26
PA/DNA	33.68	30.23	35.16	32.13	35.93	32.04	35.32	29.68	32.64

*Relationship between the bases composing the base pair.
‡DNA corresponds to 0.73 Å structure of duplex DNA solved by Rees and coworkers (PDB 1D8G, 5'-CCAGTACTGG-3').

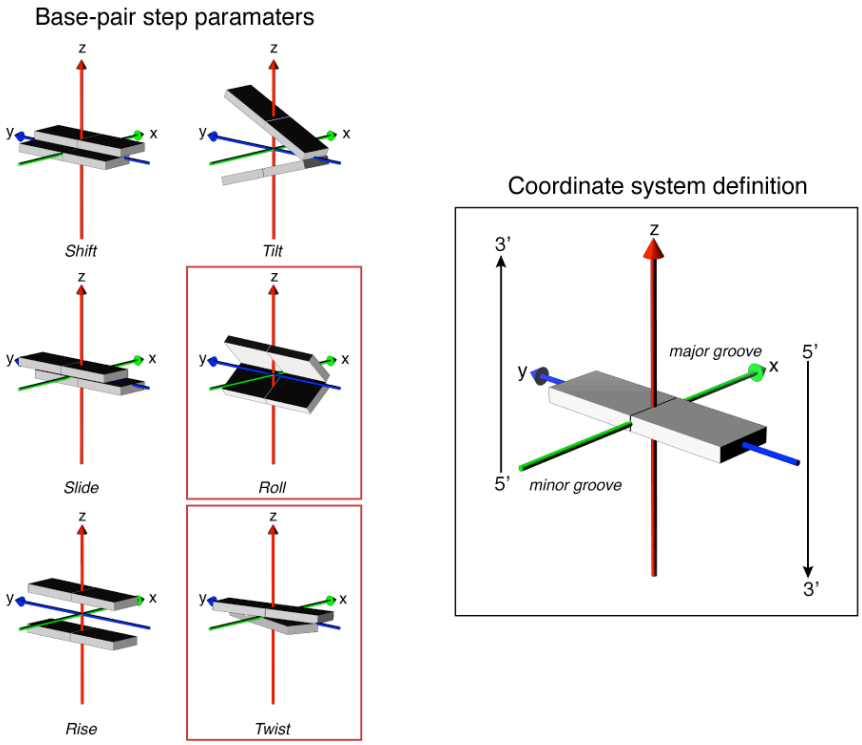

Figure S3. Local base-pair step parameters for DNA in the absence and presence of polyamide.

Local base-pair parameters and sugar pucker

Parameter*	C•G	C•G	A•T	G•C	T•A	A•T	C•G	T•A	G•C	G•C
Shear, Å										
DNA	0.15	0.32	0.02	-0.19	-0.09	0.09	0.19	-0.02	-0.32	-0.15
PA/DNA	0.15	0.19	0.13	-0.12	-0.13	0.13	0.12	-0.10	-0.16	-0.16
Stretch, Å										
DNA	-0.15	-0.16	-0.11	-0.07	-0.03	-0.03	-0.07	-0.11	-0.16	-0.15
PA/DNA	-0.14	-0.10	-0.11	-0.07	-0.10	-0.09	-0.10	-0.13	-0.04	-0.10
Stagger, Å										
DNA	0.09	0.12	0.08	0.25	0.00	0.00	0.25	0.08	0.12	0.09
PA/DNA	0.27	-0.02	-0.10	0.09	-0.02	0.04	0.09	-0.14	0.07	0.61
Buckle, °										
DNA	-6.41	-0.43	-1.63	10.75	13.15	-13.15	-10.74	1.63	0.44	6.42
PA/DNA	-10.59	-7.08	6.15	-2.23	0.37	1.17	2.39	-2.93	16.58	23.00
Propeller, °										
DNA	-15.16	-11.87	-3.23	-5.12	-10.90	-10.90	-5.15	-3.23	-11.87	-15.15
PA/DNA	-16.87	-6.31	-10.92	-4.05	-14.69	-16.26	-4.66	-7.96	-5.00	-17.05
Opening, °										
DNA	0.99	-1.15	1.35	1.26	-0.27	-0.27	1.27	1.34	-1.13	1.00
PA/DNA	0.68	1.71	3.84	-0.78	-4.87	-4.88	-1.10	3.78	0.87	-0.15
Sugar pucker										
DNA	O4'-endo C1'-exo	C2'-endo C3'-exo	C2'-endo C2'-endo	C1'-exo O4'-endo	C2'-endo C2'-endo	C2'-endo C2'-endo	O4'-endo C1'-exo	C2'-endo C2'-endo	C3'-exo C2'-endo	C1'-exo O4'-endo
PA/DNA	C3'-endo C2'-endo	C1'-exo C2'-endo	C2'-endo O4'-endo	C2'-endo C1'-exo	O4'-endo C1'-exo	C1'-exo O4'-endo	C1'-exo C2'-endo	O4'-endo C2'-endo	C2'-endo C2'-endo	C1'-exo C3'-endo

*Relationship between the bases composing the base pair.
‡DNA corresponds to 0.73 Å structure of duplex DNA solved by Rees and coworkers (PDB 1D8G, 5'-CCAGTACTGG-3').

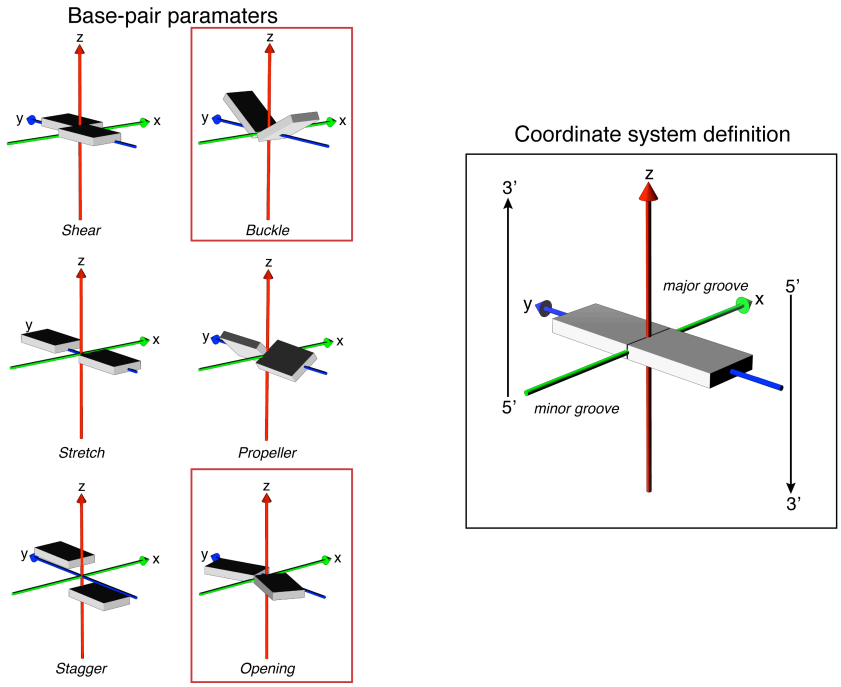

Figure S4. Local base-pair parameters and sugar pucker values for DNA in the absence and presence of polyamide.

Local base-pair helical parameters

Parameter*	CC/GG	CA/TG	AG/CT	GT/AC	TA/TA	AC/GT	CT/AG	TG/CA	GG/CC
X-displacement, Å									
DNA	-0.42	3.84	-1.31	0.57	-0.41	0.57	-1.32	3.84	-0.42
PA/DNA	-1.36	-0.07	-1.21	-0.76	0.42	-0.81	-1.07	0.59	-0.34
Y-displacement, Å									
DNA	1.83	-0.36	-2.71	1.50	0.00	-1.50	2.71	0.36	-1.84
PA/DNA	0.98	-0.68	1.45	1.36	0.05	-1.34	-1.59	1.60	-1.52
Inclination, °									
DNA	17.85	-9.25	25.08	-1.20	3.96	-1.20	25.12	-9.26	17.85
PA/DNA	12.96	16.43	17.68	5.14	11.58	4.47	16.74	18.10	6.29
Tip, °									
DNA	-6.56	1.59	9.92	-3.62	0.00	3.60	-9.90	-1.59	6.59
PA/DNA	-9.78	-1.38	13.33	-0.33	0.26	-0.73	-12.56	-1.20	9.97

*Relationship between the bases composing the base pair.
‡DNA corresponds to 0.73 Å structure of duplex DNA solved by Rees and coworkers (PDB 1D8G, 5'-CCAGTACTGG-3').

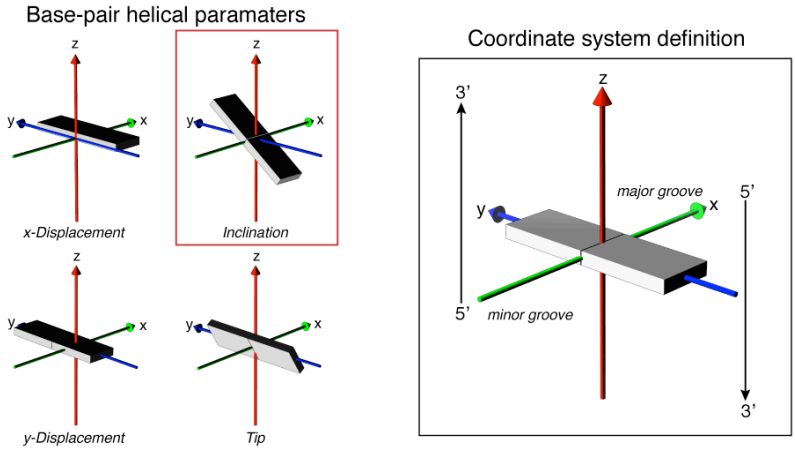

Figure S5. Local base-pair helical parameters for DNA in the absence and presence of polyamide.

Table S1. DNA sequence alignment for GR crystal structures from the literature.

DNA Sequence Alignment for GR Structures																		
Gene				FkBp	FkBp	FkBp	FkBp	FkBp	GilZ	GilZ	GilZ	Pal	Pal	Pal	Sgk	Sgk	Sgk	Cgt
PDB #	1R4R	1R4O	1GLU	3G6P	3G6T	3G6R	3G6Q_1	3G6U	3G8X	3G8U	3G97	3G9J	3G99	3G9I	3G9P	3G9O	3G9M	3FYL
0																		
1																		
2	**A**	**A**	**A**	**A**		**A**												
3	**G**	**G**	**G**	**G**	**G**	**G**	**G**	**G**	**G**	**G**	**G**	**G**	**G**	**G**	**G**	**G**	**G**	**G**
4	**A**	**A**	**A**	**A**	**A**	**A**	**A**	**A**	**A**	**A**	**A**	**A**	**A**	**A**	**A**	**A**	**A**	**A**
5	**A**	**A**	**A**	**A**	**A**	**A**	**A**	**A**	**A**	**A**	**A**	**A**	**A**	**A**	**A**	**A**	**A**	**A**
6	**C**	**C**	**C**	**C**	**C**	**C**	**C**	**C**	**C**	**C**	**C**	**C**	**C**	**C**	**C**	**C**	**C**	**C**
7	A	A	A	A	A	A	A	A	C	C	C	A	A	A	A	A	A	A
8	T	T	T	C	C	G	G	G	C	C	C	A	A	A	T	T	T	T
9	G	C	C	C	C	G	G	G	A	A	A	A	A	A	T	T	T	T
10	A	G	G	C	C	G	G	G	A	A	A	A	A	A	T	T	T	T
11	T	A	A	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T
12	G	T	T	G	G	G	G	G	G	G	G	G	G	G	G	G	G	G
13	T	G	G	T	T	T	T	T	T	T	T	T	T	T	T	T	T	T
14	T	T	T	T	T	T	T	T	T	T	T	T	T	T	C	C	C	C
15	C	T	T	C	C	C	C	C	C	C	C	C	C	C	C	C	C	C
16	T	C	C	T		T						T						
17	C	T	T															