Supplementary Material
Interaction of Zn with losartan. Activation of intrinsic apoptotic signaling pathway in lung cancer cells and effects on alkaline and acid phosphatases

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Table S1. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å x 10^3) for chloro*losartanate*zinc complex. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor. To be deposited.

Atom	x	y	z	U(eq)
C(1)	5848(3)	7585(5)	8565(2)	47(1)
C(2)	6028(3)	8422(5)	8038(2)	47(1)
C(3)	4410(3)	7474(4)	7942(2)	43(1)
C(4)	6956(4)	9292(6)	7846(3)	62(1)
C(5)	3319(4)	7103(5)	7677(2)	46(1)
C(6)	2434(4)	7995(5)	7951(3)	51(1)
C(7)	1348(4)	7560(6)	7676(3)	61(1)
C(8)	446(5)	8180(8)	8021(4)	104(3)
C(9)	4934(4)	9010(5)	6987(2)	49(1)
C(10)	5484(3)	8185(4)	6456(2)	42(1)
C(11)	5925(5)	8881(5)	5929(3)	63(1)
C(12)	6454(5)	8130(6)	5447(3)	63(1)
C(13)	6555(3)	6680(5)	5482(2)	41(1)
C(14)	6079(4)	5979(5)	5999(2)	47(1)
C(15)	5561(4)	6731(5)	6481(2)	50(1)
C(16)	7188(3)	5853(4)	5007(2)	42(1)
C(17)	8266(3)	6160(4)	4921(2)	40(1)
C(18)	8841(4)	5356(5)	4480(2)	47(1)
C(19)	8369(4)	4250(6)	4129(2)	55(1)
C(20)	7314(4)	3935(5)	4217(2)	58(1)
C(21)	6732(4)	4734(5)	4647(2)	52(1)
C(22)	8818(3)	7229(4)	5343(2)	40(1)
N(1)	4854(3)	6983(4)	8515(2)	44(1)
N(2)	5083(3)	8350(4)	7648(2)	43(1)
N(3)	8923(3)	7154(4)	6017(2)	49(1)
N(4)	9503(3)	8292(4)	6209(2)	50(1)
N(5)	9731(3)	9011(4)	5682(2)	46(1)
N(6)	9319(3)	8376(4)	5124(2)	42(1)
O	6739(3)	10740(4)	7774(2)	71(1)
Cl(1)	6694(1)	7246(2)	9243(1)	74(1)
Cl(2)	2634(1)	4854(1)	8991(1)	60(1)
Zn	4255(1)	5691(1)	9207(1)	45(1)

Table S2. Full bond lengths [Å] and angles [°] for chloro*losartanate*zinc complex.

C(1)-C(2)	1.345(6)	O-C(4)-C(2)	114.5(4)
C(1)-N(1)	1.372(5)	C(3)-C(5)-C(6)	114.8(4)
C(1)-Cl(1)	1.715(4)	C(7)-C(6)-C(5)	112.6(4)
C(2)-N(2)	1.394(5)	C(8)-C(7)-C(6)	115.1(5)
C(2)-C(4)	1.491(7)	N(2)-C(9)-C(10)	111.8(4)
C(3)-N(1)	1.335(5)	C(15)-C(10)-C(11)	118.2(4)
C(3)-N(2)	1.338(5)	C(15)-C(10)-C(9)	121.6(4)
C(3)-C(5)	1.490(6)	C(11)-C(10)-C(9)	120.2(4)
C(4)-O	1.401(7)	C(10)-C(11)-C(12)	120.5(4)
C(5)-C(6)	1.517(6)	C(13)-C(12)-C(11)	121.2(4)
C(6)-C(7)	1.507(7)	C(12)-C(13)-C(14)	118.2(4)
C(7)-C(8)	1.474(8)	C(12)-C(13)-C(16)	122.7(4)
C(9)-N(2)	1.467(5)	C(14)-C(13)-C(16)	119.1(4)
C(9)-C(10)	1.509(6)	C(15)-C(14)-C(13)	120.5(4)
C(10)-C(15)	1.378(6)	C(10)-C(15)-C(14)	121.4(4)
C(10)-C(11)	1.380(6)	C(21)-C(16)-C(17)	118.1(4)
C(11)-C(12)	1.391(7)	C(21)-C(16)-C(13)	120.7(4)
C(12)-C(13)	1.377(7)	C(17)-C(16)-C(13)	121.1(4)
C(13)-C(14)	1.386(6)	C(18)-C(17)-C(16)	119.8(4)
C(13)-C(16)	1.488(5)	C(18)-C(17)-C(22)	119.6(4)
C(14)-C(15)	1.383(6)	C(16)-C(17)-C(22)	120.3(4)
C(16)-C(21)	1.390(6)	C(19)-C(18)-C(17)	120.9(4)
C(16)-C(17)	1.404(6)	C(18)-C(19)-C(20)	119.6(4)
C(17)-C(18)	1.391(6)	C(21)-C(20)-C(19)	120.2(5)
C(17)-C(22)	1.471(5)	C(20)-C(21)-C(16)	121.4(4)
C(18)-C(19)	1.378(7)	N(6)-C(22)-N(3)	110.0(4)
C(19)-C(20)	1.378(7)	N(6)-C(22)-C(17)	125.9(3)
C(20)-C(21)	1.378(7)	N(3)-C(22)-C(17)	124.1(4)
C(22)-N(6)	1.337(5)	C(3)-N(1)-C(1)	105.3(4)
C(22)-N(3)	1.350(5)	C(3)-N(1)-Zn	130.1(3)
N(1)-Zn	2.016(3)	C(1)-N(1)-Zn	124.5(3)
N(3)-N(4)	1.345(5)	C(3)-N(2)-C(2)	108.9(4)
N(4)-N(5)	1.296(5)	C(3)-N(2)-C(9)	127.0(4)
N(5)-N(6)	1.350(4)	C(2)-N(2)-C(9)	123.8(4)
N(5)-Zn#1	2.041(3)	C(22)-N(3)-N(4)	105.7(3)
N(6)-Zn#2	2.034(3)	N(5)-N(4)-N(3)	108.8(3)
Cl(2)-Zn	2.2107(13)	N(4)-N(5)-N(6)	110.4(3)
Zn-N(6)#3	2.034(3)	N(4)-N(5)-Zn#1	118.6(3)
Zn-N(5)#4	2.041(3)	N(6)-N(5)-Zn#1	130.5(3)
		C(22)-N(6)-N(5)	105.0(3)
C(2)-C(1)-N(1)	111.7(4)	C(22)-N(6)-Zn#2	130.3(3)
C(2)-C(1)-Cl(1)	127.5(4)	N(5)-N(6)-Zn#2	123.5(3)
N(1)-C(1)-Cl(1)	120.7(3)	N(1)-Zn-N(6)#3	110.84(14)
C(1)-C(2)-N(2)	104.0(4)	N(1)-Zn-N(5)#4	107.14(14)
C(1)-C(2)-C(4)	133.4(4)	N(6)#3-Zn-N(5)#4	103.83(13)
N(2)-C(2)-C(4)	122.6(4)	N(1)-Zn-Cl(2)	116.86(11)
N(1)-C(3)-N(2)	110.1(4)	N(6)#3-Zn-Cl(2)	109.29(10)
N(1)-C(3)-C(5)	124.5(4)	N(5)#4-Zn-Cl(2)	108.02(11)
N(2)-C(3)-C(5)	125.4(4)		

Symmetry transformations used to generate equivalent atoms:

(#1) -x+3/2,y+1/2,-z+3/2; (#2) x+1/2,-y+3/2,z-1/2; (#3) x-1/2,-y+3/2,z+1/2; (#4) -x+3/2,y-1/2,-z+3/2

Table S3. Anisotropic displacement parameters ($Å^2$ x 10^3) for chloro*losartanate*zinc complex. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$. To be deposited.

Atom	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	42(2)	60(3)	39(2)	-5(2)	-1(2)	6(2)
C(2)	40(2)	57(3)	45(2)	-8(2)	0(2)	2(2)
C(3)	45(2)	49(2)	36(2)	-5(2)	5(2)	3(2)
C(4)	51(3)	77(4)	58(3)	-10(3)	9(2)	-6(3)
C(5)	45(2)	56(3)	36(2)	-2(2)	-1(2)	-2(2)
C(6)	44(2)	49(3)	60(3)	-6(2)	-2(2)	-1(2)
C(7)	46(3)	63(3)	74(4)	-5(3)	-4(2)	5(2)
C(8)	55(3)	101(5)	156(7)	-52(5)	1(4)	12(4)
C(9)	51(3)	55(3)	41(2)	2(2)	7(2)	9(2)
C(10)	36(2)	46(2)	42(2)	1(2)	4(2)	-1(2)
C(11)	88(4)	43(2)	59(3)	9(2)	28(3)	15(3)
C(12)	80(4)	55(3)	56(3)	8(2)	31(3)	4(3)
C(13)	36(2)	47(2)	41(2)	-2(2)	0(2)	1(2)
C(14)	45(2)	43(2)	52(2)	2(2)	8(2)	-2(2)
C(15)	56(3)	47(2)	48(2)	5(2)	13(2)	-6(2)
C(16)	44(2)	44(2)	37(2)	2(2)	1(2)	1(2)
C(17)	41(2)	45(2)	33(2)	1(2)	1(2)	0(2)
C(18)	43(2)	57(3)	41(2)	3(2)	2(2)	7(2)
C(19)	63(3)	61(3)	39(2)	-11(2)	1(2)	14(3)
C(20)	74(3)	54(3)	44(2)	-11(2)	-10(2)	-6(2)
C(21)	45(2)	59(3)	50(2)	-7(2)	-3(2)	-5(2)
C(22)	38(2)	43(2)	38(2)	1(2)	4(2)	1(2)
N(1)	46(2)	52(2)	35(2)	-1(2)	1(1)	1(2)
N(2)	43(2)	50(2)	36(2)	-2(2)	6(1)	5(2)
N(3)	55(2)	54(2)	38(2)	3(2)	2(2)	-11(2)
N(4)	59(2)	57(2)	35(2)	5(2)	-2(2)	-15(2)
N(5)	54(2)	52(2)	33(2)	2(2)	0(2)	-10(2)
N(6)	46(2)	47(2)	32(2)	0(1)	2(1)	-5(2)
O	86(3)	68(2)	60(2)	-11(2)	17(2)	-14(2)
Cl(1)	60(1)	105(1)	55(1)	5(1)	-17(1)	-2(1)
Cl(2)	56(1)	63(1)	61(1)	1(1)	-2(1)	-5(1)
Zn	51(1)	50(1)	34(1)	-1(1)	0(1)	8(1)

Table S4. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^2 x 10^3) for chloro*losartanate*zinc complex. To be deposited.

Atom	x	y	z	U(eq)
H(8A)	477	7884	8480	156
H(8B)	-211	7866	7807	156
H(8C)	486	9194	7999	156
H	6570(50)	11030(70)	8090(30)	90(20)
H(4A)	7520(40)	9050(50)	8200(20)	63(15)
H(4B)	7200(30)	8970(50)	7410(20)	50(12)
H(5A)	3290(40)	7380(60)	7220(30)	79(18)
H(5B)	3200(40)	6050(60)	7770(30)	85(18)
H(6A)	2450(30)	7890(40)	8460(20)	39(11)
H(6B)	2570(40)	8960(50)	7890(20)	53(13)
H(7A)	1370(40)	7800(60)	7220(30)	76(18)
H(7B)	1350(50)	6620(70)	7650(30)	90(20)
H(9A)	4150(40)	9100(40)	6890(20)	45(12)
H(9B)	5200(40)	9890(50)	7000(20)	52(14)
H(11)	5810(40)	9860(50)	5880(20)	54(13)
H(12)	6710(50)	8610(60)	5150(30)	80(18)
H(14)	6150(40)	5090(50)	6030(20)	59(15)
H(15)	5270(40)	6280(50)	6790(20)	55(14)
H(18)	9480(30)	5560(40)	4470(20)	41(12)
H(19)	8740(40)	3780(50)	3840(20)	53(13)
H(20)	6980(40)	3120(60)	3990(20)	66(15)
H(21)	6110(40)	4520(50)	4720(30)	65(16)

Table S5. Hydrogen bond distances (Å) and angles (º) for chloro*losartanate*zinc complex. To be deposited.

D-H	d(D-H)	d(H..A)	∠(D-H..A)	d(D..A)	A	Symmetry operation
O	0.73(6)	2.19(6)	173(7)	2.917(5)	N(3)	[-x+3/2, y+1/2, -z+3/2]

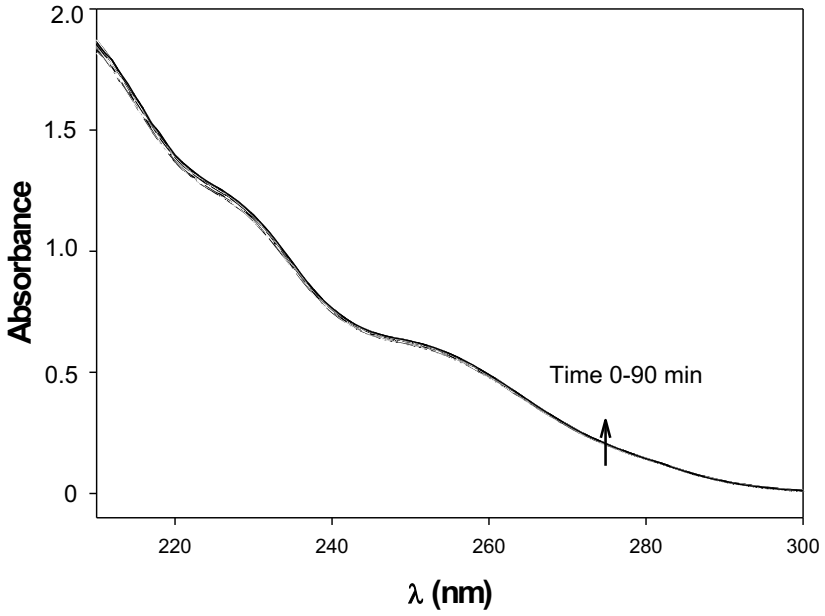

Fig. S1. Time variation of the electronic absorption spectra of the zinc complex in 96 % EtOH (5×10^{-5} mol L^{-1}), room temperature.

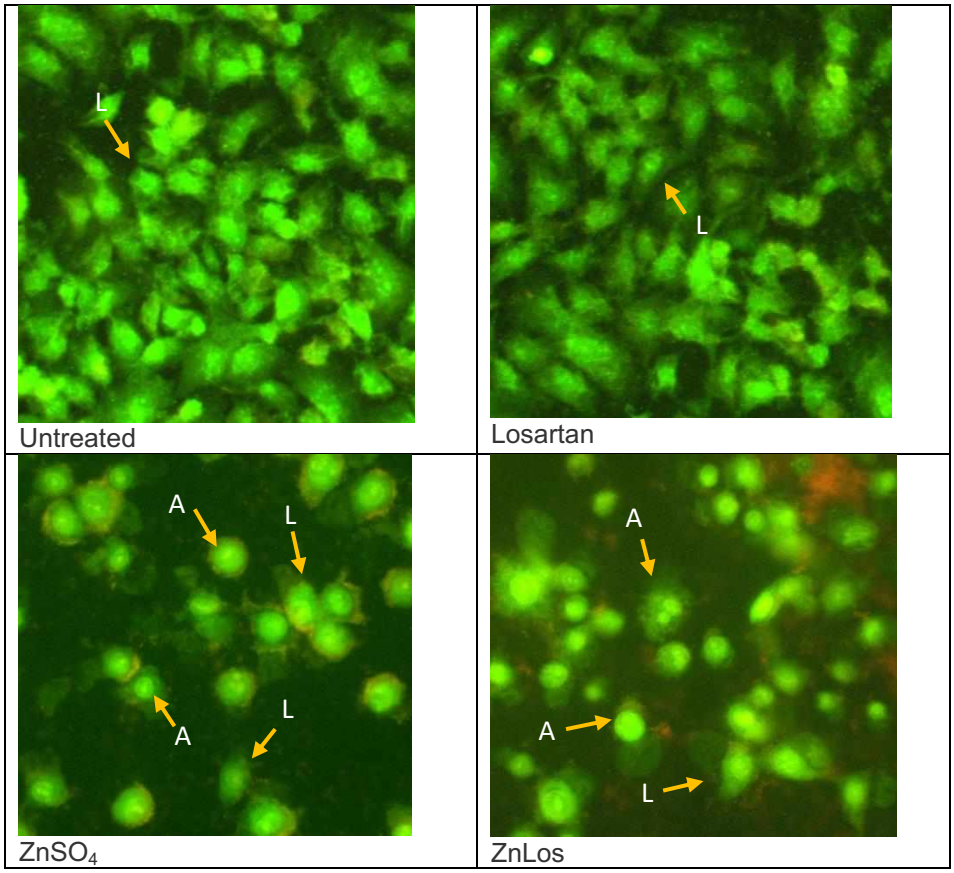

Fig. S2. Morphologic changes of A549 cells double stained with AO/EtBr. Untreated cells and cells exposed to losartan exhibit normal morphology. Cells exposed to $ZnSO_4$ and ZnLos showed that apoptotic cells became the increasingly predominant cell type. Necrotic cells were not observed. Arrows next to "L" point to live cells; arrows next to "A" indicate apoptotic cells.