

### Raw data

## **Two Zn sources (ZnO nanoparticles and ZnSO<sub>4</sub>) differentially affect lipid metabolism via ferroptosis pathway and SLC7A11<sup>K23</sup> acetylation by HDAC8 and HDAC6 in a freshwater teleost**

Yi-Chuang Xu,<sup>‡</sup><sup>a</sup> Hua Zheng,<sup>‡</sup><sup>a</sup> Xiao-Ying Tan,<sup>a</sup> Christer Hogstrand,<sup>c</sup> Tao Zhao,<sup>a</sup> Xiao-Lei Wei<sup>a</sup> and Zhi Luo<sup>\*ab</sup>

<sup>a</sup>Hubei Hongshan Laboratory, Fishery College, Huazhong Agricultural University, Wuhan 430070, China

<sup>b</sup>Laboratory for Marine Fisheries Science and Food Production Processes, Qingdao National Laboratory for Marine Science and Technology, Qingdao 266237, China

<sup>c</sup>Diabetes and Nutritional Sciences Division, School of Medicine, King's College London, Franklin-Wilkins Building, 150 Stamford Street, London SE1 9NH, UK

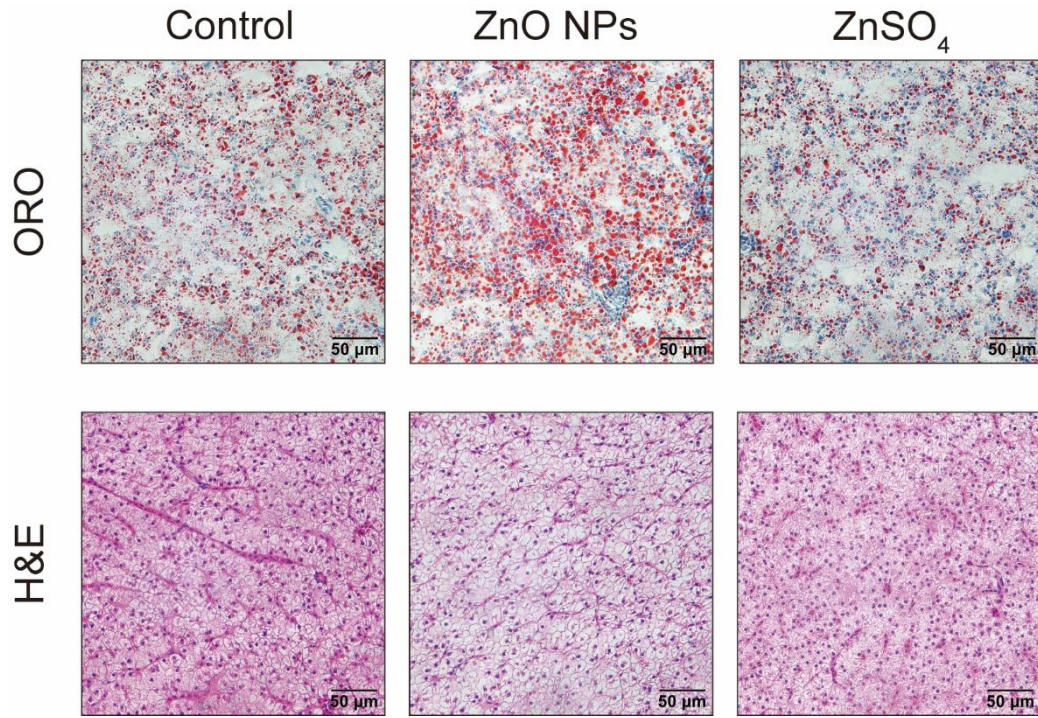
\*Corresponding author at: Zhi Luo, Hubei Hongshan Laboratory, Fishery College, Huazhong Agricultural University, Wuhan 430070, China, Tel.: +86-27-8728-2113; Fax: +86-27-8728-2114;

E-mail address: luozhi99@mail.hzau.edu.cn; luozhi99@aliyun.com (Z. Luo).

<sup>‡</sup> These two authors contributed equally.

**Fig. 1**

**Fig. 1A**



**Fig. 1B**

	Control			ZnO NPs			ZnSO <sub>4</sub>		
ORO	104.3632	93.47531	102.1615	126.8533	119.1429	131.2484	70.53249	74.14587	84.11147
H&E	94.32622	107.102	98.57183	127.7537	128.2744	129.2343	78.69475	79.89375	84.43586

**Fig. 1C**

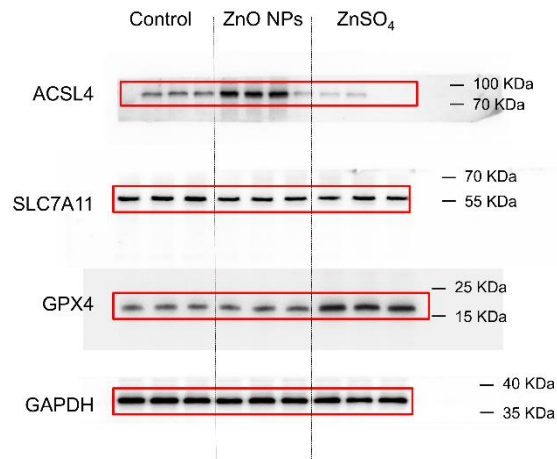
	Control			ZnO NPs			ZnSO <sub>4</sub>		
TG	1.033558	1.073225	1.120001	1.255237	1.39605	1.564342	0.793699	0.89046	0.827252

**Fig. 1D**

	Control			ZnO NPs			ZnSO <sub>4</sub>		
NEFA	996.7976	1071.773	903.7281	2168.637	2709.909	2530.962	1723.371	1892.842	1985.981

**Fig. 1E**

	Control			ZnO NPs			ZnSO <sub>4</sub>		
<i>atgl</i>	1.002313	0.985094	1.012789	0.341116	0.374577	0.382447	1.221229	1.212793	1.359742
<i>hsla</i>	1.138131	0.967053	0.908568	0.5328	0.53465	0.614152	1.528023	1.455653	1.316463
<i>cpt1alb</i>	0.974905	1.012789	1.012789	0.677519	0.703847	1.313425	0.839926	0.80571	0.961483
<i>cpt1a2a</i>	1.044877	1.012789	0.944965	0.581694	0.703847	0.544624	1.4323	1.412581	1.295342
<i>acs1la</i>	1.214195	1.261377	0.65293	1.29684	1.433955	1.265757	0.560583	0.49827	0.50698
<i>acadsb</i>	0.937354	1.043671	1.022192	0.624887	0.44648	0.512871	1.528023	1.415848	1.430646
<i>acca</i>	0.909618	1.100633	0.998845	1.545778	1.52979	1.3692	0.405657	0.446996	0.398688
<i>fas</i>	1.052145	1.005793	0.944965	1.493123	1.76949	1.650992	1.212793	0.938438	0.99539
<i>elovl6</i>	1.011619	1.00812	0.980552	1.881218	1.914101	1.836128	0.429779	0.480186	0.39685
<i>srebpl</i>	0.963707	1.00812	1.029302	0.85362	0.93088	0.997692	1.073012	1.103179	0.97041
<i>ppara</i>	0.99539	1.070536	0.938438	0.397309	0.401461	0.364334	1.005793	0.887816	0.922316

**Fig. 2****Fig. 2A****Fig. 2B**

	Control			ZnO NPs			ZnSO <sub>4</sub>		
ACSL4	1	0.87601	0.75343	1.36699	1.74192	1.80161	0.4881	0.44473	0.46479

SLC7A11	1	0.7559	0.67197	0.58437	0.79468	0.8094	1.1727	0.97041	0.78578
GPX4	1	0.72324	0.67162	0.87376	0.92936	0.83616	2.59254	2.25147	2.24975

**Fig. 2C**

	Control			ZnO NPs			ZnSO <sub>4</sub>		
<i>acs14</i>	1.047294	0.99424	0.960373	2.087342	2.214018	2.009263	0.727827	0.758734	0.63581

**Fig. 2D**

	Control			ZnO NPs			ZnSO <sub>4</sub>		
Cys	1.086983	1.148008	1.179255	0.80959	0.895072	0.949668	1.235312	1.347383	1.402978

**Fig. 2E**

	Control			ZnO NPs			ZnSO <sub>4</sub>		
Reduced									
GSH	99.27469	111.917	88.80833	64.30327	60.16761	38.73422	153.9915	138.8916	121.6833

**Fig. 2F**

	Control			ZnO NPs			ZnSO <sub>4</sub>		
GSH:									
GSSG	5.074794	4.758245	5.098925	7.212806	6.970724	7.990305	5.202281	6.028979	4.952163

**Fig. 2G**

	Control			ZnO NPs			ZnSO <sub>4</sub>		
<i>cbsa</i>	0.96929	1.231144	0.837987	1.197479	0.929805	0.90125	1.351911	0.989657	0.91067
<i>cbsb</i>	0.828362	1.081725	1.115997	0.915945	1.063141	1.104454	1.026927	1.4323	0.985094
<i>cth</i>	1.060688	1.197479	0.787308	0.864537	1.287882	0.876606	0.91067	1.098093	0.815072
<i>gclc</i>	0.929805	0.933033	1.152686	0.406126	0.367292	0.296273	0.952638	0.694959	0.635075
<i>gclm</i>	1.008120	0.983957	1.008120	0.405189	0.398228	0.432768	1.091768	1.087991	0.953739
<i>gss</i>	0.881684	0.948246	1.196096	1.341022	1.281944	0.925518	1.350350	1.364463	1.383510

<i>gpx4</i>	1.019833	1.016305	0.964821	1.089249	0.875594	0.780967	1.472567	1.442262	1.273089
<i>gsr</i>	0.927659	1.040060	1.036462	0.730353	1.267220	1.258466	1.245450	1.339474	1.293847

**Fig. 2H**

	Control			ZnO NPs			ZnSO <sub>4</sub>		
MDA	6.186559	5.830637	5.610867	7.773924	7.372122	7.067338	4.820292	5.365986	5.415312

**Fig. 2I**

	Control			ZnO NPs			ZnSO <sub>4</sub>		
4-HNE	6.186559	5.830637	5.610867	7.773924	7.372122	7.067338	4.820292	5.365986	5.415312

**Fig. 2J**

	Control			ZnO NPs			ZnSO <sub>4</sub>		
<i>ptgs2</i>	1.105731	0.97942	0.923382	1.474269	1.244012	1.265757	0.787308	0.820742	0.78187

**Fig. 3**

**Fig. 3A**

	Cell viability, %						
0	99.99999	100.8474	101.7484	99.58051	102.2411	95.58265	
0.1	101.3244	100.5803	101.4788	99.31669	101.9702	95.32942	
0.2	76.9234	100.2573	97.91272	94.96439	94.10797	84.84178	
0.4	66.56212	84.61714	89.9101	93.19539	87.94455	87.50932	
0.6	85.54377	84.96814	83.90112	82.17424	54.55819	69.52449	
0.8	79.59094	76.19334	68.65403	66.82887	66.67444	73.56792	
1	70.24051	66.42172	70.50727	74.91572	47.2014	53.23846	
2	42.96142	34.97284	27.09658	18.06907	20.2031	39.97096	
3	31.96835	21.21396	17.78828	19.5292	13.07094	24.87831	
4	25.49606	24.70983	21.52283	22.08441	20.55409	23.76917	

**Fig. 3B**

		Cell viability, %					
Control		96.80647	99.34962	101.184	104.486	100.8505	97.32344
	25	99.31627	102.1346	111.4567	96.78979	96.33953	96.58134
ZnO	50	106.3787	104.4609	93.86308	94.30501	68.0647	106.9207
NPs	75	89.28542	100.5003	97.04828	97.69032	100.7421	106.337
	100	88.88518	91.04477	89.04361	75.32728	90.57784	91.89527
	25	102.293	95.3056	109.4055	107.1208	102.3764	103.6355
	50	102.7349	102.4514	95.48904	109.6139	109.9308	109.8891
ZnSO <sub>4</sub>	75	95.78921	97.18169	107.7295	107.6378	99.30793	110.2226
	100	100.8588	110.306	111.957	96.03102	97.62361	108.2048

**Fig. 3C**

		Cell viability, %					
Control		95.92719	91.44749	110.2313	112.3012	99.48005	90.61335
ZnO NPs		85.57756	79.33688	79.76941	78.47184	83.97105	88.6979
ZnSO <sub>4</sub>		108.3838	99.31557	103.4315	94.00617	96.01716	99.40014
ZnO NPs+Fer-1		90.24262	90.05725	93.05401	92.55969	94.38247	120.4883
ZnSO <sub>4</sub> +RSL3		77.49534	79.86343	76.33009	87.00528	74.68558	80.88771

**Fig. 3D**

		MDA					
Control		2.152468	1.853738	1.731632	1.899635	1.917601	2.070739
ZnO NPs		2.84723	2.782328	2.869924	3.001828	3.334086	2.408523
ZnSO <sub>4</sub>		1.733383	1.739168	1.636188	1.742329	1.860889	1.608162
ZnO NPs+Fer-1		1.739574	1.869964	1.777217	1.782864	2.152605	2.106166
ZnSO <sub>4</sub> +RSL3		2.166734	2.546513	1.8706	1.850025	1.83049	2.202484

**Fig. 3E**

	4-HNE			
Control	107.2205	92.98227	106.9442	92.85309
ZnO NPs	115.4999	129.243	141.393	142.0959
ZnSO <sub>4</sub>	85.80792	89.61116	85.81996	74.94378
ZnO NPs+Fer-1	90.78713	95.49242	102.0275	91.26217
ZnSO <sub>4</sub> +RSL3	96.88998	104.9899	93.80553	98.04482

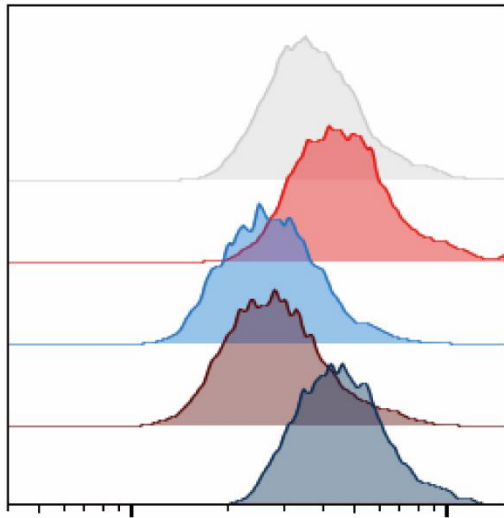
**Fig. 3F**

	C11-BODIPY			
Control	95.99476	105.5668	96.70998	101.7285
ZnO NPs	160.7343	160.7462	161.1873	149.4934
ZnSO <sub>4</sub>	71.45071	66.32495	87.126	77.32745
ZnO NPs+Fer-1	50.85231	71.96329	60.36476	53.54631
ZnSO <sub>4</sub> +RSL3	175.9208	176.8626	189.5458	191.2266

**Fig. 3G**

	TG					
Control	0.035733	0.03686	0.035884	0.040361	0.042164	0.037249
ZnO NPs	0.057416	0.054899	0.065479	0.055365	0.067106	0.057545
ZnSO <sub>4</sub>	0.036629	0.025589	0.036827	0.03545	0.024342	0.028289
ZnO NPs+Fer-1	0.057056	0.039631	0.039821	0.024018	0.039138	0.027954
ZnSO <sub>4</sub> +RSL3	0.043712	0.044383	0.04353	0.047968	0.051444	0.04672

**Fig. 3H**

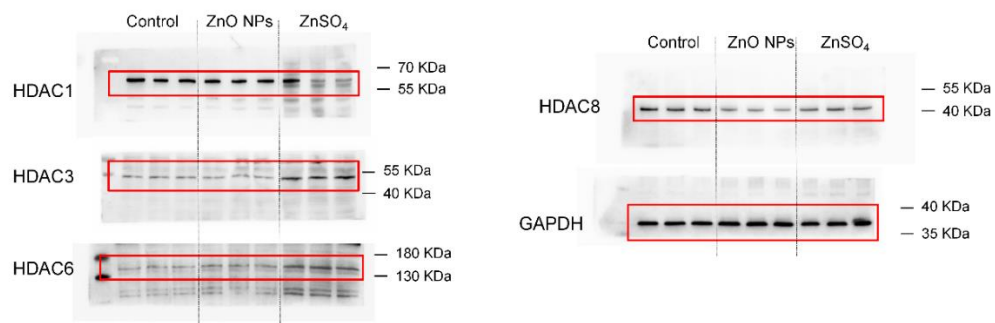


**Fig. 3I**

BODIPY 493/503				
Control	101.2996	100.8841	99.39403	98.42232
ZnO NPs	124.4161	122.0529	123.1428	105.4308
ZnSO <sub>4</sub>	76.22565	75.53731	73.96412	74.27853
ZnO NPs+Fer-1	72.11184	76.45093	73.96982	72.12864
ZnSO <sub>4</sub> +RSL3	124.6232	123.6016	124.3734	115.7923

**Fig. 4**

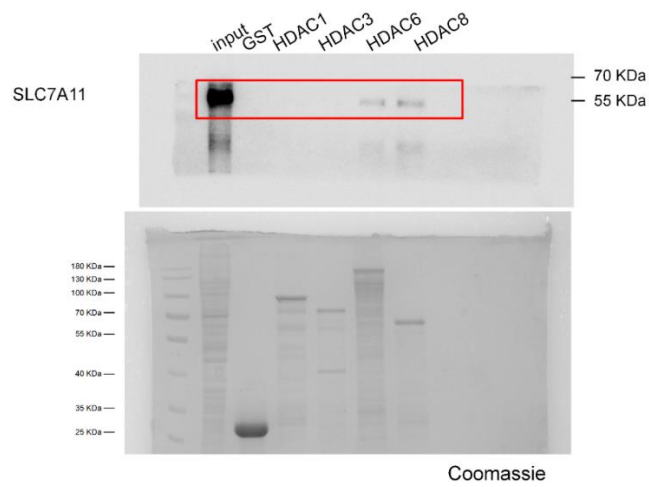
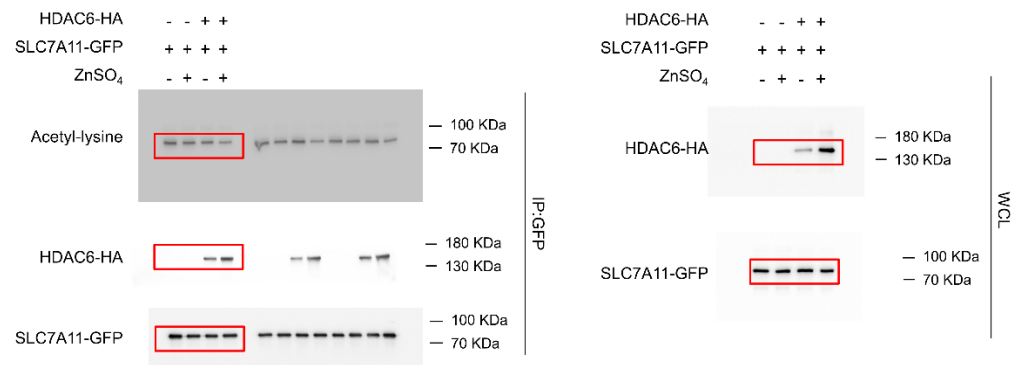
**Fig. 4A**



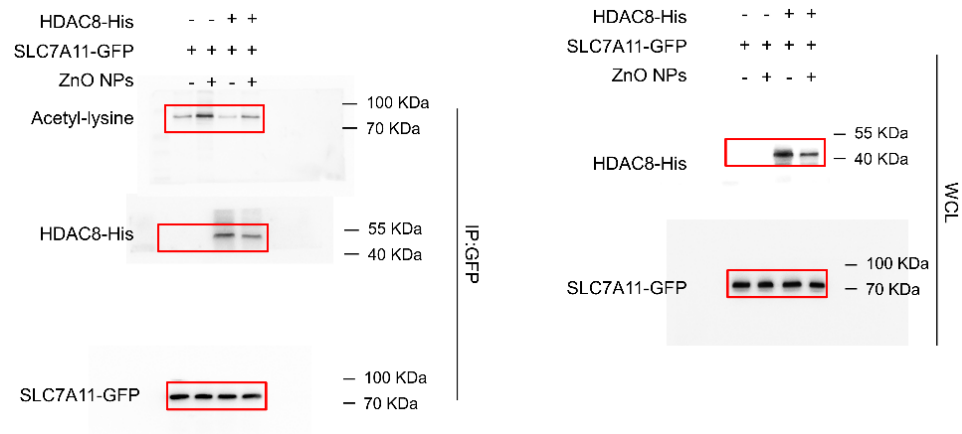


**Fig. 4B**

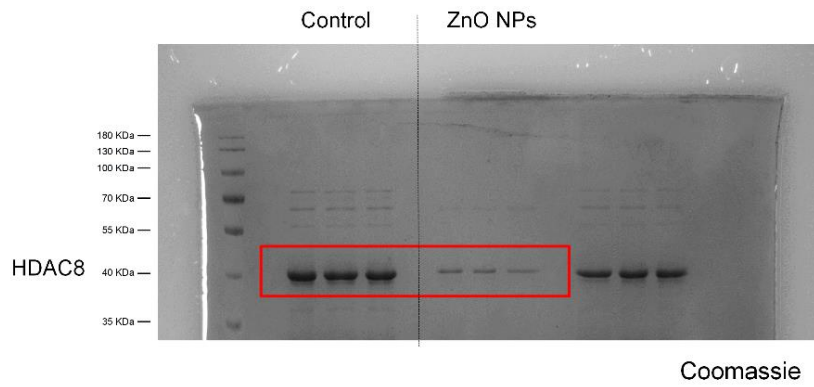
		Control		ZnO NPs			ZnSO <sub>4</sub>		
HDAC1	1	0.75828	0.89413	0.86048	0.7897	0.87063	1.12006	0.60826	0.43779
HDAC3	1	1.11299	1.19716	1.01323	0.97224	0.98399	2.43126	2.06114	2.99985
HDAC6	1	1.03172	0.76331	1.14603	1.09149	1.10697	1.54469	1.82498	1.69284
HDAC8	1	0.90941	0.74239	0.50429	0.40589	0.35026	0.62488	0.73119	0.6625

**Fig. 4C****Fig. 4D**

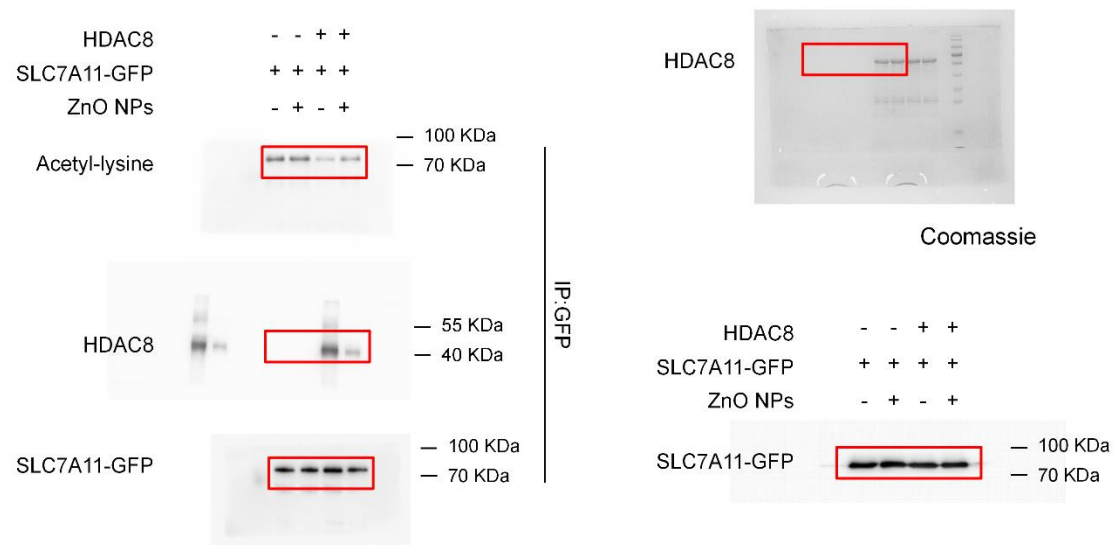
**Fig. 4E**



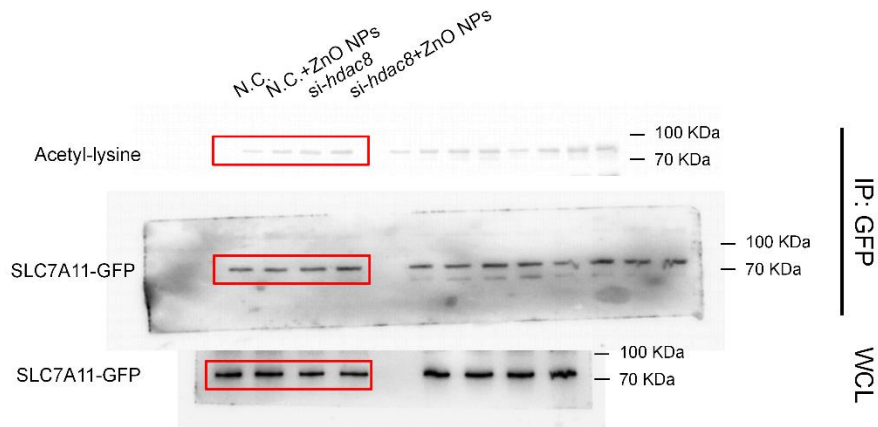
**Fig. 4F**



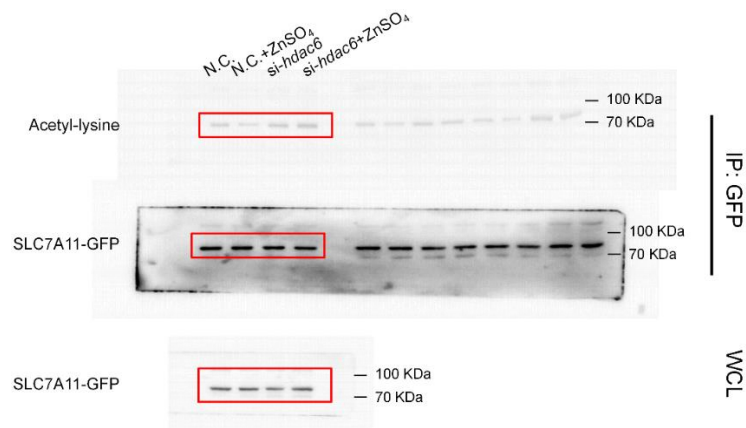
**Fig. 4G**



**Fig. 4H**

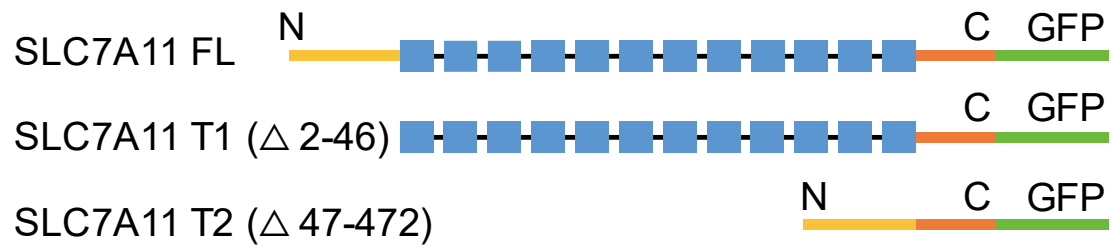


**Fig. 4I**

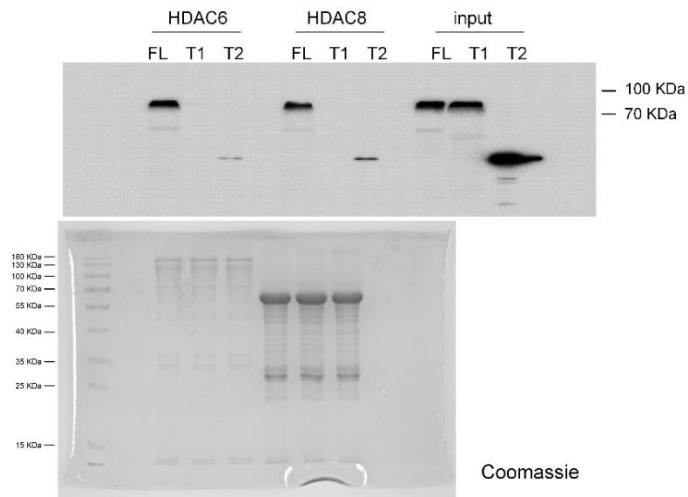


**Fig. 5**

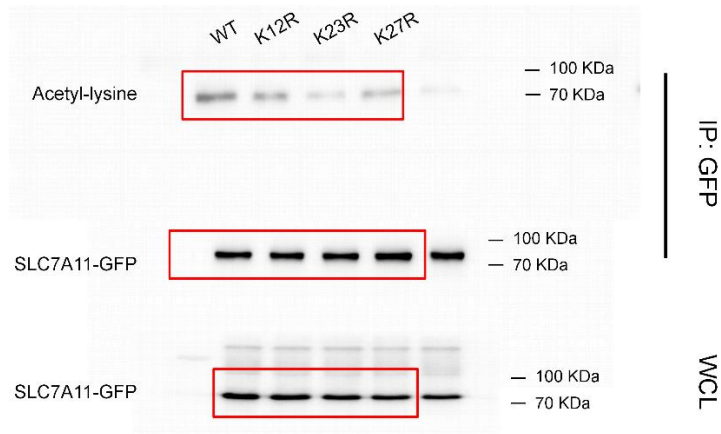
**Fig. 5A**



**Fig. 5B**



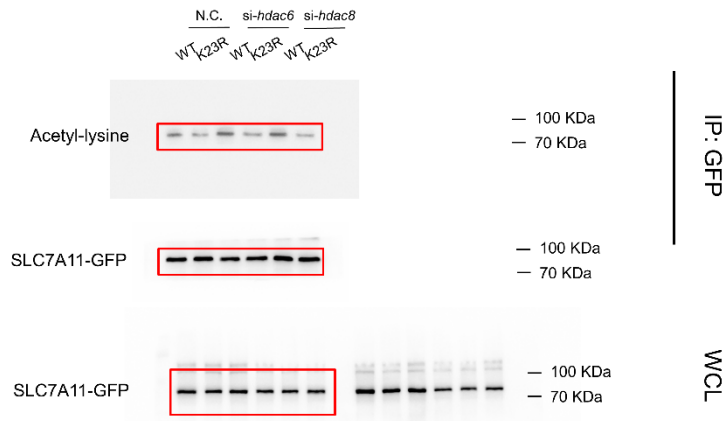
**Fig. 5C**



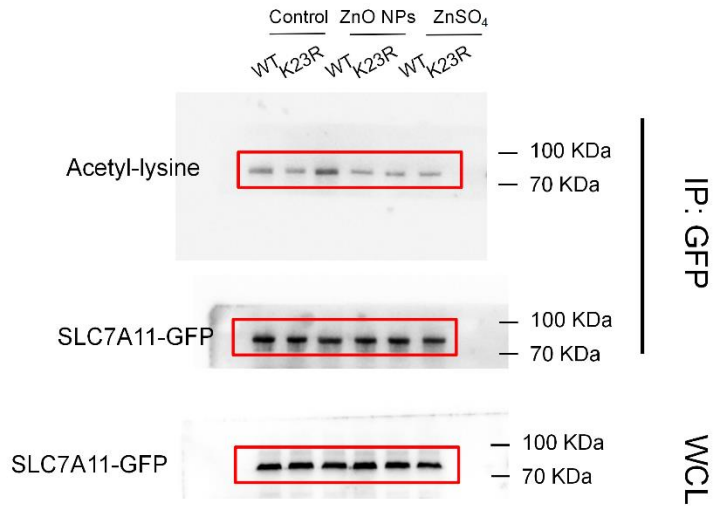
**Fig. 5D**

WT	K12R	K23R	K27R
100	100	110.672	137.789
83.884	57.387	79.60533	132.395
66.66667	31.883	30.987	62.141
103.6587	65.321	50.072	108.085

**Fig. 5E**



**Fig. 5F**



**Fig. 6**

**Fig. 6A**

		Cell viability					
Control	WT	96.76725	100.2593	94.31787	104.2644	104.4961	99.89519
	K23R	101.5171	106.1841	107.5412	106.813	90.80929	104.7112
ZnO NPs	WT	76.49363	76.26193	84.75203	85.03338	87.84686	83.94108
	K23R	93.65587	91.90159	87.15176	92.48083	87.76411	90.23005
RSL3	WT	81.50825	84.66928	73.91184	82.76604	74.73934	76.59292

K23R	88.83985	84.38793	89.8163	80.48215	89.386	82.96464
------	----------	----------	---------	----------	--------	----------

**Fig. 6B**

		Cystine uptake					
Control	WT	0.145486	0.142442	0.13691	0.115992	0.130366	0.181679
	K23R	0.186679	0.177792	0.216002	0.184996	0.199953	0.211332
ZnO	WT	0.066977	0.097151	0.095015	0.115081	0.102338	0.073463
NPs	K23R	0.145332	0.174911	0.135226	0.134801	0.141005	0.107208
ZnSO <sub>4</sub>	WT	0.196052	0.193396	0.192353	0.201588	0.192353	0.150586
	K23R	0.200571	0.192399	0.226808	0.202911	0.19317	0.20583

**Fig. 6C**

			Relative expression			
<i>gclc</i>	Control	WT	1.084853	0.970971	0.931418	1.019244
		K23R	1.523617	1.285652	1.539541	1.37316
	ZnO NPs	WT	0.557676	0.60395	0.599778	0.551908
		K23R	1.199556	1.354256	1.487098	1.303599
	ZnSO <sub>4</sub>	WT	0.761808	0.967612	0.61664	1.246169
		K23R	1.555631	1.37316	1.340248	1.250496
<i>gclm</i>	Control	WT	1.022783	1.008702	1.001734	0.967612
		K23R	1.416666	1.162717	1.154686	1.57189
	ZnO NPs	WT	0.427057	0.478802	0.516736	0.561555
		K23R	0.905948	1.022783	1.212093	1.138789
	ZnSO <sub>4</sub>	WT	1.285652	1.290115	0.627419	1.029897
		K23R	1.183041	1.358957	1.392329	1.471717
<i>gss</i>	Control	WT	1.152686	0.982821	0.989657	0.891929
		K23R	1.075494	1.148698	1.172835	1.136817
	ZnO NPs	WT	0.709562	0.835088	0.858565	1.042466
		K23R	0.757858	0.719467	0.687771	0.952638

<i>gpx4</i>	ZnSO <sub>4</sub>	WT	1.71119	1.681793	1.670176	1.872544	
		K23R	1.808759	1.783857	1.474269	1.180993	
	Control	WT	1.069918	1.099997	0.970971	0.875088	
		K23R	1.492261	1.23328	1.436442	1.402013	
	ZnO NPs	WT	0.964264	0.836536	0.890384	0.866037	
		K23R	1.377928	1.14671	1.267952	1.199556	
	ZnSO <sub>4</sub>	WT	1.290115	1.33099	1.33099	1.20372	
		K23R	1.392329	1.492261	1.33099	1.732073	
	Control	WT	0.959264	0.965936	0.993092	1.086735	
		K23R	1.164734	1.209994	1.287882	1.319508	
	<i>gsr</i>	ZnO NPs	WT	0.806642	1.060688	0.929805	0.861546
			K23R	1.235419	1.140764	1.201636	1.201636
ZnSO <sub>4</sub>	WT	1.239708	1.105731	1.209994	1.301342		
	K23R	1.265757	1.283426	1.342573	1.252664		

**Fig. 6D**

		Reduced GSH		
Control	WT	103.6975	96.18015	100.1223
	K23R	127.3139	126.233	124.0345
ZnO NPs	WT	68.66277	70.87017	72.97748
	K23R	97.39783	100.0979	114.8435
ZnSO <sub>4</sub>	WT	117.4423	131.5318	123.4918
	K23R	127.6508	132.7017	132.288

**Fig. 6E**

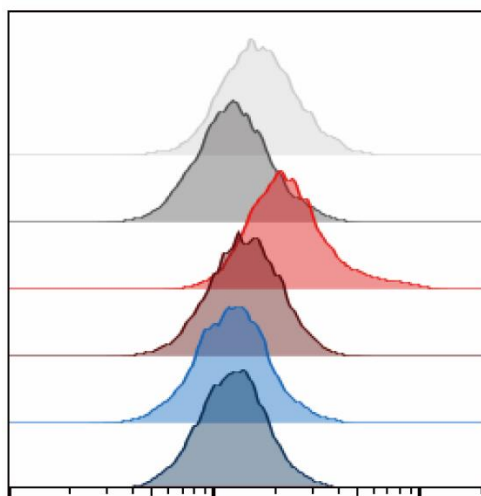
		MDA			
Control	WT	2.000662	2.192151	2.297818	2.494457
	K23R	1.477955	1.541081	1.455004	1.785388
ZnO NPs	WT	3.471696	2.709948	3.308911	2.953441

	K23R	1.252156	1.30795	1.308716	1.906647
ZnSO <sub>4</sub>	WT	1.590691	1.513302	1.70402	1.559604
	K23R	1.169716	1.092287	1.23439	1.509283

**Fig. 6F**

		4-HNE			
Control	WT	103.1402	107.3318	85.77514	103.7529
	K23R	79.07667	79.80761	80.1683	72.51685
ZnO NPs	WT	129.9416	124.2915	134.147	141.026
	K23R	78.10814	95.70568	73.29907	64.25267
ZnSO <sub>4</sub>	WT	70.23481	82.71337	71.87335	72.20847
	K23R	75.68318	67.51806	77.27275	61.24713

**Fig. 6G**



**Fig. 6H**

		C11-BODIPY			
Control	WT	97.38725	99.23297	103.8382	99.5416
	K23R	70.96023	72.46706	71.94663	75.48072
ZnO NPs	WT	119.5782	141.6542	141.7692	142.4832
	K23R	81.93165	104.1589	74.42775	78.41571



ZnSO <sub>4</sub>	WT	71.05705	71.051	70.81499	73.97389
	K23R	52.03104	57.30193	60.91469	70.30666

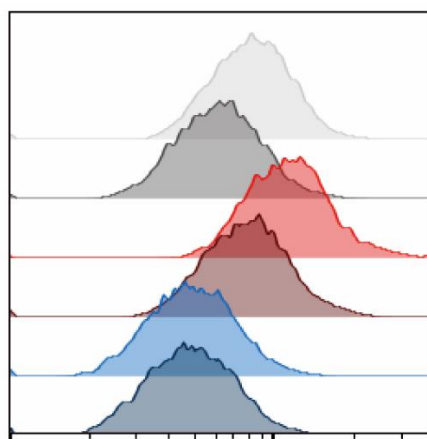
**Fig. 6I**

		<i>ptgs2</i>			
Control	WT	1.193336	0.976032	1.01748	0.843816
	K23R	0.600818	0.598739	0.757858	0.630689
ZnO NPs	WT	1.664397	1.94531	1.892115	1.918528
	K23R	1.132884	1.333299	1.356604	1.172835
ZnSO <sub>4</sub>	WT	0.765779	0.757858	0.726986	0.744839
	K23R	0.515842	0.534033	0.510506	0.80107

**Fig. 6J**

		TG					
Control	WT	0.049867	0.04908	0.0423	0.037546	0.045113	0.054747
	K23R	0.041824	0.030602	0.036301	0.029101	0.04053	0.028184
ZnO NPs	WT	0.078096	0.069355	0.065715	0.054734	0.085365	0.065959
	K23R	0.043118	0.045943	0.047949	0.039589	0.046284	0.047555
ZnSO <sub>4</sub>	WT	0.040528	0.042108	0.037938	0.033444	0.036591	0.045707
	K23R	0.03793	0.028165	0.033307	0.033204	0.039067	0.026095

**Fig. 6K**



**Fig. 6L**

		BODIPY 493/503			
Control	WT	116.3912	94.58849	95.33355	93.68671
	K23R	85.66174	71.7318	71.1459	70.66689
ZnO NPs	WT	126.1	128.6466	125.4682	141.5111
	K23R	90.55641	89.03974	91.10641	104.0172
ZnSO <sub>4</sub>	WT	90.55641	70.07386	70.73297	89.03974
	K23R	57.38063	69.10741	56.61229	56.19631

**Fig. 6M**

			Relative expression			
<i>atgl</i>	Control	WT	0.936272	0.982821	1.010451	1.075494
		K23R	1.274561	1.244012	1.526259	1.394744
	ZnO NPs	WT	0.787308	0.817902	0.784584	0.755236
		K23R	1.176907	1.156688	1.021012	1.641483
	ZnSO <sub>4</sub>	WT	1.342573	1.474269	1.505247	1.337928
		K23R	1.500039	1.664397	1.670176	1.892115
<i>hsla</i>	Control	WT	1.084853	0.998269	1.062527	0.869043
		K23R	1.456494	1.726081	1.85639	1.518345
	ZnO NPs	WT	0.667806	0.684205	0.753929	0.75132
		K23R	0.977725	1.174869	1.207899	1.220523
	ZnSO <sub>4</sub>	WT	1.481953	1.250496	1.19127	1.397163
		K23R	2.458026	2.475123	2.518387	2.333507
<i>cpt1a2a</i>	Control	WT	1.172835	0.986233	0.933033	0.926588
		K23R	1.201636	1.301342	1.510473	1.69937
	ZnO NPs	WT	0.697372	0.72951	0.792784	0.812252
		K23R	1.172835	1.053361	1.136817	1.042466
	ZnSO <sub>4</sub>	WT	1.231144	1.261377	1.21841	1.489677

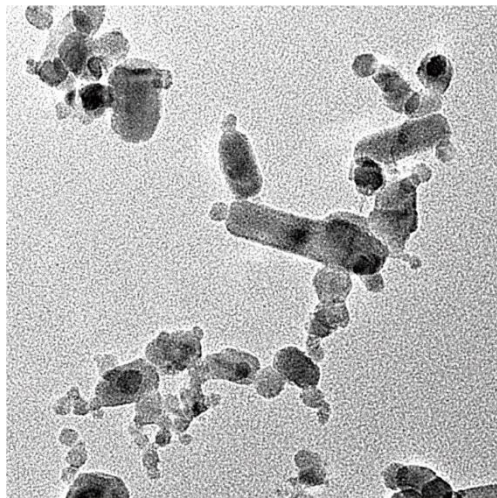
		K23R	2.219139	2.17347	1.925189	1.735077
	Control	WT	1.019244	0.957603	1.005212	1.019244
		K23R	1.267952	1.411765	1.321796	1.103816
<i>acadsb</i>	ZnO NPs	WT	0.816486	0.743549	0.733312	0.767107
		K23R	0.857079	0.684205	0.674785	0.645058
	ZnSO <sub>4</sub>	WT	1.392329	1.744121	1.843567	1.518345
		K23R	1.431473	1.513092	1.111494	1.638641
<i>acca</i>	Control	WT	1.160704	1.010451	0.982821	0.867539
		K23R	0.566442	0.626332	0.678302	0.582367
	ZnO NPs	WT	1.479388	1.453973	1.591073	1.438934
		K23R	1.031683	1.214195	1.356604	1.287882
<i>fas</i>	ZnSO <sub>4</sub>	WT	0.776469	0.768438	0.707107	0.80107
		K23R	0.534033	0.643941	0.812252	0.562529
	Control	WT	1.125058	1.006956	0.913831	0.965936
		K23R	0.82645	0.673617	0.690159	1.082975
<i>elov6</i>	ZnO NPs	WT	1.840375	1.747146	2.034959	1.164734
		K23R	1.117287	0.898132	0.929805	0.97942
	ZnSO <sub>4</sub>	WT	0.82932	1.270151	0.82645	0.750019
		K23R	0.673617	0.598739	0.545254	0.662044
<i>ppara</i>	Control	WT	1.055188	1.055188	0.912249	0.984525
		K23R	0.934651	1.14671	0.921784	1.19127
	ZnO NPs	WT	1.237561	1.387512	1.507857	1.229013
		K23R	1.154686	1.387512	1.539541	1.354256
<i>ppara</i>	ZnSO <sub>4</sub>	WT	0.597703	0.651799	0.670124	0.629597
		K23R	0.606046	0.645058	0.660898	0.836536
	Control	WT	1.058851	1.001734	1.022783	0.921784
		K23R	0.893475	0.921784	1.555631	1.263565
<i>ppara</i>	ZnO NPs	WT	0.354167	0.298851	0.355396	0.291688
		K23R	0.387562	0.373065	0.373065	0.349291

ZnSO <sub>4</sub>	WT	0.718221	0.672451	1.14671	1.237561
	K23R	1.19127	1.001734	1.012204	0.931418

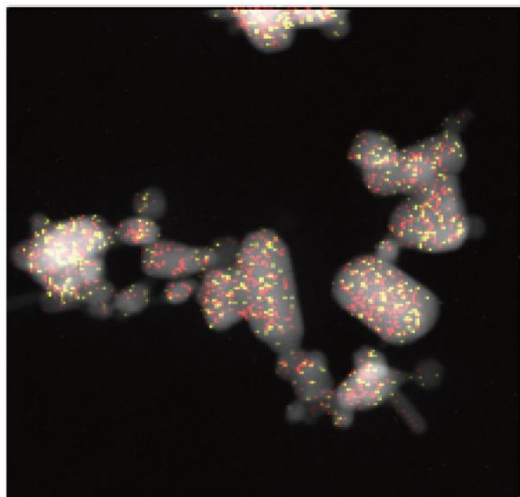
---

**Fig. S1**

**Fig. S1A**



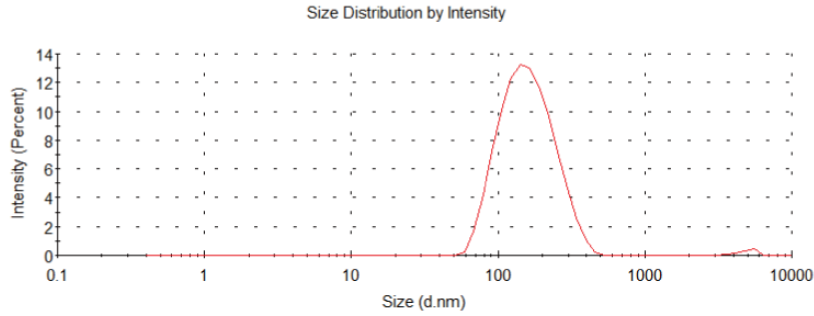
**Fig. S1B**



**Fig. S1C**

	Size (d. nm)	% Intensity	St Dev (d. nm)
Z-Average (d. nm): 147.7	Peak 1: 168.4	99.0	69.86
PdI: 0.170	Peak 2: 4979	1.0	620.0
Intercept: 0.959	Peak 3: 0.000	0.0	0.000

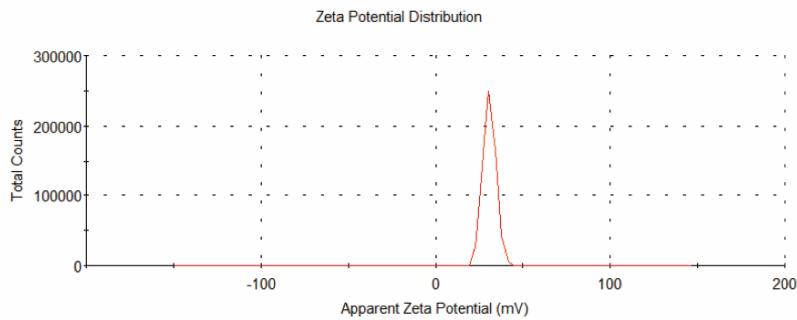
Result quality: Good



**Fig. S1D**

	Mean (mV)	Area (%)	St Dev (mV)
Zeta Potential (mV): 30.8	Peak 1: 30.8	100.0	3.73
Zeta Deviation (mV): 3.73	Peak 2: 0.00	0.0	0.00
Conductivity (mS/cm): 0.0686	Peak 3: 0.00	0.0	0.00

Result quality: Good



**Fig. S2**

**Fig. S2A**

	Control		ZnO NPs			ZnSO <sub>4</sub>			
Zn									
content	39.91454	39.4719	37.74343	49.31817	56.65319	53.86408	41.51663	43.68898	43.85137

**Fig. S2B**

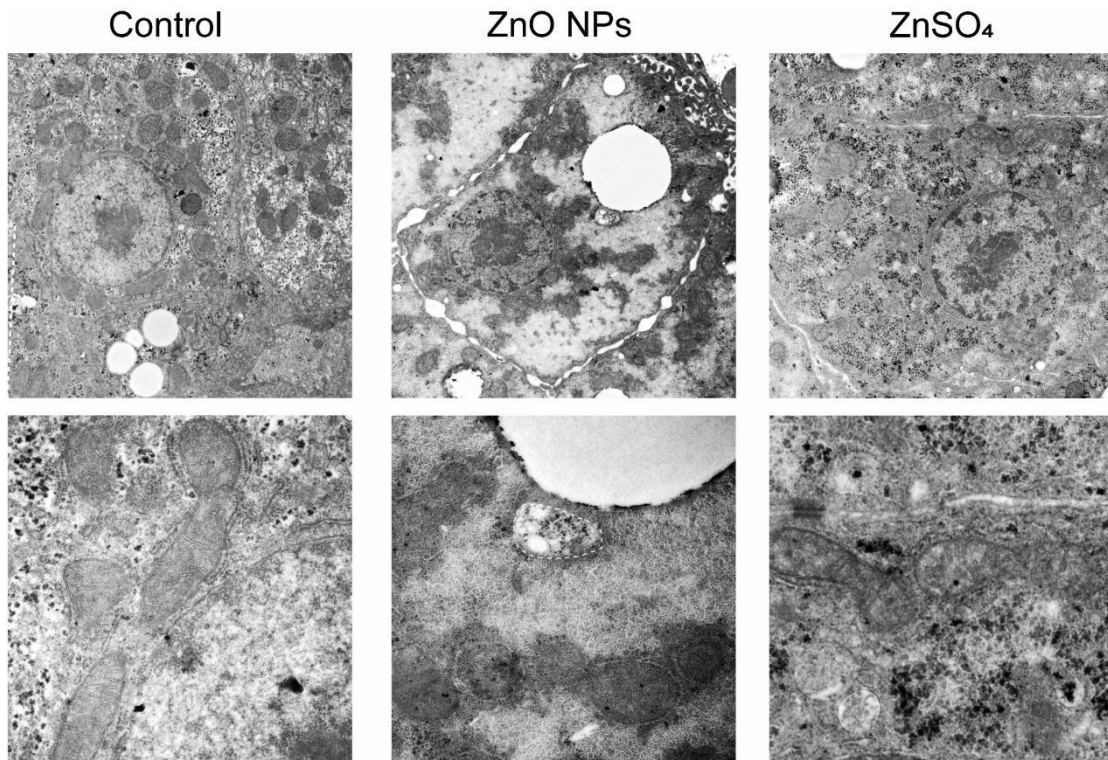
	Control			ZnO NPs			ZnSO <sub>4</sub>		
<i>znt1</i>	1.241141	0.97041	0.830278	0.97041	1.073012	1.076738	1.358172	1.538652	1.377132
<i>znt4</i>	1.168777	0.986233	0.867539	1.580083	1.270151	1.292353	0.724471	0.976032	0.962594
<i>znt5</i>	1.026927	1.052145	0.925518	1.477679	1.229723	1.251218	1.139447	1.041262	0.944965
<i>znt6</i>	1.131576	0.99539	0.887816	1.104454	1.163389	0.941696	1.204416	1.012789	1.108288
<i>znt7</i>	1.019833	1.104454	0.887816	0.728668	1.246889	1.217004	0.80571	1.171481	1.09303
<i>znt8</i>	0.99654	1.013959	0.989657	1.180993	0.898132	1.071773	0.588453	0.568408	1.046085
<i>znt9</i>	1.30586	1.22264	0.626332	1.231144	1.235419	1.086735	1.500039	1.075494	1.176907
<i>znt10</i>	0.953739	1.186463	0.883723	1.076738	0.665111	0.605696	1.150026	1.293847	1.150026

**Fig. S2C**

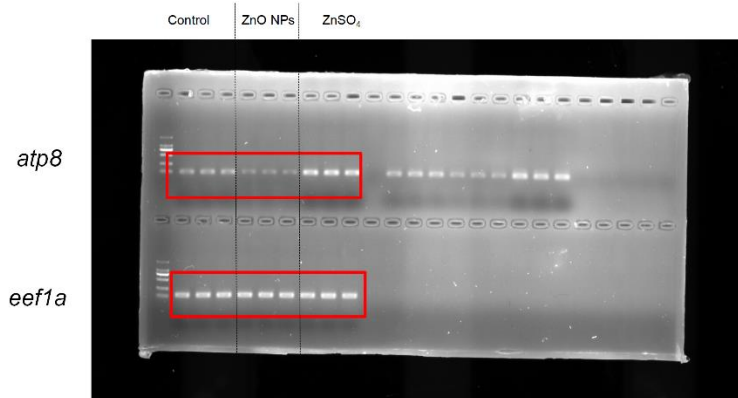
	Control			ZnO NPs			ZnSO <sub>4</sub>		
<i>zip1</i>	1.126359	1.04006	0.85362	1.004632	0.737987	0.735433	0.551589	0.575013	0.629233
<i>zip4</i>	1.063141	1.002313	0.938438	0.718636	1.196096	1.112136	0.783678	1.131576	1.08548
<i>zip5</i>	1.100633	1.044877	0.869545	0.99539	0.778265	0.708742	0.834124	0.925518	0.863539
<i>zip6</i>	1.065601	0.990801	0.947151	1.0693	0.717806	0.730353	0.865537	0.732889	0.813191
<i>zip7</i>	1.121166	0.97942	0.91067	1.071773	0.942785	1.853176	0.474671	0.505226	0.787308
<i>zip8</i>	1.128964	1.101905	0.803851	0.946058	1.075494	1.729074	0.82645	0.898132	0.776469
<i>zip9</i>	0.985094	1.016305	0.998845	0.848704	1.063141	1.447269	0.811315	0.686977	0.663576
<i>zip10</i>	1.185093	1.117287	0.755236	1.094294	1.121166	0.752623	1.209994	0.873573	0.744839
<i>zip13</i>	1.215598	0.943874	0.871557	0.777366	0.58304	0.437291	0.50406	0.521835	0.796456
<i>zip14</i>	1.16608	0.97716	0.877619	0.918064	0.980552	1.146047	1.339474	1.001156	0.74312

**Fig. S3**

**Fig. S3A**



**Fig. S3B**



**Fig. S3C**

Control		ZnO NPs			ZnSO <sub>4</sub>			
1.028114	1.021012	0.952638	0.655197	0.742262	0.737135	2.234574	2.250117	2.188587

**Fig. S3D**

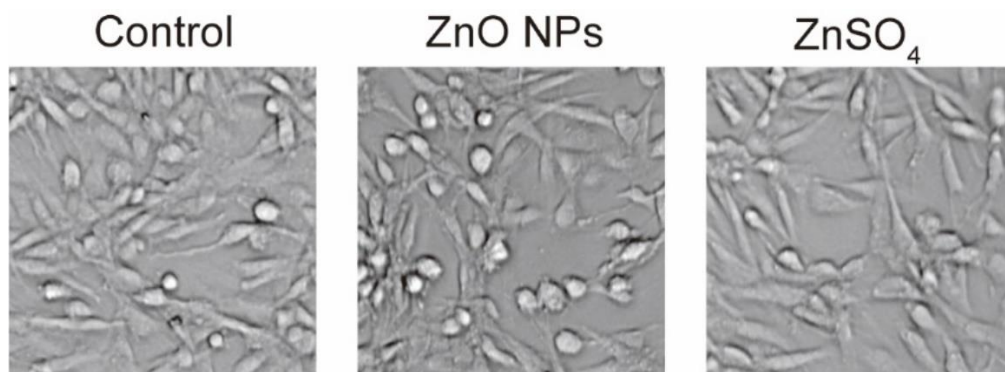
Control			ZnO NPs			ZnSO <sub>4</sub>		
81.94566	117.2979	100.7564	38.20949	56.17136	48.18563	138.8003	142.8649	125.5621

**Fig. S3E**

Control			ZnO NPs			ZnSO <sub>4</sub>		
15.78914	13.44038	20.30551	9.375015	9.290799	10.2976	33.7514	26.04105	31.94291

**Fig. S4**

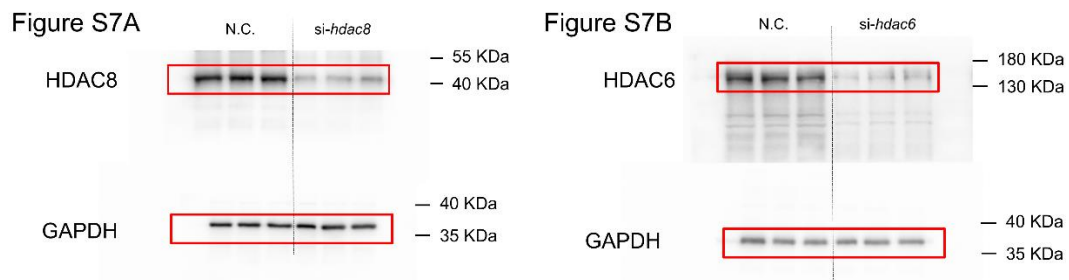
Cell viability, %						
0	87.33929	87.52355	102.8171	107.6284	101.8754	100.1556
0.2	107.2394	109.2867	90.41029	109.3072	95.54909	92.8671
0.4	95.63099	93.58366	96.20424	91.31112	93.84981	109.471
0.6	106.359	100.217	93.25608	90.12366	85.92663	97.43264
0.8	95.65147	91.5568	105.1306	84.7187	94.46401	88.67006
1	106.6252	94.34117	99.95087	83.98165	83.65409	93.21511

**Fig. S5**



**Fig. S6**

	Control			ZnO NPs			ZnSO <sub>4</sub>		
<i>hdac1</i>	1.046085	1.006956	0.949342	0.926588	0.91067	0.986233	1.563739	1.652901	1.71119
<i>hdac3</i>	1.0693	0.963707	0.97041	1.211393	0.850667	0.990801	1.773583	1.481098	1.632029
<i>hdac4</i>	1.152686	0.939523	0.923382	0.615572	0.635075	0.619854	0.843816	0.923382	0.849685
<i>hdac5</i>	1.057018	1.028114	0.920188	1.125058	1.086735	0.913831	0.870551	0.888843	0.812252
<i>hdac6</i>	1.132884	0.993092	0.888843	0.946058	0.888843	0.726986	1.248331	1.239708	1.42405
<i>hdac7</i>	1.407694	0.866537	0.819794	1.54043	1.159364	1.183724	1.167428	1.208597	1.286395
<i>hdac8</i>	1.030492	1.066832	0.909618	0.749154	0.643197	0.571701	1.225468	1.200249	1.259921
<i>hdac9</i>	1.086735	1	0.920188	1.156688	0.858565	0.840896	0.946058	1.248331	1.172835
<i>hdac10</i>	1.307369	0.886791	0.862542	1.420764	1.154019	1.076738	1.512219	1.307369	1.430646
<i>hdac11</i>	1.098093	0.965936	0.942785	0.870551	0.898132	1.464086	1.30586	1.370783	0.99654
<i>hdac12</i>	1.302846	0.89296	0.859558	0.937354	0.940609	0.983957	1.224054	1.293847	1.110852

**Fig. S7****Fig. S7A-B****Fig. S7C**

	Relative <i>hdac8</i> expression			
Control	1.077733	1.033831	0.964598	0.918913
ZnO NPs	0.848508	0.670356	0.672684	0.531448
<i>si-hdac8</i>	0.157454	0.31165	0.175921	0.332863
ZnO NPs + <i>si-hdac8</i>	0.389043	0.184667	0.150517	0.146401

**Fig. S7D**

	Relative <i>hdac6</i> expression			
Control	1.066586	1.092778	1.023137	0.839731
ZnSO <sub>4</sub>	1.422077	1.412254	1.929196	1.91587
<i>si-hdac6</i>	0.269433	0.319303	0.271307	0.25139
ZnSO <sub>4</sub> + <i>si-hdac6</i>	0.483974	0.381036	0.529609	0.387697