Supporting Information

On the mechanism of action of Arsenoplatins: Arsenoplatin-1 binding to a B-DNA dodecamer

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Table S1 Data collection and refinement statistics. Values in brackets refer to the highest resolution shell.

	cisplatin/DNA adduct	AP-1/DNA adduct (4 h soaking)	AP-1/DNA adduct (48 h soaking)	transplatin/DNA adduct (48h soaking)	transplatin/DNA adduct (7d soaking)
Crystal data					
Space group	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$
Unit-cell parameters					
a, b, c (Å)	24.72, 41.00, 66.48	25.51, 40.73, 65.85	39.97, 65.67, 23.56	25.50 40.20, 65.60	25.56, 40.39, 65.67
α, β, γ (°)	90.00, 90.00, 90.00	90.00, 90.00, 90.00	90.00, 90.00, 90.00	90.00, 90.00, 90.00	90.00, 90.00, 90.00
No. of molecules in the asymmetric unit	1 duplex	1 duplex	1 duplex	1 duplex	1 duplex
Data collection					
Resolution limits (Å)	23.17 – 2.31 (2.35 – 2.31)	34.64 – 1.52 (1.55 – 1.52)	34.14 – 2.51 (2.55 – 2.51)	25.47 – 1.41 (1.45 – 1.41)	34.40 – 1.40 (1.42 – 1.40)
No. of observations	38543 (1937)	126537 (6273)	24779 (1249)	121269 (2369)	135194 (6641)
No. of unique reflections	3221 (148)	11057 (530)	2357 (118)	12070 (490)	13972 (698)
Completeness (%)	99.1 (100.0)	99.7 (100.0)	99.8 (100.0)	89.9 (51.9)	98.9 (100.0)
<I/σ(I)>	22.0 (2.5)	22.4 (2.3)	13.7 (2.1)	30.50 (2.5)	13.2 (0.9)
Average multiplicity	12.0 (13.1)	11.4 (11.8)	10.5 (10.6)	10.0 (4.8)	9.7 (9.5)
$CC_{1/2}$	1.0 (0.9)	1.0 (0.8)	1.0 (0.9)	0.999 (0.832)	0.998 (0.601)
Refinement					
Resolution limits (Å)	23.17 – 2.31	34.64 – 1.52	34.14 – 2.51	25.45 – 1.41	34.40 – 1.40
No. of reflections	2894	10514	2064	11444	11739
R_{factor}/R_{free}	0.231/0.266	0.238/0.261	0.179/0.232	0.189/0.229	0.218/ 0.256
No. of atoms	499	569	493	610	603
Mean B value (Å²)	52.8	33.6	59.1	17.2	19.1
RMSD from ideal values					
Bond lengths (Å)	0.003	0.004	0.007	0.011	0.010

Bond angles (°)	1.730	2.132	2.344	3.199	1.931
Pt occupancy	0.50/0.60/0.50/0.65	0.20/0.20	0.15/0.40/0.25	0.20	0.25/0.30/0.30
Pt B-factors (Å^2)	84.1/78.8/71.8/85.5	57.9/39.3	62.3/86.9/66.4	38.83	27.44/61.52/65.28
As occupancy	-	0.20	0.25	-	-
As B-factors (Å^2)	-	44.1	54.4	-	-
PDB code	8C62	8C63	8C64	8RI5	8RI3

Table S2 Anomalous signal close to Pt and As atoms in the structures of cisplatin/DNA, transplatin/DNA and AP-1/DNA adducts. Pt and As occupancies are also reported.

Structure	Resolution (Å)	Sigma level (σ)/Occupancy					
		Pt 1	Pt 2	Pt 3	Pt 4	As 2	As 3
Cisplatin/DNA adduct	2.31	9.91/0.50	11.65/0.60	10.01/0.50	13.85/0.65	-	-
AP-1/DNA adduct (4 h)	1.52	8.24/0.20	23.55/0.20	-	-	5.21/0.20	-
AP-1/DNA adduct (48 h)	2.51	3.26/0.15	5.92/0.40	2.89/0.25	-	-	4.04/0.25
Transplatin/DNA adduct (48 h)	1.41	12.46/0.20	-	-	-	-	-
Transplatin/DNA adduct (7 d)	1.40	10.32/0.25	6.35/0.30	4.24/0.30	-	-	-

Table S3. X-ray structures of Pt-based drugs/DNA adducts reported in the PDB. Our structures are in bold

DNA	Metallodrug	Resolution (Å)	PDB code	Space group	Reference	Cocristallization or Soaking (time)	Binding sites
$[d(CGCGAATTCGCG)]_2$	**cisplatin**	**2.31**	**8C62**	**P 2_1 2_1 2_1**	**-**	**Soaking (6 days)**	**Binding of Pt to Gua4, Gua10, Gua16 and Gua22**
$[d(CGCGAATTCGCG)]_2$	**AP-1**	**1.54**	**8C63**	**P 2_1 2_1 2_1**	**-**	**Soaking (4h)**	**Binding of Pt to Gua10 and Gua14**
$[d(CGCGAATTCGCG)]_2$	**AP-1**	**2.51**	**8C64**	**P 2_1 2_1 2_1**	**-**	**Soaking (48h)**	**Binding of Pt to Gua2, Gua10 and Gua14**
$[d(CGCGAATTCGCG)]_2$	**transplatin**	**1.41**	**8RI5**	**P 2_1 2_1 2_1**	**-**	**Soaking (48 h)**	**Binding of Pt to Gua16**
$[d(CGCGAATTCGCG)]_2$	**transplatin**	**1.40**	**8RI3**	**P 2_1 2_1 2_1**	**-**	**Soaking (7 days)**	**Binding of Pt to Gua4, Gua10 and Gua16**
5'-D(*DCP*DCP*DTP*DCP*DTP*DCP*DGP*DTP*DCP*DTP*DCP*DC)-3'	*cis*-$\{Pt(NH_3)_2(pyridine)\}^{2+}$	2.16	3CO3	C 2 2 2_1	(2008) Proc Natl Acad Sci U S A 105: 8902-8907	n/A	Binding of Pt to Gua7
$[d(CGCGAATTCGCG)]_2$	$\{Pt(ammine)(cyclohexylamine)\}^{2+}$	2.40	1LU5	P 1	(2002) J. Biol. Chem. 277: 49743-49749	n/A	Binding of Pt to Gua6 and Gua7
$[d(CGCGAATTCGCG)]_2$	[{*trans*-Pt-$(NH_3)_2(NH_2(CH_2)_6(NH_3^+)\}_2$-μ-{*trans*-$Pt(NH_3)_2(NH_2(CH_2)_6NH_2)_2\}$] (TriplatinNC)	1.13	2DYW	P 2_1 2_1 2_1	(2006) J. Am. Chem. Soc. 128: 16092-16103	Cocristallization	-
5'-D(*CP*CP*(BRU)P*CP*TP*[PT(NH3)2(GP*GP)]*TP*CP*TP*CP*C)-3'	cisplatin	2.60	1AIO	P 1	(1995) Nature. **377**: 649-652	Cocristallization	Binding of Pt to Gua6 and Gua7

5'-D(*CP*CP*TP*CP*TP*GP*GP*TP*CP*TP*CP*C)-3'	oxaliplatin	2.40	1IHH	I 2 2 2	(2001) Inorg. Chem. **40**: 5596-5602	Cocristallization	Binding of Pt to Gua6 and Gua7
5'-D(*CP*GP*TP*(1AP)P*CP*(PT(NH3)3)G)-3'	$[(NH_3)_3ClPt]Cl$	1.60	211D	P 3_2 2 1	(1995) Biochem. 34: 15487-15495	Soaking (3 weeks)	Binding of Pt to Gua6
5'-D(*CP*CP*TP*CP*TP*GP*GP*TP*CP*TP*CP*C)-3'	cisplatin	1.77	3LPV	P 1	(2010) J. Inorg. Biochem. **104**: 902-908	Cocristallization	Binding of Pt to Gua6 and Gua7
(5'-D(*GP*(2ST)P*GP*GP*CP*CP*AP*C)-3'	-	1.42	4H5A	P 4_3 2_1 2	n/A	n/A	Binding of Pt to Gua4
5'-D(*GP*(2ST)P*GP*GP*CP*CP*AP*C)-3'	-	1.25	4I1G	P 4_3 2_1 2	n/A	n/A	Binding of Pt to Gua 1 and Gua4
5'-D(*GP*TP*AP*CP*G)-3'	$Pt(H_2bapbpy)]$	2.30	6F3C	P 3_2 2 1	(2019) Angew. Chem. Int. Ed. Engl. 58: 9378-9382	Soaking	Close to Gua2
$[d(CGCGAATTCGCG)]_2)$	cisplatin	2.60	5BNA	P 2_1 2_1 2_1	(1984) EMBO J. 3: 1201-1206	Soaking	Binding of Pt to Gua4 and Gua10
5'-D(*CP*CP*TP*CP*GP*CP*TP*CP*TP*C)-3'	cisplatin	1.63	1I1P	C 1 2 1	(2002) Acta Crystallogr. D. Biol. Crystallogr. 58: 431-440	Cocristallization	Binding of Pt to Gua5
5'-D(*CP*CP*TP*CP*GP*CP*TP*CP*TP*C)-3'	cisplatin	1.63	1A2E	C 1 2 1	(1999) Nucleic Acids Res. 27: 1837-1846	Cocristallization	Binding of Pt to Gua5

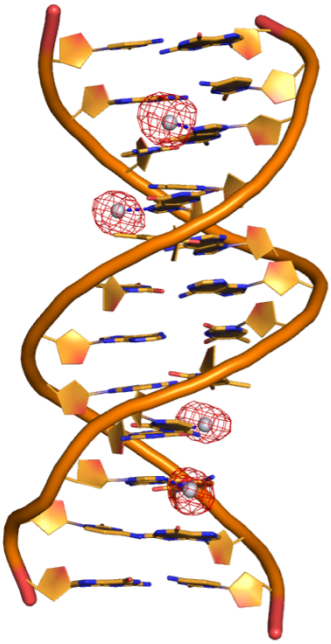

Fig. S1 Anomalous difference electron density maps (red, 3.0 σ) around the Pt centers in the cisplatin/DNA adduct.

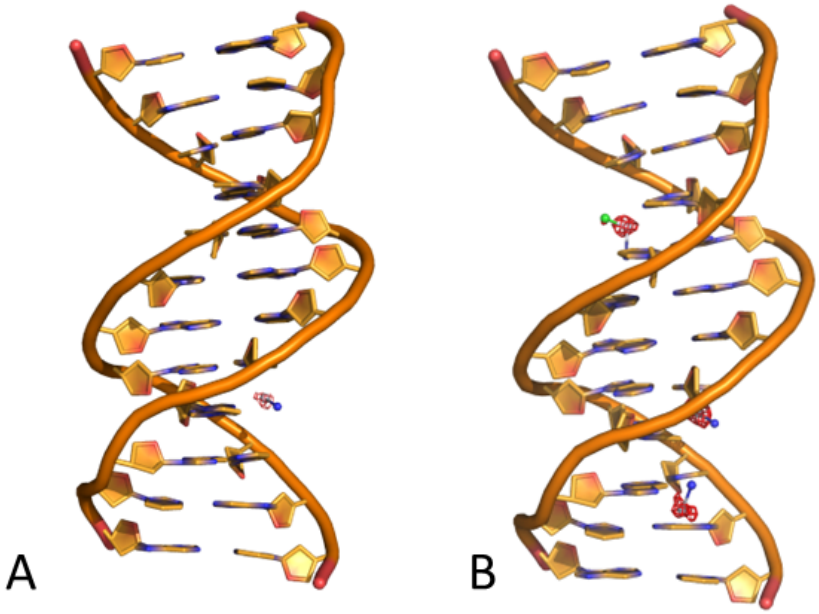

Fig. S2 Anomalous difference electron density maps at 3.0 σ (red) around Pt centers in the transplatin/DNA adducts obtained upon (A) 48 h and (B) 7 days of soaking.

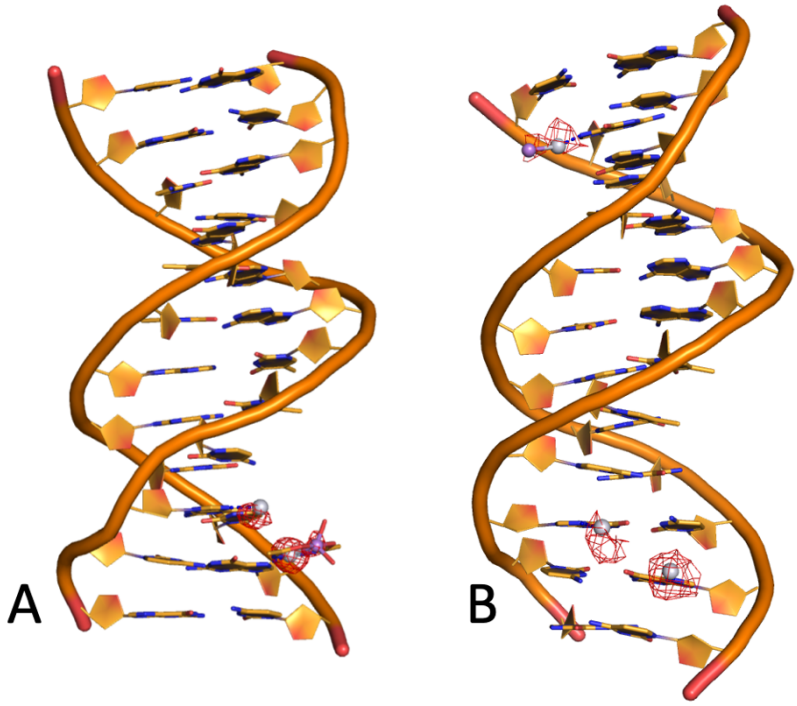

Fig. S3 Anomalous difference electron density maps (red) around Pt and As in the AP-1/DNA adducts obtained upon (A) 4 h (3.0 σ value) and (B) 48 h (2.0 σ value) of soaking.

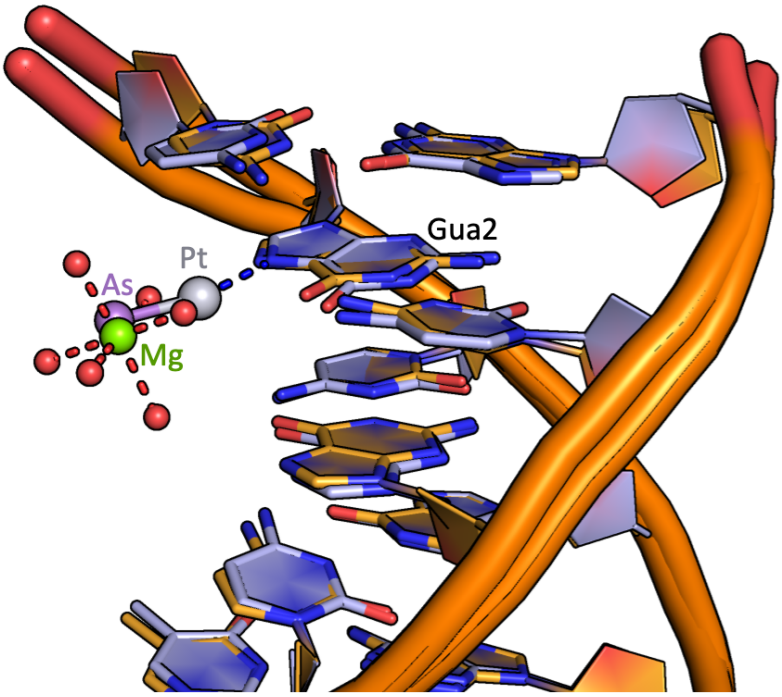

Fig. S4 Superimposed structures of AP-1/DNA adducts formed upon 4 (orange) and 48 h (light blue) of soaking. The hexaaqua magnesium ion observed in the structure of the adduct formed upon 4 h of soaking occupies almost the same position adopted by Pt-As bimetallic center in the AP-1/DNA adducts obtained upon 48 h of soaking.

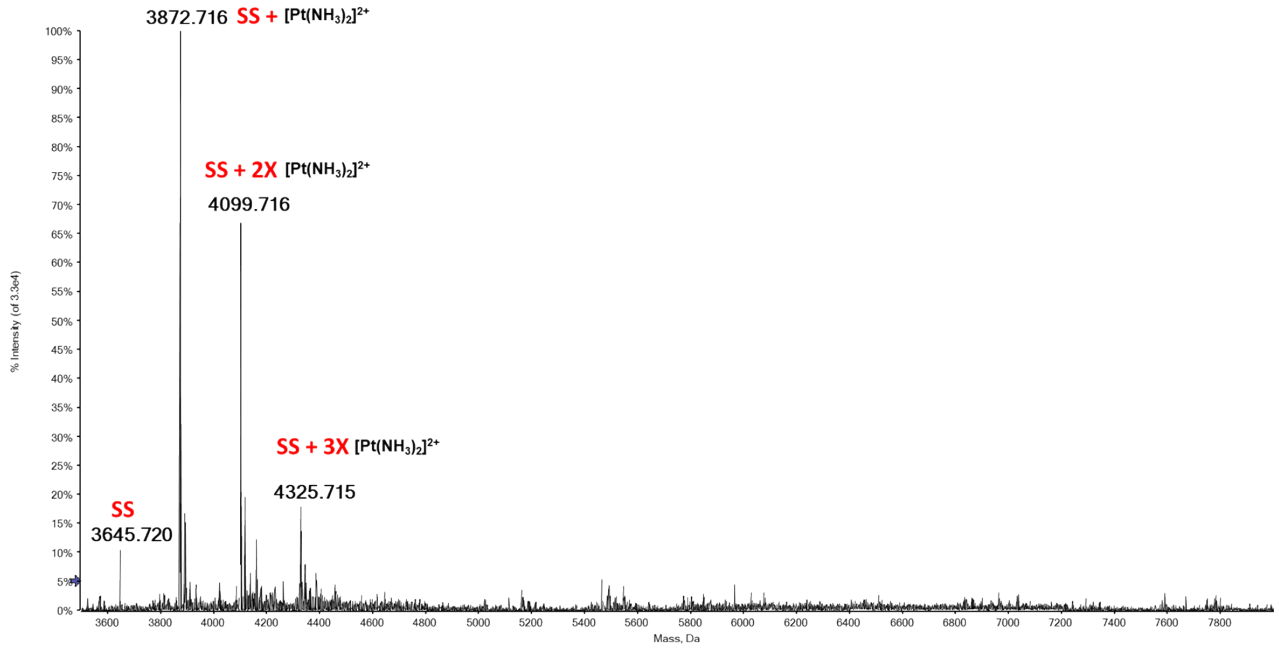

Fig. S5 ESI MS spectrum of the Dickerson sequence (5'-CGCGAATTCGCG-3') and cisplatin, metal complex to DNA ratio 3:1, incubated for 48 h in 100 mM ammonium acetate buffer (pH=6.8) at the concentration of 10^{-4} M.

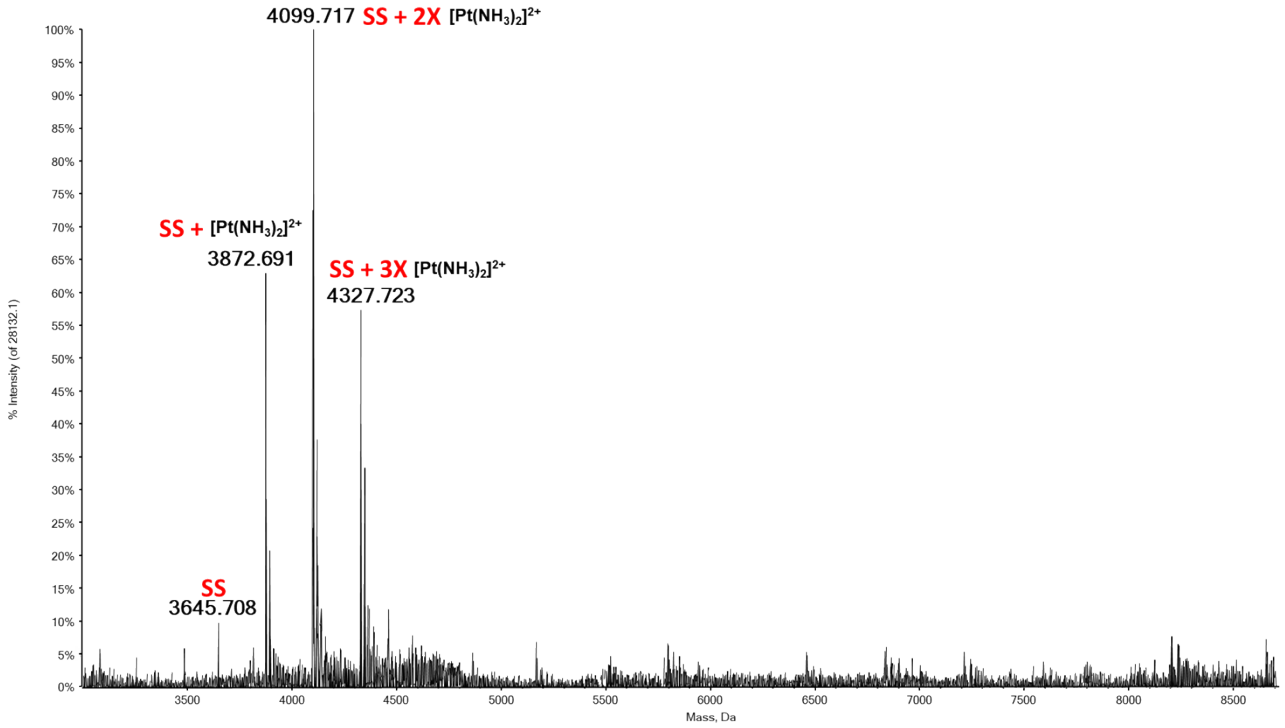

Fig. S6 ESI MS spectrum of the Dickerson sequence (5'-CGCGAATTCGCG-3') and transplatin, metal complex to DNA ratio 3:1, incubated for 48 h in 100 mM ammonium acetate buffer (pH=6.8) at the concentration of 10^{-4} M.

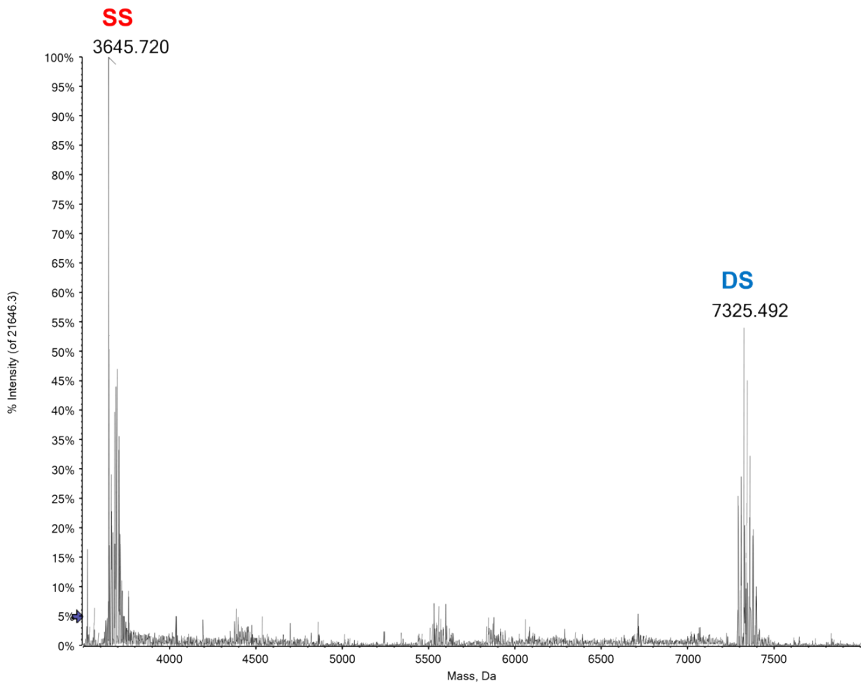

Fig. S7 ESI MS spectrum of the Dickerson sequence (5'-CGCGAATTCGCG-3') and AP-1, metal complex to DNA ratio 3:1, incubated for 24 h in 100 mM ammonium acetate buffer (pH=6.8) at the concentration of 10^{-4} M.