Table 1S. Energy of $UvrA_2$ dimer and its complexes with DNA(1) before and after SA. The docking default structure, Holo-0 is the initial dimer (Methods); C01, C02 and C03 are the complexes before SA; Holo-1, C1, C2 and C3 are the same molecules after one step SA, where DNA(1) was kept as aggregate. E(Interact) = E(Tot) - [E(DNA) + E(Prot)]; E(Prot) = E(Protein-SA) - E(Protein-0), *i.e.* the protein energy change after SA. Averaged data ± stdev from three independent SA runs for C1, C2 and C3 DNA-protein complexes.

Molecule	Energy (kcal/mol)				
	E (Tot)	E (DNA)	E (Prot)	E (Interact)	ΔE (Prot)
Holo-0	-23369.8	-	-23369.8	-	-
Holo-1	-27025.9 3	-	-27025.9	-	-3656.1
C01	-25618.8	-857.0	-23740.6	-1021.2	-
C02	-24897.2	-924.4	-23741.2	-231.6	-
C03	-24784.6	-924.4	-23783.6	-76.6	-
C1	-28525.9 ± 61.3	-856.3 ± 8.2	-26209.2 ± 58.6	-1460.4 ± 16.7	-2468.6 ±43.4
C2	-28313.0 ± 87.3	-909.0 ± 11.1	-26441.1 ± 69.4	-962.9 ± 27.5	-2699.9 ± 76.8
C3	-26326.2 ± 76.8	-379.6 ± 16.3	-25527.9 ± 64.6	-418.7 ± 29.4	-1744.3 ± 61.1

Table 2S - A,B,C. List of Complex - 1, 2 and 3 residues in vdW contacts (< 3.5 Å) with DNA(1), per chain, domain, mutated ones (in bold) and total number. These residues might be primary candidates for structure-based mutation studies. C-01,02,03 are the original complexes; C-1,2,3 are the complexes submitted to SA with DNA(1) as Aggregate. C1T (also denoted also, C1/DNA(1)-ARlx) is the C1 complex submitted to a subsequent SA run with unrestrained (relaxed) DNA.

(A) Complexes C01 (C/DNA(1)-0), C1 (C/DNA(1)-A) and C1T (C/DNA(1)-ARlx) after second SA run with unrestrained DNA(1), see also Table 3.

Complex						Domain
C01 or C/DNA(1)-0		C1 or C/DNA(1)-A		C1T or C/DNA(1)-ARlx		
ChainA	ChainB	ChainA	ChainB	ChainA	ChainB	
				ALA59		ATP-BD1
TYR60	TYR60	TYR60	TYR60	TYR60	TYR60	ATP-BD1
				GLN63		ATP-BD1
				PHE64	PHE64	ATP-BD1
				GLN67	GLN67	ATP-BD1
					MET68	ATP-BD1
		ASN93	ASN93	ASN93	ASN93	SGN1
		PRO94	PRO94	PRO94	PRO94	SGN1
		ARG95	ARG95	ARG95	ARG95	SGN1
					SER96	SGN1
					SER266	SGN1
					ASN268	SGN1
					SER269	SGN1
		PRO270		PRO270		SGN1
		CYS277		CYS277		SGN1
		ASP278		ASP278		SGN1
		GLY279		GLY279		SGN1
		LEU280		LEU280		SGN1
		LYS283				SGN1
			ASN294			ID
LEU297	LEU297		LEU297		LEU297	ID
		LYS300		LYS300		ID
GLU301		GLU301		GLU301		ID
HIS302		HIS302	HIS302	HIS302	HIS302	ID
ALA305						ID
GLU308	GLU308	GLU308	GLU308	GLU308	GLU308	ID
PRO309	PRO309	PRO309	PRO309	PRO309	PRO309	ID
GLN310	GLN310	GLN310	GLN310	GLN310	GLN310	ID
SER311	SER311	SER311	SER311	SER311	SER311	ID
					SER312	ID
		GLN313		GLN313	GLN313	ID
					TYR314	ID
					TYR315	ID
					TYR358	ID

					THR359	ID
					ASN360	ID
					PHE362	ID
					GLY363	ID
					GLN364	ID
					ARG366	ID
					GLN368	ID
				TYR383		ID
					SER387	ID
					SER388	ID
ASP389		ASP389		ASP389	ASP389	ID
TYR390	TYR390	TYR390	TYR390	TYR390	TYR390	ID
ARG392		**ARG392**	**ARG392**	**ARG392**	**ARG392**	ID
GLU393	GLU393	GLU393	GLU393	GLU393	GLU393	ID
GLN394	GLN394	GLN394	GLN394	GLN394	GLN394	ID
				GLU396		ID
LYS397	LYS397	LYS397	LYS397	LYS397	LYS397	ID
TYR398	TYR398	TYR398	TYR398			ID
				ARG608		Linker
	TYR652		TYR652		TYR652	ATP-BD2
ALA656	ALA656	ALA656	ALA656	ALA656	ALA656	ATP-BD2
			LYS658		LYS658	ATP-BD2
LEU659	LEU659	LEU659	LEU659	LEU659	LEU659	ATP-BD2
HIS660	HIS660	HIS660	HIS660	HIS660	HIS660	ATP-BD2
ARG661	ARG661	ARG661	ARG661	ARG661	ARG661	ATP-BD2
ALA662	ALA662	ALA662	ALA662	ALA662	ALA662	ATP-BD2
LYS663	LYS663	LYS663	LYS663	LYS663	LYS663	ATP-BD2
	ALA664		ALA664		ALA664	ATP-BD2
					LEU675	ATP-BD2
				GLU676	GLU676	ATP-BD2
				HIS677		ATP-BD2
ASP679	ASP679	ASP679	ASP679	ASP679	ASP679	ATP-BD2
LYS680	**LYS680**	**LYS680**	**LYS680**	**LYS680**	**LYS680**	ATP-BD2
	VAL681		VAL681	VAL681	VAL681	ATP-BD2
ILE682	ILE682	ILE682	ILE682	ILE682	ILE682	ATP-BD2
	PRO688	PRO688	PRO688		PRO688	SGN2
	ILE689	ILE689	ILE689	ILE689	ILE689	SGN2
GLY690	GLY690		GLY690	GLY690	GLY690	SGN2
ARG691	**ARG691**	**ARG691**	**ARG691**	**ARG691**	**ARG691**	SGN2
THR692	THR692	THR692	THR692	THR692	THR692	SGN2
ARG694	ARG694	ARG694	ARG694	ARG694	ARG694	SGN2
SER695	SER695	SER695	SER695	SER695	SER695	SGN2
		THR699		THR699	THR699	SGN2
					TYR700	SGN2
					THR701	SGN2
					GLY702	SGN2
			PHE704	PHE704	PHE704	SGN2
					ASP705	SGN2
		ARG708		**ARG708**	**ARG708**	SGN2
				LYS724	LYS724	SGN2
					GLY725	SGN2
		SER728		SER728	SER728	SGN2
		PHE729		PHE729	PHE729	SGN2
ASN730	ASN730	ASN730	ASN730	ASN730	ASN730	SGN2

		VAL731		VAL731		SGN2
		LYS732		**LYS732**		SGN2
	ARG735	**ARG735**	**ARG735**	**ARG735**	**ARG735**	SGN2-Zn3
HIS740	HIS740	HIS740		HIS740		SGN2-Zn3
	GLY741	GLY741	GLY741	GLY741	GLY741	SGN2-Zn3
	ASP742	ASP742	ASP742	ASP742	ASP742	SGN2-Zn3
LYS746	LYS746	LYS746	LYS746	ILE745	ILE745	SGN2-Zn3
GLU748	GLU748			LYS746	LYS746	SGN2-Zn3
				ILE747	ILE747	SGN2-Zn3
		GLU748	GLU748	GLU748	GLU748	SGN2-Zn3
				MET749	MET749	SGN2-Zn3
HIS750	HIS750	HIS750	HIS750	HIS750	HIS750	SGN2-Zn3
				PHE751	PHE751	SGN2-Zn3
TYR756	TYR756	TYR756	TYR756	TYR756		SGN2-Zn3
					LYS801	SGN2
					LYS803	SGN2
			THR824		ARG804	SGN2
					LYS805	SGN2
					VAL834	SGN2
				GLU839	GLU839	SGN2
					HIS841	SGN2
	ARG842	ARG842	ARG842	ARG842	ARG842	SGN2
ARG843	ARG843	ARG843	ARG843	ARG843	ARG843	ATP-BD2
					SER844	ATP-BD2
ASN845	ASN845	ASN845	ASN845	ASN845	ASN845	ATP-BD2
				GLY846		ATP-BD2
ARG847	ARG847	ARG847	ARG847	ARG847	ARG847	ATP-BD2

Number per chain						
39	43	59	52	75	83	
Total number per dimer						
82		111		158		
Mutated per chain						
3	3	6	4	6	5	
Mutated per dimer						
6		10		11		

(B) Complexes C02 and C2.

Complex				
C02		C2		
ChainA	ChainB	ChainA	ChainB	Domain
			PRO251	BBD
		CYS253	CYS253	BBD
		GLY254	GLY254	BBD
			PHE255	BBD
		CYS274	CYS274	SGN1
PRO275	PRO275	PRO275	PRO275	SGN1
ASP276	ASP276	ASP276	ASP276	SGN1
		CYS277		SGN1
		ASP278		SGN1
LYS283		LYS283	LYS283	SGN1
		TYR315		ID
		PHE362		ID
		ARG381		ID
ARG384		**ARG384**	**ARG384**	ID
SER387	SER387	GLU385		ID
	ARG392	THR386		ID
	THR406	SER387	SER387	ID
	LYS413	SER388		ID
		ASP389		ID
		TYR390		ID
		ARG392	**ARG392**	ID
		CYS404		SGN1
			THR406	SGN1
			LYS413	SGN1
LYS414	LYS414	LYS414	LYS414	SGN1
		LYS732		SGN2
			SER156	BBD
			GLY157	BBD
		LYS158	LYS158	BBD
		LYS159	LYS159	BBD
			GLY160	BBD
			HIS162	BBD
		ARG181		BBD
			GLU193	BBD
		ASN195	ASN195	BBD
		LYS196	LYS196	BBD
		LYS197	LYS197	BBD
Number per chain				
6	7	28	24	
Total number per dimer				
13		52		
Mutated per chain				
1	0	4	2	
Mutated per dimer				
1		6		

(C) Complexes C03 and C3.

Complex				
C-03		C-3		
ChainA	ChainB	ChainA	ChainB	Domain
		LYS226		BBD
		LEU227		BBD
		PHE255		BBD
		SER256		BBD
		ILE257		SGN1
			ARG263	SGN1
	GLU716		GLU716	SGN2
	ALA717		ALA717	SGN2
			LYS718	SGN2
VAL719	VAL719	VAL719	VAL719	SGN2
ARG720	**ARG720**	**ARG720**	**ARG720**	SGN2
	GLY721		GLY721	SGN2
TYR722	TYR722	TYR722	TYR722	SGN2
		LYS723	LYS723	SGN2
ARG726	**ARG726**	**ARG726**	**ARG726**	SGN2
	LYS732	**LYS732**	**LYS732**	SGN2
	GLY733		GLY733	SGN2
	GLY734			SGN2
	ARG735	**ARG735**	**ARG735**	SGN2
	CYS736		CYS736	SGN2
GLU737	GLU737	GLU737	GLU737	SGN2
ALA738	ALA738	ALA738	ALA738	SGN2
HIS740	HIS740	CYS739	CYS739	SGN2
		HIS740	HIS740	SGN2
			GLY741	SGN2
			VAL761	SGN2
			HIS763	SGN2
			TYR767	SGN2
	ASN768		ASN768	SGN2
ARG769	**ARG769**	**ARG769**	**ARG769**	SGN2
GLU770	GLU770	GLU770	GLU770	SGN2
GLU773	GLU773	GLU773	GLU773	SGN2
	VAL774		VAL774	SGN2
		ILE154	ILE154	BBD
		VAL155	VAL155	BBD
			SER156	BBD
		LYS158	LYS158	BBD
			LYS159	BBD
			GLY160	BBD
			THR161	BBD
	HIS162	HIS162	HIS162	BBD
	ALA163	ALA163	ALA163	BBD
LYS164	LYS164	LYS164	LYS164	BBD
THR165		THR165	THR165	BBD
GLU167				BBD
ASP168				BBD
LYS171				BBD

		LYS194		BBD
Number per chain				
15	23	26	39	
Total number per dimer				
38		65		
Mutated per chain				
3	5	5	6	
Mutated per dimer				
8		11		

Table 3S. Translational domain displacement at the end of the SA run. The reference coordinates are of the starting structures (before SA). C-1T (labeled also C1/DNA(1)-ARlx) is the C-1 complex submitted to a second, DNA-unrestrained DNA run. Mean RMSD is the average per two identical domains in dimer molecule, Std. Dev. < 20%. **See Fig. 5**.

		Molecule (RMSD, Å)					
Domain	Chain	Holo-1	Holo-2	C-1	C-1T	C-2	C-3
SGN2	A	3.5	3.1	2.2	1.1	4.2	1.3
	B	4	3.4	1.7	3	4.4	1.6
	Mean	3.75	3.25	1.95	2.05	4.3	1.45
ID	A	15.6	12.5	3.2	6.9	10.9	7.7
	B	11.5	9.4	1.8	11.4	5.9	4.6
	Mean	13.55	10.95	2.5	9.15	8.4	6.15
BBD	A	8.3	8	8.7	5.2	8.2	7.6
	B	14.1	11	10.2	3.3	12.9	8.2
	Mean	11.2	9.5	9.45	4.25	10.55	7.9
ATP-BD2	A	0.6	0.6	0.4	2.5	2.1	0.6
	B	0.6	0.3	0.5	2.8	1.8	0.3
	Mean	0.6	0.45	0.45	2.65	1.95	0.45
SGN1	A	2	1.7	2.9	0.9	2.3	3.5
	B	1.4	1.5	2.2	1.1	1.3	2.6
	Mean	1.7	1.6	2.55	1	1.8	3.05

Table. 4S - A. Relative (same) domain (inter-chain) plane angles (backbone atoms only) in the starting structure (Holo-0) and after one SA round of all studied dimers. The relative rotation of domain pairs after SA, Δ(Holo-0) is the difference from the values in Holo-0. C-1T (labeled also C1/DNA(1)-ARIx) is the C-1 complex submitted to a second, DNA-unrestrained DNA run. See also, **Fig. 6S-A**.

	Deg					
Complex	Holo-0	Holo-1	C-1	C-1T	C-2	C-3
ID(A):ID(B)	165,3	147,8	131	133	26	176,9
Δ(Holo-0)	0	17,5	34,3	32,3	139,3	-11,6
BBD(A):BBD(B)	154,7	104,7	100,5	66,6	102,9	126,6
Δ(Holo-0)	0	50	54,2	88,1	51,8	28,1
SGN1(A):SGN1(B)	149,8	155	167,7	165,6	154,7	168,1
Δ(Holo-0)	0	-5,2	-17,9	-15,8	-4,9	-18,3
SGN2(A):SGN2(B)	84,7	69,8	78,9	85,2	79,5	86,7
Δ(Holo-0)	0	14,9	5,8	-0,5	5,2	-2
SGN1(A):SGN1(B)	149,8	155	167,7	165,6	154,7	168,1
Δ(Holo-0)	0	-5,2	-17,9	-15,8	-4,9	-18,3
ID(A):BBD(B)	74	104,1	52,7	71,4	127,9	90,1
Δ(Holo-0)	0	-30,1	21,3	2,6	-53,9	-16,1
ID(B):BBD(A)	73,7	142,7	87	85,8	107,7	138,9
Δ(Holo-0)	0	-69	-13,3	-12,1	-34	-65,2
ID(A):SGN1(A)	93,1	36,5	100,9	78,7	60,4	73,5
Δ(Holo-0)	0	56,6	-7,8	14,4	32,7	19,6
ID(B):SGN1(B)	93,2	73,4	100,7	73,7	97,8	87,6
Δ(Holo-0)	0	19,8	-7,5	19,5	-4,6	5,6
SGN1(A):BBD(A)	9,7	17,5	32,5	47,8	24,5	35,2
Δ(Holo-0)x	0	-7,8	-22,8	-38,1	-14,8	-25,5
SGN1(B):BBD(B)	9,6	38	36,4	51,5	33,9	17,4
Δ(Holo-0)	0	-28,4	-26,8	-41,9	-24,3	-7,8
ATP1(A):ATP1(B)	64,86	64,63	64,98	69,19	64,05	65,04
Δ(Holo-0)	0	-0,27	0,08	4,29	-0,85	0,14
ATP2(A):ATP2(B)	162,31	166,22	160,77	173,36	179,57	168,62
Δ(Holo-0)	0	3,92	-1,53	11,06	17,27	6,32

Table 4S-B. Intra-chain domain rotation. Similar to **Table 4S-A**, but the domain plane rotation is relative to the plane of ATP-BD1(A) for chain (A), or ATP-BD1(B) for chain (B) domains, both kept immobilized with the exception in C-1T. The rotation after SA is the difference, Δ(Holo-0) from the starting Holo-dimer. See also, **Fig. 6S-B**.

	Deg					
Complex	Holo-0	Holo-1	C-1	C-1T	C-2	C-3
ATP2A:ATP1A	113,01	111,4	111,18	116,88	122,26	114,86
Δ(Holo-0)	0	-1,6	-1,82	3,88	9,26	1,86
ATP2B:ATP1B	113,88	120,05	114,55	121,53	121,49	118,69
Δ(Holo-0)	0	6,15	0,65	7,63	7,59	4,79
SGN1A:ATP1A	106,4	104,94	116,5	115,68	112,72	118,48
Δ(Holo-0)	0	-1,46	10,1	9,28	6,32	12,08
SGN1B:ATP1B	17,62	104,94	24,99	26,77	26,35	30,04
Δ(Holo-0)	0	-2,66	7,39	9,17	8,75	12,44
SGN2A:ATP1A	23,21	27,04	25,43	19,79	35,1	24,27
Δ(Holo-0)	0	3,84	2,23	-3,41	11,9	1,07
SGN2B:ATP1B	23,66	19,45	19,6	25,41	22,54	28,41
Δ(Holo-0)	0	-4,25	-4,1	1,71	-1,16	4,71
IDA:ATP1A	86,67	118,44	69,51	77,29	95,85	74,14
Δ(Holo-0)	0	31,74	-17,19	-9,41	9,15	-12,56
IDB:ATP1B	87,54	161,84	79,44	82,63	105,96	140,97
Δ(Holo-0)	0	-15,66	-8,06	-4,87	18,46	53,47
BBDA:ATP1A	107,43	90,89	91,41	68,39	100,57	98,3
Δ(Holo-0)	0	-16,51	-15,99	-39,01	-6,83	-9,1
BBDB:ATP1B	107,91	80	75,08	67,9	73,23	97,75
Δ(Holo-0)	0	-27,9	-32,82	-40	-34,67	-10,15