

SUPPLEMENTARY FILES

N. Zhu, *et al.*, “X-ray crystallographic study of preferred spacing by the NF- κ B p50 homodimer on κ B DNA.”

Figure S1. Close up view of interactions between NF- κ B p50 subunit loop L1 amino acid side chains (labeled) and DNA bases from NGAL κ B DNA packed end-to-end in the p50:(NGAL)₂ complex crystal structure. A) The interface between two double-stranded 10-mer NGAL κ B DNA molecules in asymmetric unit of the p50:(NGAL)₂ complex X-ray co-crystal structure is depicted as a ribbon diagram with key amino acid side chains and DNA bases shown as sticks. One NGAL κ B DNA (colored magenta and orange, consistent with Figure 1D) is bound by the NF- κ B p50 homodimer (green). The other (two-tone grey) packs against the end of the first and contributes only a 5'-G base, which is bound by p50 loop L1 residue H64. B) A similar interaction is observed at the other end where the p50-bound NGAL κ B DNA stacks end-to-end with an unbound NGAL κ B DNA from a neighboring asymmetric unit, which contributes a 5'-G to the complex. The consequence is that one NF- κ B p50 homodimer binds to one blunt-ended 10-mer NGAL κ B DNA with 12-bp spacing.

Table S1. Results of analysis of structural changes to κ B DNA as a consequence of p50 homodimer binding. Ideal B-DNA models for each of the κ B DNA sequences employed in the X-ray crystallographic studies were generated in WinCoot [22]. Base pair geometric parameters (shear, stretch, stagger, buckle, propeller, and opening) are measured for the 17-mer IL-6 κ B DNA in its p50-bound and ideal B-DNA conformations as well as their differences (Page 1). An analysis of major and minor groove width at each base pair for p50-bound and ideal B-DNA conformations of the 17-mer IL-6 κ B DNA (Page 2). Similar analysis was performed on both p50-bound (“Central DNA”), p50-unbound (“Terminal DNA”), and Ideal B-DNA conformations of blunt-ended 10-mer NGAL κ B DNA (Pages 3 and 4) and with p50-bound and ideal B-DNA conformations of 16-mer Test κ B-like DNA (Pages 5 and 6). Analysis was performed with Web 3DNA 2.0 at <https://web.x3dna.org> [26]. Details on the definitions of each of the parameters measured are provided at the website.

Figure S2. The dimerization domains of p50 homodimer contact DNA differently as a consequence of 11- or 12-bp spacing. A) Ribbon diagram representation of the p50:IL-6 κ B DNA complex X-ray co-crystal structure. The two p50 subunits are green and the double-stranded DNA is pink and yellow (consistent with Figure 1C). A similar representation of the p50:NGAL κ B DNA complex, with p50 in blue and DNA strands as magenta and orange, is superimposed via least-squares fit of the dimerization domains. The pseudo-dyad axis of symmetry is shown as a black line. B) A close up view of the 2-fold symmetry axis as it passes through the DNA reveals that it passes between A₀:T₀ of IL-6 κ B DNA and between A₋₀T₊₀:T₀A₊₀ of NGAL κ B DNA. Therefore, despite the dimerization domains being in the same place, the DNA they contact is in a different position. C) Close up view of superimposed p50 dimerization domains from Figure 5B, with DNA ribose-phosphate backbone-contacting amino acid residues from the dimerization domains depicted as sticks. The amino acids, like the dimerization domains, overlay with one another but interact with the bound IL-6 and NGAL κ B DNA molecules via distinct modes.

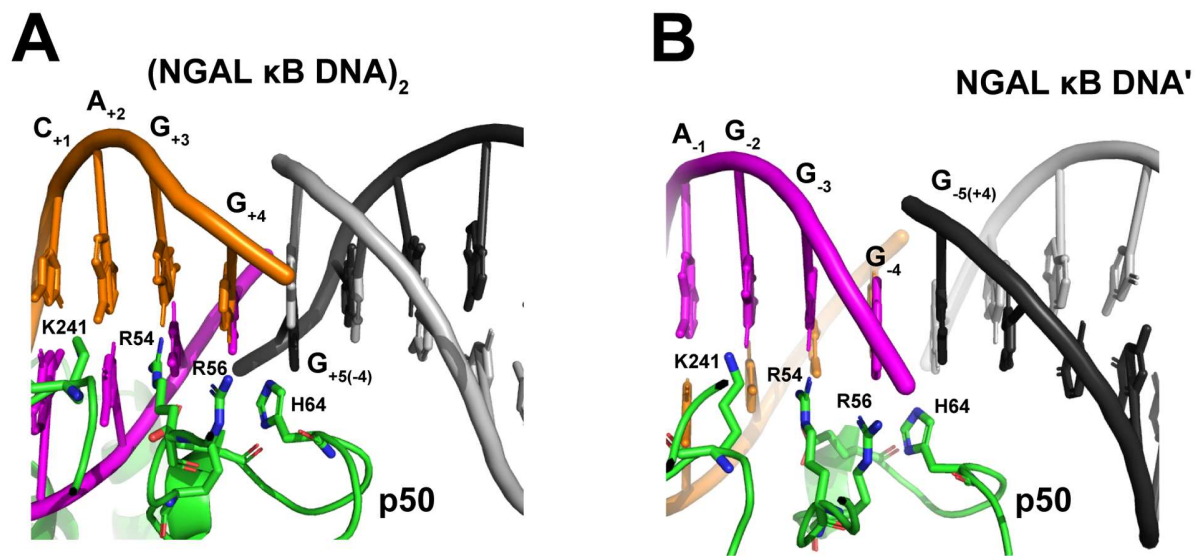


Figure S1

IL-6 κB DNA bound by p50							
Pair ID	Base Pair	Shear	Stretch	Stagger	Buckle	Propeller	Opening
1	T-A	-0.15	-0.14	-0.38	-0.56	-3.01	0.13
2	G-C	-0.24	-0.12	-0.08	-3.45	-6.42	4.02
3	T-A	-0.05	-0.11	0.13	-0.03	-6.78	1.34
4	G-C	-0.16	-0.17	0.33	0.06	-4.48	-2.22
5	G-C	-0.22	-0.18	-0.02	2.08	-1.88	0.98
6	G-C	-0.2	-0.16	0.2	5.39	-6.49	0.39
7	A-T	0.06	-0.13	0.27	4.2	-11.16	1.73
8	T-A	-0.3	-0.2	0.43	-1.49	-16.97	-0.23
9	T-A	-0.19	-0.18	0.22	-2.44	-18.53	3.29
10	T-A	-0.15	-0.15	-0.02	-3.46	-16.04	1.86
11	T-A	-0.14	-0.18	-0.29	-7.82	-11.49	3.21
12	C-G	0.21	-0.13	-0.12	-3.93	-5.34	-0.25
13	C-G	0.23	-0.19	-0.32	2.6	-1.55	2.28
14	C-G	0.2	-0.17	0.18	-1.63	-4.03	-0.38
15	A-T	0.05	-0.14	0.05	-3.84	-2.85	2.99
16	T-A	-0.07	-0.17	0.3	3.89	-1.65	2.73
17	G-C	-0.16	-0.15	-0.27	6.56	0.31	-2.47

Ideal B-DNA versus IL-6 κB DNA							
Pair ID	Base Pair	Shear	Stretch	Stagger	Buckle	Propeller	Opening
1	T-A	0.1	-0.17	0.08	-0.09	-14.46	-1.1
2	G-C	-0.3	-0.2	0.11	0.31	-14.67	0.24
3	T-A	0.1	-0.17	0.08	-0.08	-14.46	-1.09
4	G-C	-0.3	-0.2	0.11	0.31	-14.67	0.22
5	G-C	-0.3	-0.2	0.11	0.31	-14.67	0.24
6	G-C	-0.3	-0.2	0.11	0.31	-14.67	0.24
7	A-T	-0.1	-0.17	0.08	0.08	-14.46	-1.09
8	T-A	0.1	-0.17	0.08	-0.08	-14.46	-1.1
9	T-A	0.1	-0.17	0.08	-0.08	-14.46	-1.09
10	T-A	0.1	-0.17	0.08	-0.08	-14.46	-1.1
11	T-A	0.1	-0.17	0.08	-0.08	-14.46	-1.1
12	C-G	0.3	-0.2	0.11	-0.31	-14.68	0.22
13	C-G	0.3	-0.2	0.11	-0.31	-14.68	0.23
14	C-G	0.3	-0.2	0.11	-0.31	-14.69	0.23
15	A-T	-0.1	-0.17	0.08	0.09	-14.46	-1.09
16	T-A	0.1	-0.17	0.08	-0.09	-14.46	-1.09
17	G-C	-0.3	-0.2	0.11	0.32	-14.69	0.25

Difference in Base Geometries							
Pair ID	Base Pair	Shear	Stretch	Stagger	Buckle	Propeller	Opening
1	T-A	0.25	0.03	0.46	0.47	11.45	1.23
2	G-C	0.06	0.08	0.19	3.76	8.25	3.78
3	T-A	0.15	0.06	0.05	0.05	7.68	2.43
4	G-C	0.14	0.03	0.22	0.25	10.19	2.44
5	G-C	0.08	0.02	0.13	1.77	12.79	0.74
6	G-C	0.1	0.04	0.09	5.08	8.18	0.15
7	A-T	0.16	0.04	0.19	4.12	3.3	2.82
8	T-A	0.4	0.03	0.35	1.41	2.51	0.87
9	T-A	0.29	0.01	0.14	2.36	4.07	4.38
10	T-A	0.25	0.02	0.1	3.38	1.58	2.96
11	T-A	0.24	0.01	0.37	7.74	2.97	4.31
12	C-G	0.09	0.07	0.23	3.62	9.34	0.47
13	C-G	0.07	0.01	0.43	2.91	13.13	2.05
14	C-G	0.1	0.03	0.07	1.32	10.66	0.61
15	A-T	0.15	0.03	0.03	3.93	11.61	4.08
16	T-A	0.17	0	0.22	3.98	12.81	3.82
17	G-C	0.14	0.05	0.38	6.24	15	2.72

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IL-6 κB DNA bound by p50					
Pair ID	Base Pair	Minor Groove		Major Groove	
		P-P	Refined	P-P	Refined
1	TG/CA	---	---	---	---
2	GT/AC	---	---	---	---
3	TG/CA	13.7	---	18.3	---
4	GG/CC	12.7	12.7	20.7	20.7
5	GG/CC	11.8	11.8	22.3	22.2
6	GA/TC	10.6	10.6	20.8	20.7
7	AT/AT	9.5	9.5	18.3	18
8	TT/AA	9.9	9.8	16.6	16.2
9	TT/AA	9.9	9.9	16.8	16.4
10	TT/AA	9.8	9.7	18.1	18
11	TC/GA	11	11	21.1	21
12	CC/GG	11.9	11.9	22.4	22.2
13	CC/GG	12.5	12.4	21.4	21.3
14	CA/TG	14.1	---	18.4	---
15	AT/AT	---	---	---	---
16	TG/CA	---	---	---	---

Ideal B-DNA versus IL-6 κB DNA					
Pair ID	Base Pair	Minor Groove		Major Groove	
		P-P	Refined	P-P	Refined
1	TG/CA	---	---	---	---
2	GT/AC	---	---	---	---
3	TG/CA	11.7	---	17.2	---
4	GG/CC	11.7	11.7	17.2	17.2
5	GG/CC	11.7	11.7	17.2	17.2
6	GA/TC	11.7	11.7	17.2	17.2
7	AT/AT	11.7	11.7	17.2	17.2
8	TT/AA	11.7	11.7	17.2	17.2
9	TT/AA	11.7	11.7	17.2	17.2
10	TT/AA	11.7	11.7	17.2	17.2
11	TC/GA	11.7	11.7	17.2	17.2
12	CC/GG	11.7	11.7	17.2	17.2
13	CC/GG	11.7	11.7	17.2	17.2
14	CA/TG	11.7	---	17.2	---
15	AT/AT	---	---	---	---
16	TG/CA	---	---	---	---

Differences in Minor and Major Grooves					
Pair ID	Base Pair	Minor Groove		Major Groove	
		P-P	Refined	P-P	Refined
1	TG/CA	---	---	---	---
2	GT/AC	---	---	---	---
3	TG/CA	2	---	1.1	---
4	GG/CC	1	1	3.5	3.5
5	GG/CC	0.1	0.1	5.1	5
6	GA/TC	1.1	1.1	3.6	3.5
7	AT/AT	2.2	2.2	1.1	0.8
8	TT/AA	1.8	1.9	0.6	1
9	TT/AA	1.8	1.8	0.4	0.8
10	TT/AA	1.9	2	0.9	0.8
11	TC/GA	0.7	0.7	3.9	3.8
12	CC/GG	0.2	0.2	5.2	5
13	CC/GG	0.8	0.7	4.2	4.1
14	CA/TG	2.4	---	1.2	---
15	AT/AT	---	---	---	---
16	TG/CA	---	---	---	---

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Ideal B-DNA versus NGAL κB-DNA							
Pair ID	Base Pair	Shear	Stretch	Stagger	Buckle	Propeller	Opening
1	G-C	-0.3	-0.2	0.11	0.33	-14.67	0.23
2	G-C	-0.3	-0.2	0.11	0.33	-14.67	0.22
3	G-C	-0.3	-0.2	0.11	0.33	-14.67	0.23
4	A-T	-0.1	-0.17	0.08	0.08	-14.47	-1.11
5	A-T	-0.1	-0.17	0.08	0.08	-14.47	-1.11
6	T-A	0.1	-0.17	0.08	-0.11	-14.48	-1.1
7	G-C	-0.3	-0.2	0.11	0.33	-14.67	0.23
8	T-A	0.1	-0.17	0.08	-0.11	-14.48	-1.1
9	C-G	0.3	-0.2	0.11	-0.33	-14.67	0.23
10	C-G	0.3	-0.2	0.11	-0.33	-14.67	0.23

NGAL κB DNA bound by p53							
Pair ID	Base Pair	Shear	Stretch	Stagger	Buckle	Propeller	Opening
Central DNA							
1	G-C	-0.2	-0.14	0.16	2.27	-2.07	0.05
2	G-C	-0.2	-0.2	0.43	3.63	-5.91	-1.57
3	G-C	-0.17	-0.17	0.19	2.64	-8.48	0.65
4	A-T	0.09	-0.2	0.17	4.34	-7.17	-1.47
5	A-T	0.13	-0.17	0.29	1.04	-16.02	-1.52
6	T-A	-0.22	-0.18	0.41	-6.15	-17.05	-4.01
7	G-C	-0.12	-0.13	0.21	-8.09	-3.79	0.05
8	T-A	-0.23	-0.14	0.08	-5.07	-5.19	0.09
9	C-G	0.17	-0.19	0.11	-1.82	-6.53	-0.21
10	C-G	0.2	-0.19	-0.08	-0.22	-4.19	1.6
Terminal DNA							
1	G-C	-0.19	-0.14	0.13	0.75	-2.31	-0.83
2	G-C	-0.21	-0.15	0.21	-0.67	-2.45	-1.3
3	G-C	-0.2	-0.13	0.32	5.31	-1.81	-0.03
4	A-T	0.14	-0.17	0.25	3.47	-6.19	-0.24
5	A-T	0.1	-0.17	0.01	-1.68	-8.94	4.93
6	T-A	-0.14	-0.05	-0.04	-3.09	-7.06	-6.24
7	G-C	-0.2	-0.16	-0.18	-2.28	-0.25	0.36
8	T-A	-0.06	-0.18	0.1	-2.45	-2.53	1.4
9	C-G	0.16	-0.18	-0.17	3	2.41	-0.62
10	C-G	0.23	-0.13	-0.04	-0.12	0.92	1.88

Difference in Base Geometries							
Pair ID	Base Pair	Shear	Stretch	Stagger	Buckle	Propeller	Opening
Central DNA							
1	G-C	0.1	0.06	0.05	1.94	12.6	0.18
2	G-C	0.1	0	0.32	3.3	8.76	1.79
3	G-C	0.13	0.03	0.08	2.31	6.19	0.42
4	A-T	0.19	0.03	0.09	4.26	7.3	0.36
5	A-T	0.23	0	0.21	0.96	1.55	0.41
6	T-A	0.32	0.01	0.33	6.04	2.57	2.91
7	G-C	0.18	0.07	0.1	8.42	10.88	0.18
8	T-A	0.33	0.03	0	4.96	9.29	1.19
9	C-G	0.13	0.01	0	1.49	8.14	0.44
10	C-G	0.1	0.01	0.19	0.11	10.48	1.37
Terminal DNA							
1	G-C	0.11	0.06	0.02	0.42	12.36	1.06
2	G-C	0.09	0.05	0.1	1	12.22	1.52
3	G-C	0.1	0.07	0.21	4.98	12.86	0.26
4	A-T	0.24	0	0.17	3.39	8.28	0.87
5	A-T	0.2	0	0.07	1.76	5.53	6.04
6	T-A	0.24	0.12	0.12	2.98	7.42	5.14
7	G-C	0.1	0.04	0.29	2.61	14.42	0.13
8	T-A	0.16	0.01	0.02	2.34	11.95	2.5
9	C-G	0.14	0.02	0.28	3.33	17.08	0.85
10	C-G	0.07	0.07	0.15	0.21	15.59	1.65

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NGAL κB DNA bound by p50					
		Minor Groove		Major Groove	
Central DNA					
Pair ID	Base Pair	P-P	Refined	P-P	Refined
1	GG/CC	---	---	---	---
2	GG/CC	---	---	---	---
3	GA/TC	10.8	---	19.3	---
4	AA/TT	9.7	9.7	17.9	17.9
5	AT/AT	9.5	9.5	16.1	16
6	TG/CA	9.3	9.3	18.3	18.3
7	GT/AC	10.4	---	20.1	---
8	TC/GA	---	---	---	---
9	CC/GG	---	---	---	---
Terminal DNA					
1	GG/CC	---	---	---	---
2	GG/CC	---	---	---	---
3	GA/TC	12.9	---	19.4	---
4	AA/TT	12.7	12.6	19.9	19.3
5	AT/AT	12.7	12.5	20.2	19.5
6	TG/CA	12.4	12	19.6	18.2
7	GT/AC	12.9	---	17.9	---
8	TC/GA	---	---	---	---
9	CC/GG	---	---	---	---

Ideal B-DNA versus NGAL κB-DNA					
		Minor Groove		Major Groove	
Pair ID	Base Pair	P-P	Refined	P-P	Refined
1	GG/CC	---	---	---	---
2	GG/CC	---	---	---	---
3	GA/TC	11.7	---	17.2	---
4	AA/TT	11.7	11.7	17.2	17.2
5	AT/AT	11.7	11.7	17.2	17.2
6	TG/CA	11.7	11.7	17.2	17.2
7	GT/AC	11.7	---	17.2	---
8	TC/GA	---	---	---	---
9	CC/GG	---	---	---	---

Differences in Minor and Major Grooves					
		Minor Groove		Major Groove	
Central DNA					
Pair ID	Base Pair	P-P	Refined	P-P	Refined
1	GG/CC				
2	GG/CC				
3	GA/TC	0.9		2.1	
4	AA/TT	2	2	0.7	0.7
5	AT/AT	2.2	2.2	1.1	1.2
6	TG/CA	2.4	2.4	1.1	1.1
7	GT/AC	1.3		2.9	
8	TC/GA				
9	CC/GG				
Terminal DNA					
1	GG/CC				
2	GG/CC				
3	GA/TC	1.2		2.2	
4	AA/TT	1	0.9	2.7	2.1
5	AT/AT	1	0.8	3	2.3
6	TG/CA	0.7	0.3	2.4	1
7	GT/AC	1.2		0.7	
8	TC/GA				
9	CC/GG				

Table S1-page 4

Test κB DNA bound by p50							
Pair ID	Base Pair	Shear	Stretch	Stagger	Buckle	Propeller	Opening
1	C-G	0.22	-0.14	0.11	-2.35	-5.33	2.64
2	A-T	0.09	-0.15	-0.03	-2.08	-3.21	1.88
3	G-C	-0.16	-0.14	0.18	3.97	-8.16	-1.74
4	G-C	-0.23	-0.25	-0.96	-5.99	-2.11	1.69
5	G-C	-0.21	-0.19	-0.54	0.12	-0.43	0.59
6	G-C	-0.2	-0.14	-0.19	4.85	-5.35	2.83
7	A-T	0.08	-0.14	-0.31	-2.42	-7.38	3.87
8	A-T	0.07	-0.15	-0.45	-4.34	-11.89	4
9	T-A	-0.05	-0.17	-0.52	-2.71	-10.95	6.57
10	T-A	-0.18	-0.22	-0.67	-4.08	-9.72	1.17
11	C-G	0.22	-0.2	-0.61	-3.84	-6.09	1.8
12	C-G	0.22	-0.17	-0.36	-2.54	-6.06	1.8
13	C-G	0.2	-0.13	-0.33	-4.04	-5.42	0.58
14	C-G	0.21	-0.18	-0.63	2.85	-7.18	3.15
15	T-A	-0.08	-0.1	-0.46	6.45	-13.28	1.09
16	C-G	-1.63	0.2	0.55	1.31	-23.59	9.86

Ideal B-DNA versus Test κB DNA							
Pair ID	Base Pair	Shear	Stretch	Stagger	Buckle	Propeller	Opening
1	T-A	0.1	-0.17	0.08	-0.08	-14.47	-1.1
2	C-G	0.3	-0.2	0.11	-0.33	-14.67	0.23
3	A-T	-0.1	-0.17	0.08	0.11	-14.47	-1.11
4	G-C	-0.3	-0.2	0.11	0.33	-14.67	0.22
5	G-C	-0.3	-0.2	0.11	0.33	-14.67	0.24
6	G-C	-0.3	-0.2	0.11	0.33	-14.67	0.22
7	G-C	-0.3	-0.2	0.11	0.33	-14.67	0.23
8	A-T	-0.1	-0.17	0.08	0.11	-14.47	-1.11
9	A-T	-0.1	-0.17	0.08	0.11	-14.47	-1.1
10	T-A	0.1	-0.17	0.08	-0.08	-14.47	-1.1
11	T-A	0.1	-0.17	0.08	-0.08	-14.47	-1.1
12	C-G	0.3	-0.2	0.11	-0.33	-14.67	0.23
13	C-G	0.3	-0.2	0.11	-0.33	-14.67	0.24
14	C-G	0.3	-0.2	0.11	-0.33	-14.67	0.23
15	C-G	0.3	-0.2	0.11	-0.33	-14.67	0.24
16	T-A	0.1	-0.17	0.08	-0.08	-14.47	-1.09
17	C-G	0.3	-0.2	0.11	-0.33	-14.67	0.23

Difference in Base Geometries							
Pair ID	Base Pair	Shear	Stretch	Stagger	Buckle	Propeller	Opening
1	T-A	0.12	0.03	0.03	2.27	9.14	3.74
2	C-G	0.21	0.05	0.14	1.75	11.46	1.65
3	A-T	0.06	0.03	0.1	3.86	6.31	0.63
4	G-C	0.07	0.05	1.07	6.32	12.56	1.47
5	G-C	0.09	0.01	0.65	0.21	14.24	0.35
6	G-C	0.1	0.06	0.3	4.52	9.32	2.61
7	G-C	0.38	0.06	0.42	2.75	7.29	3.64
8	A-T	0.17	0.02	0.53	4.45	2.58	5.11
9	A-T	0.05	0	0.6	2.82	3.52	7.67
10	T-A	0.28	0.05	0.75	4	4.75	2.27
11	T-A	0.12	0.03	0.69	3.76	8.38	2.9
12	C-G	0.08	0.03	0.47	2.21	8.61	1.57
13	C-G	0.1	0.07	0.44	3.71	9.25	0.34
14	C-G	0.09	0.02	0.74	3.18	7.49	2.92
15	C-G	0.38	0.1	0.57	6.78	1.39	0.85
16	T-A	1.73	0.37	0.47	1.39	9.12	10.95
17	C-G	0.3	0.2	0.11	0.33	14.67	0.23

Table S1-page 5

Test κB DNA bound by p50					
Pair ID	Base Pair	Minor Groove		Major Groove	
		P-P	Refined	P-P	Refined
1	CA/TG	---	---	---	---
2	AG/CT	---	---	---	---
3	GG/CC	12.5	---	21.5	---
4	GG/CC	12.4	12.4	22.2	22.1
5	GG/CC	11.8	11.8	20.3	20.3
6	GA/TC	10.1	10	18.3	18
7	AA/TT	10	9.9	16.7	16.3
8	AT/AT	10.2	10.1	16.1	15.7
9	TT/AA	10	10	17.5	17.1
10	TC/GA	10.8	10.8	20	20
11	CC/GG	11.1	11.1	21.4	21.4
12	CC/GG	11.6	11.6	20.3	20.1
13	CC/GG	12.4	---	17.1	---
14	CT/AG	---	---	---	---
15	TC/GA	---	---	---	---

Ideal B-DNA versus Test κB DNA					
Pair ID	Base Pair	Minor Groove		Major Groove	
		P-P	Refined	P-P	Refined
1	TC/GA	---	---	---	---
2	CA/TG	---	---	---	---
3	AG/CT	11.7	---	17.2	---
4	GG/CC	11.7	11.7	17.2	17.2
5	GG/CC	11.7	11.7	17.2	17.2
6	GG/CC	11.7	11.7	17.2	17.2
7	GA/TC	11.7	11.7	17.2	17.2
8	AA/TT	11.7	11.7	17.2	17.2
9	AT/AT	11.7	11.7	17.2	17.2
10	TT/AA	11.7	11.7	17.2	17.2
11	TC/GA	11.7	11.7	17.2	17.2
12	CC/GG	11.7	11.7	17.2	17.2
13	CC/GG	11.7	11.7	17.2	17.2
14	CC/GG	11.7	---	17.2	---
15	CT/AG	---	---	---	---
16	TC/GA	---	---	---	---

Differences in Minor and Major Grooves					
Pair ID	Base Pair	Minor Groove		Major Groove	
		P-P	Refined	P-P	Refined
1	CA/TG	---	---	---	---
2	AG/CT	---	---	---	---
3	GG/CC	0.8	---	4.3	---
4	GG/CC	0.7	0.7	5	4.9
5	GG/CC	0.1	0.1	3.1	3.1
6	GA/TC	1.6	1.7	1.1	0.8
7	AA/TT	1.7	1.8	0.5	0.9
8	AT/AT	1.5	1.6	1.1	1.5
9	TT/AA	1.7	1.7	0.3	0.1
10	TC/GA	0.9	0.9	2.8	2.8
11	CC/GG	0.6	0.6	4.2	4.2
12	CC/GG	0.1	0.1	3.1	2.9
13	CC/GG	0.7	---	0.1	---
14	CT/AG	---	---	---	---
15	TC/GA	---	---	---	---
16	TC/GA	---	---	---	---

Table S1–page 6

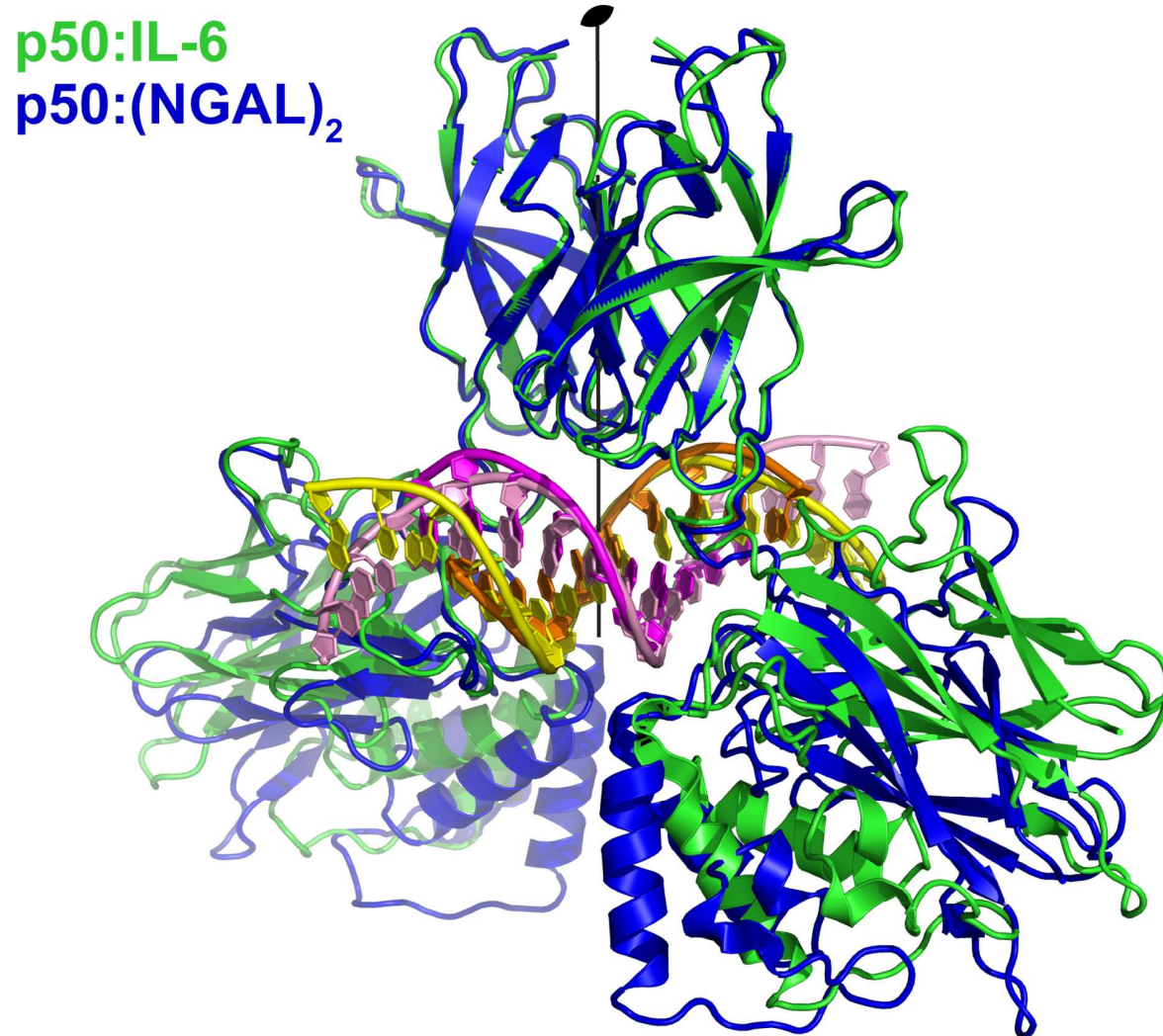


Figure S2A

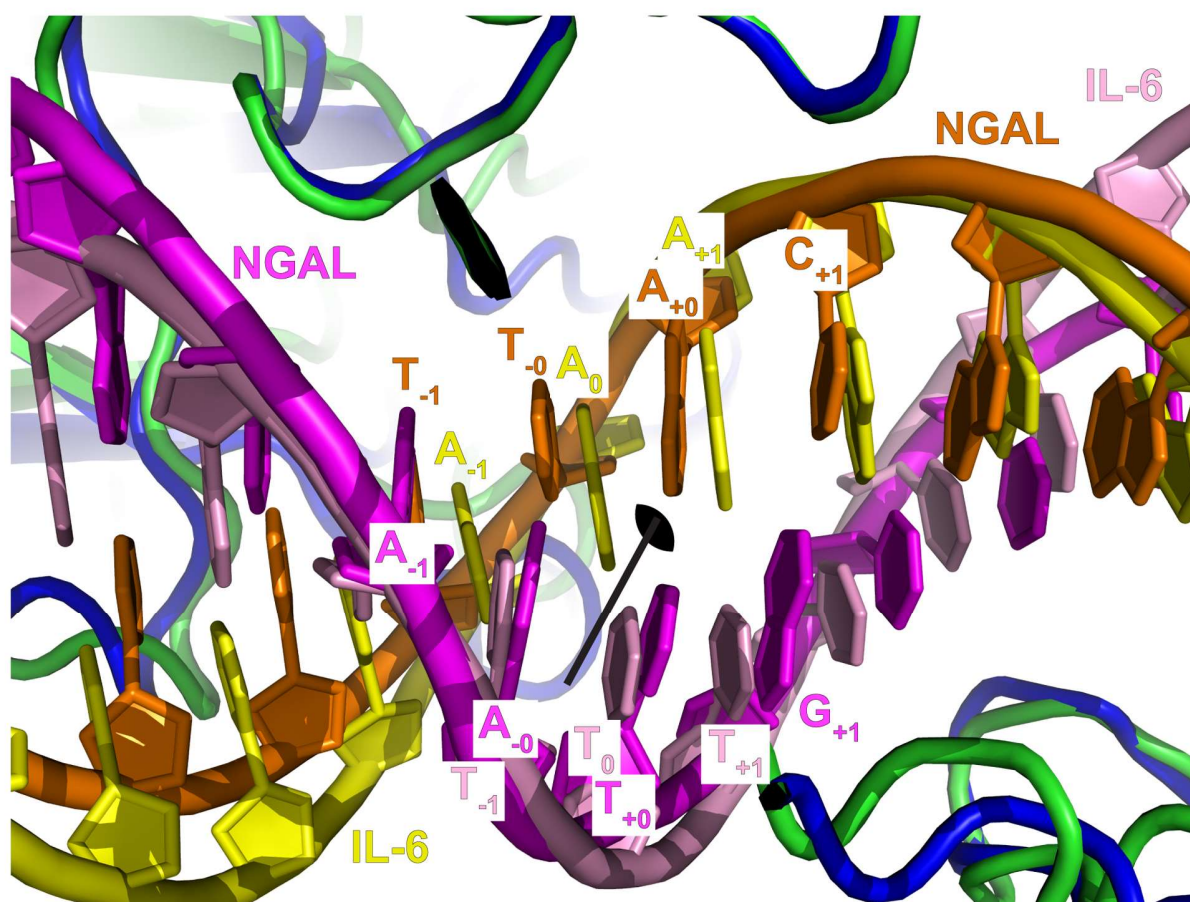


Figure S2B

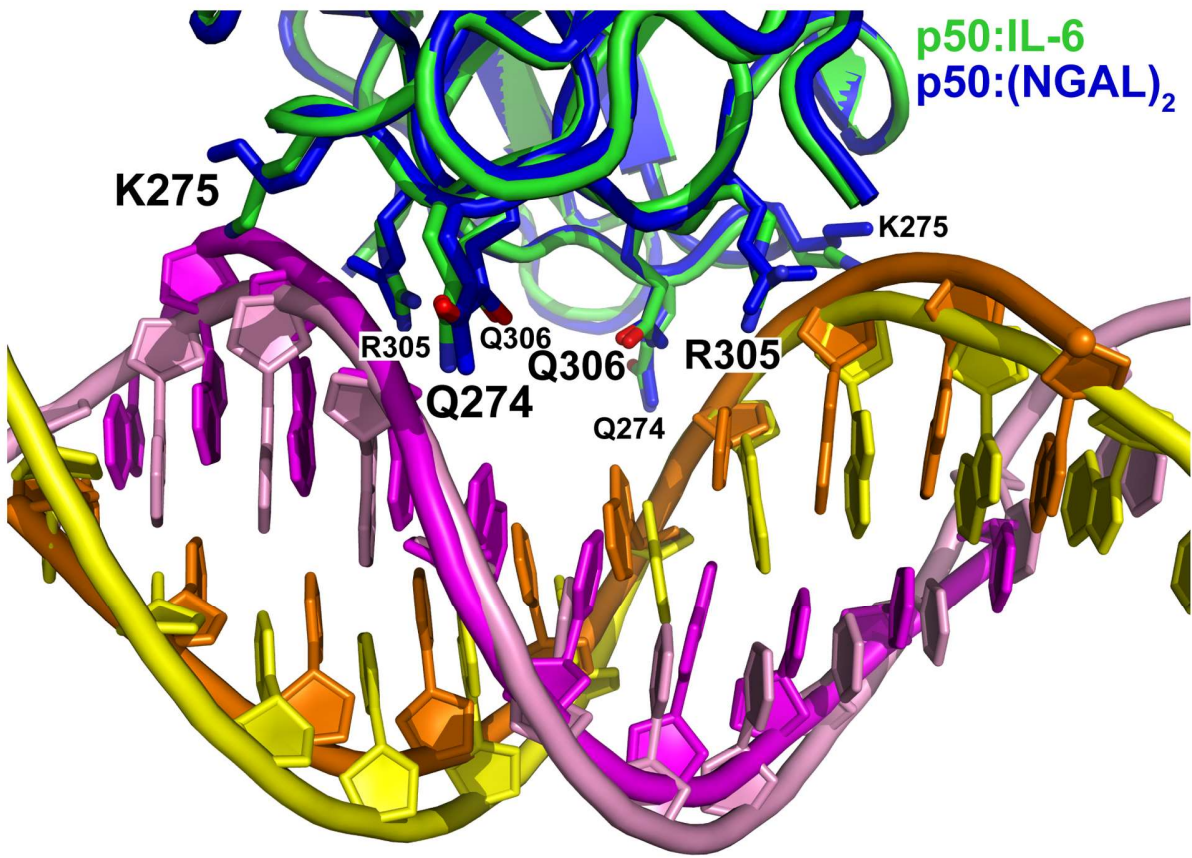


Figure S2C