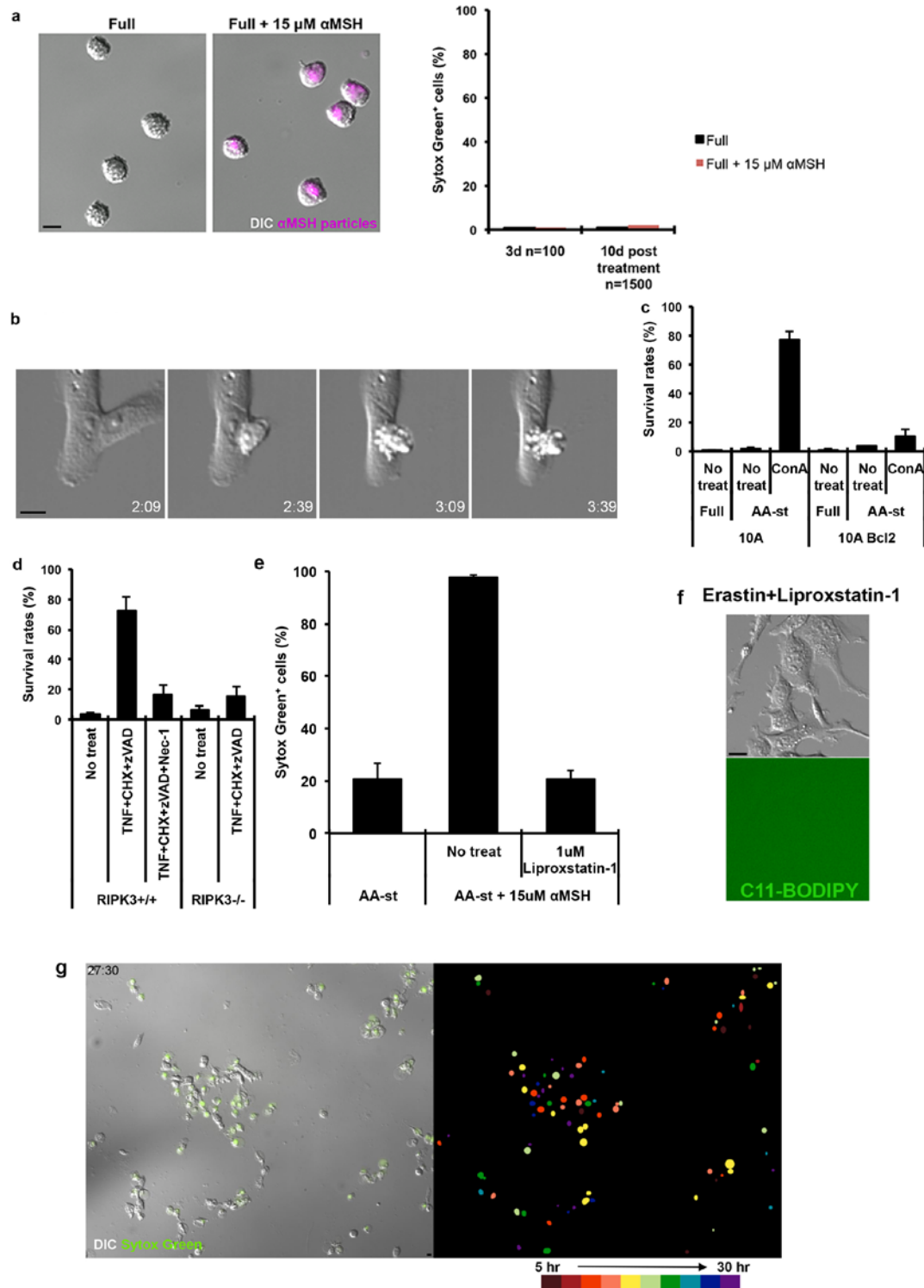
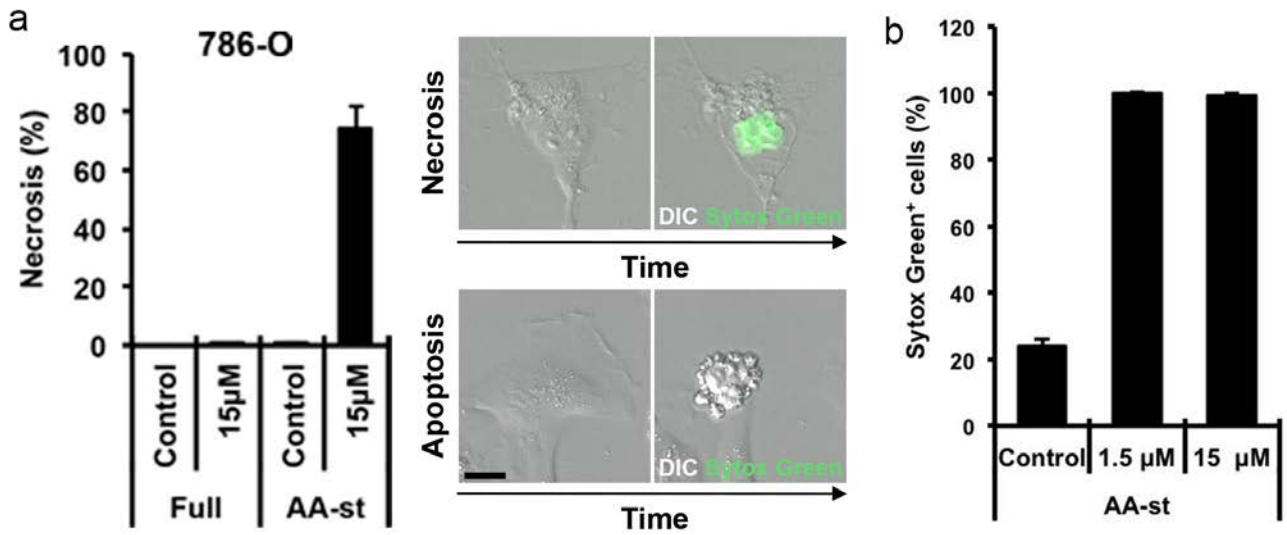


# Ultrasmall nanoparticles induce ferroptosis in nutrient-deprived cancer cells and suppress tumour growth

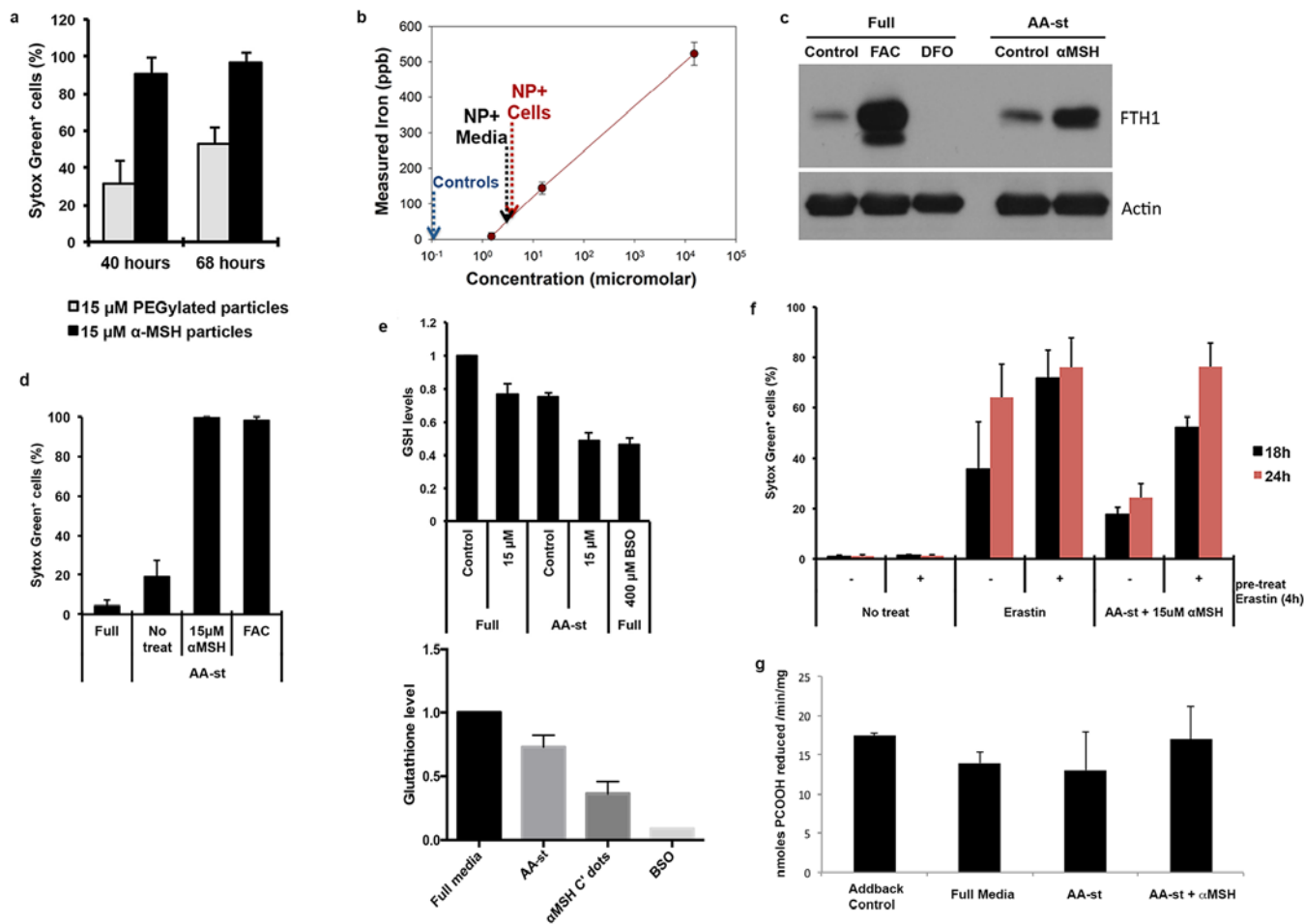
Supp Figure 1



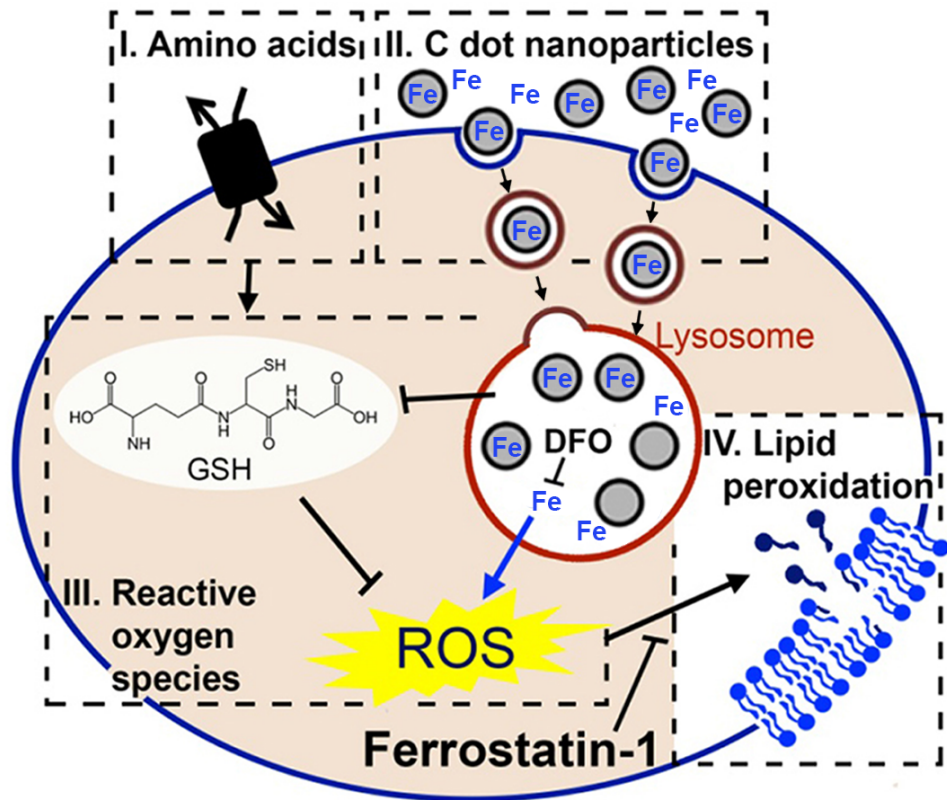
Supp Figure 2



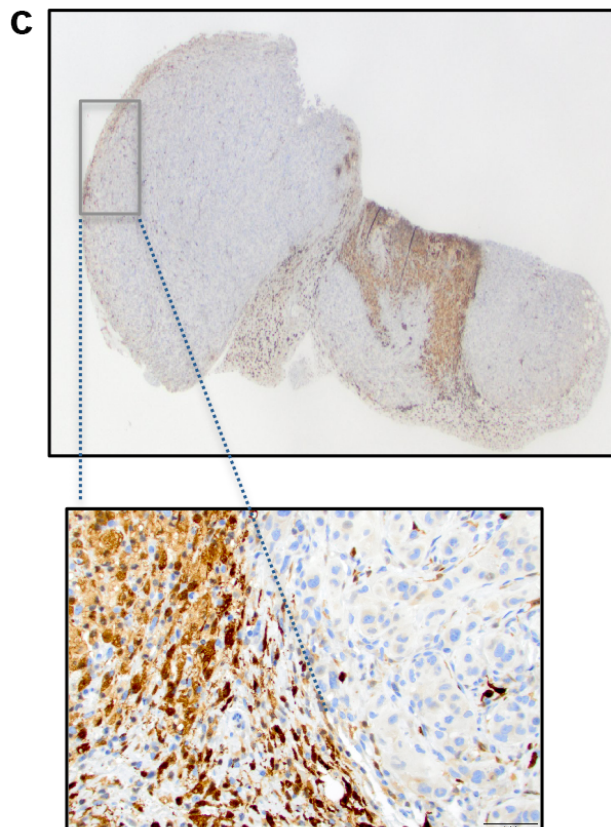
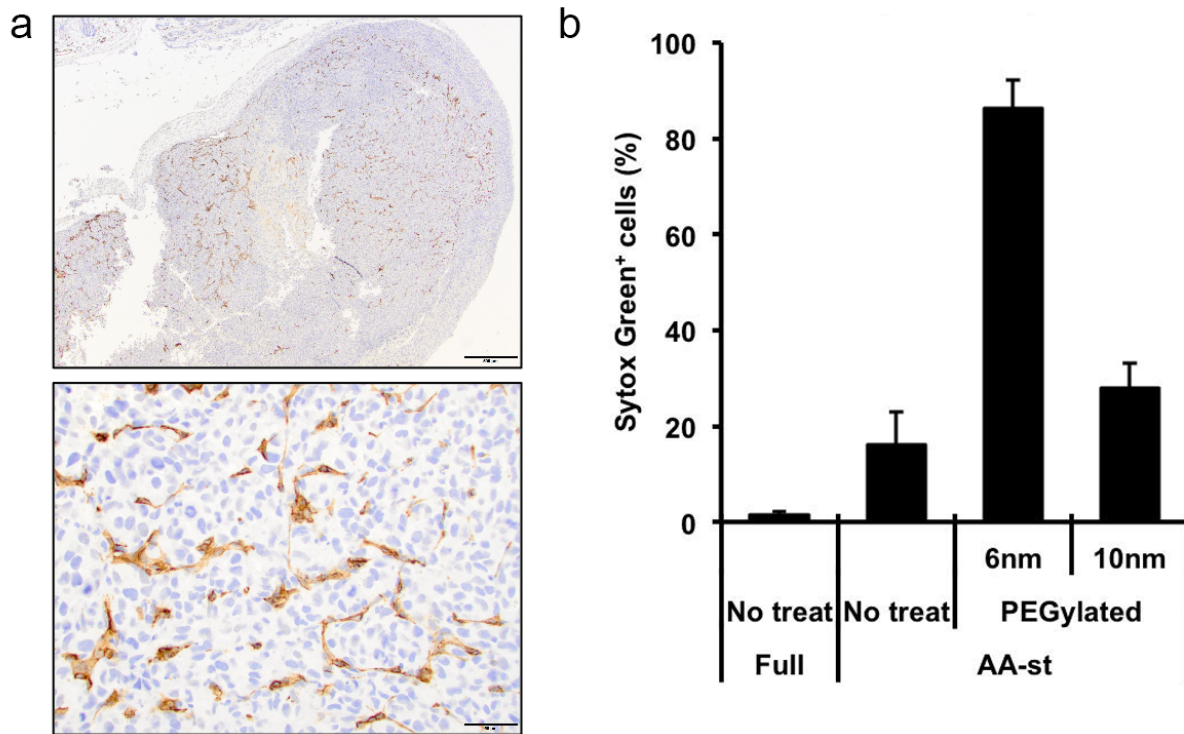
## Supp. Figure 3



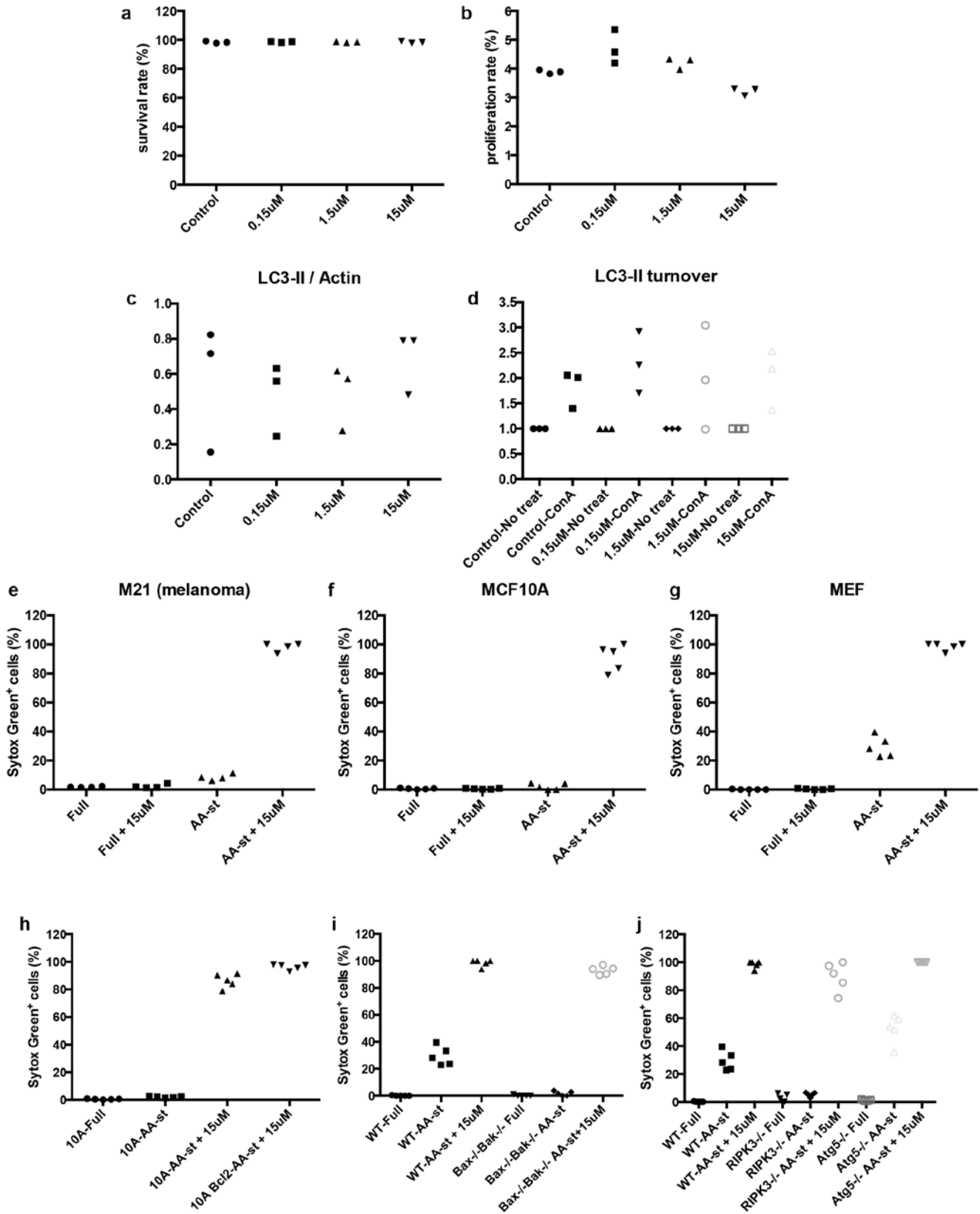
Supp Figure 4



Supp. Fig. 5

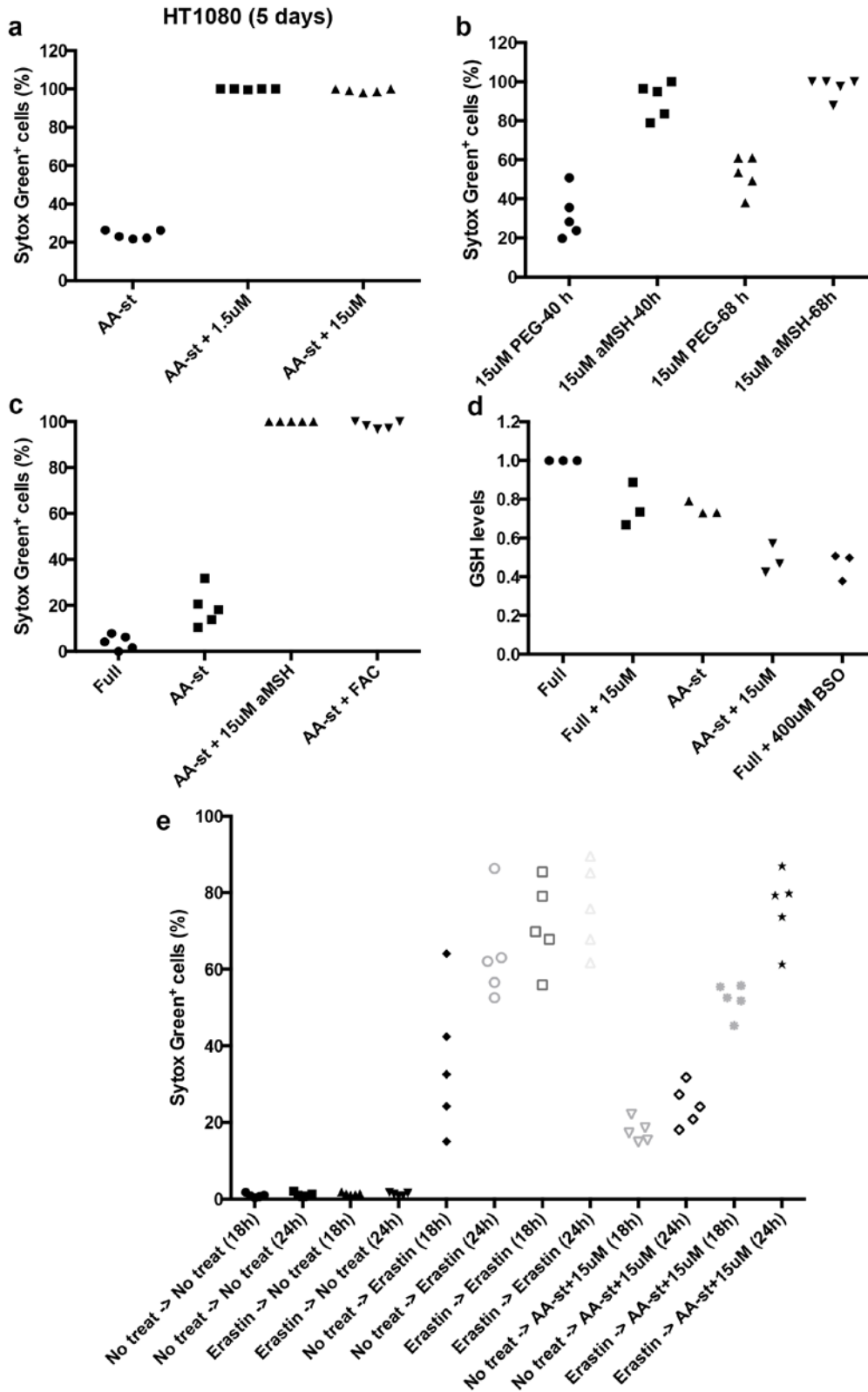


Supp. Figure 6





Supp. Figure 8





**Table S1. Iron Concentrations Measured by Microwave Plasma Atomic Emission Spectroscopy (MP-AES)**

Specimen	Iron-Containing Solution Concentrations (before purification)	<sup>†</sup> Measured Iron Concentration (ppb) +/- S.D. (after purification)	Concentration of Iron in C' dots or Cells ( $\mu\text{M}$ )	Iron-loading Capacity
C' dots, diluted full media*	$\sim 6.5 \mu\text{M}$	33.6 +/- 18.6	0.60	46.2%
C' dots, diluted AA-free media*	$\sim 6.5 \mu\text{M}$	33.9 +/- 16.3	0.61	46.9%
C' dots, $\text{Fe}^{3+}$ -doped solution	$1.5 \mu\text{M}$	8.32 +/- 12.9	0.15	50.0%
C' dots, $\text{Fe}^{3+}$ -doped solution	$15.0 \mu\text{M}$	144.7 +/- 16.3	2.58	86.0%
C' dots, $\text{Fe}^{3+}$ -doped solution	$1.5 \text{ mM}$	522.6 +/- 32.6	9.33	3.1%
C' dots only	NA	BDL	BDL	NA
C' dot-exposed HT1080 cells, AA-free media	$\sim 8.6 \mu\text{M}$	37.6 +/- 7.8	0.67	$\sim 8.0\%$
HT1080 cells, AA-free media	$\sim 8.6 \mu\text{M}$	BDL	BDL	NA

BDL, below detection limit; NA not applicable

\*iron present in undiluted full and AA-free media is  $8.6 \mu\text{M}$

<sup>†</sup>re-suspended in water or phosphate buffer solution

**Table S2.** Metabolic concentration profiles in tumor-bearing mice

		<i>HT1080</i> Particle-Exposed Female			<i>HT1080</i> Saline Vehicle Male                      Female						<i>786-O</i> Particle-Exposed Female			<i>786-O</i> Saline Vehicle Male		
<b>Metabolic profile</b>	Na (mEq/L)	151	149	153	156	156	152	152	156	152	157	157	154	155	QNS	QNS
	K (mEq/L)	8.1	9.2	8.2	9.6	9.3	10.7	9.1	8.2	8.5	8.5	8.8	10.1	8.8	QNS	QNS
	Cl (mEq/L)	111	111	111	108	109	109	117	113	112	114	115	113	110	QNS	QNS
	TCO <sub>2</sub> (mEq/L)	26	24	26	13	23	21	18	23	23	14	11	10	18	QNS	15
	Ca (mg/dL)	10.5	10.2	10.2	10.3	10.3	9.7	10.5	10.4	10.3	9.7	10.0	10.4	10.1	6.4	9.2
	P (mg/dL)	9.2	9.0	8.6	9.1	10.0	9.1	9.5	8.6	7.6	9.4	9.0	10.8	9.9	8.5	10.0
<b>Renal</b>	GLU (mg/dL)	179	184	192	108	153	149	216	164	215	142	208	224	210	149	160
	BUN (mg/dL)	12	18	19	29	28	30	19	21	23	16	17	16	24	19	21
	Crea (mg/dL)	0.2	0.2	0.24	0.12	0.12	0.03	0.20	0.23	0.21	0.10	0.11	0.13	0.18	QNS	QNS
	ALP (U/L)	29	37	58	67	71	45	73	56	48	106	95	120	71	60	55
	AST (U/L)	140	293	120	113	67	119	365	149	209	188	156	1100	68	214	43
	ALT (U/L)	15	94	30	24	18	25	158	57	71	87	66	509	34	144	21
	GGT (U/L)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	TBIL (mg/dL)	0.8*	0.8*	0.9*	0.2	0.3	0.4	0.3	0.2	0.3	0.8*	0.7*	0.9*	0.2	0.2	0.1
	DBIL (mg/dL)	0.1	0.1	0.1	0.0	0.0	0.0	0.0	0.0	0.1	0.1	0.1	0.1	0.1	0.0	0.0
	IBIL (mg/dL)	0.7*	0.7*	0.8*	0.2	0.3	0.4	0.3	0.2	0.2	0.7*	0.6*	0.8*	0.1	0.2	0.1
<b>Hepatic function</b>	TP (g/L)	4.9	4.9	5.1	5.3	5.2	5.3	5.3	5.3	5.3	4.9	5.1	5.4	5.0	5.6	5.3
	ALB (g/L)	3.8	3.9	3.9	3.3	3.1	3.1	3.3	3.2	3.2	3.1	3.2	3.3	2.9	3.3	3.0
	GLOB (g/dL)	1.9	2.0	2.0	2.0	2.1	2.2	2.0	2.1	2.1	1.8	1.9	2.1	2.1	2.3	2.3
	CHOL (mg/dL)	86	83	88	82	98	104	99	108	118	72	71	88	99	67	90
	TRIG (mg/dL)	94	74	96	89	159	127	84	88	85	95	94	94	89	151	92
	CK (U/L)	442	506	325	50	122	255	616	300	358	63	117	458	100	53	36

Na, sodium; K, potassium; Cl, chloride; TCO<sub>2</sub>, total carbon dioxide; Ca, calcium; P, phosphorus; GLU, glucose; BUN, blood urea nitrogen; Crea, creatinine; ALP, alkaline phosphatase; AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, gamma-glutamyl transferase; TBIL, total bilirubin; DBIL, direct bilirubin; IBIL, indirect bilirubin; TP, total protein; ALB, albumin; GLOB, globulin; CHOL, cholesterol; TRIG, triglyceride; CK, creatine kinase; \*, elevated relative to normal values

**Table S3.** Hematologic profiles in tumor-bearing mice

		786-O Particle-Exposed Female			786-O Saline Vehicle Male		
<b>Hematology</b>	RBC (M/uL)	9.87	9.79	10.50	9.53	9.30	9.13
	HGB (g/dL)	15.3	15.0	16.5	14.4	14.2	14.0
	HCT (%)	52.1	52.0	57.4	49.8	48.7	48.2
	MCV (fL)	52.8	53.1	54.7	52.3	52.4	52.8
	MCH (pg)	15.5	15.3	15.7	15.1	15.3	15.3
	MCHC (g/dL)	29.4	28.8	28.7	28.9	29.2	29.0
	RDW-SD (fL)	31.4	32.3	31.0	29.9	29.3	30.7
	RDW-CV (%)	23.5	23.5	23.0	22.5	22.2	22.3
	RET (K/uL)	436.3	470.9	573.3	487.9	444.5	454.7
	RET (%)	4.42	4.81	5.46	5.12	4.78	4.98
	PLT (K/uL)	908	650	682	365	294	985
	PDW (fL)	7.0	7.0	7.1	7.8	8.2	6.6
	MPV (fL)	6.2	6.1	6.5	6.7	6.9	6.1
	WBC (K/uL)	2.25	1.93	2.21	3.22	2.73	3.75
	NEUT (K/uL)	0.86	0.82	0.70	1.65	1.32	2.36
	LYMPH (K/uL)	0.84	0.84	0.80	1.06	1.01	0.93
	MONO (K/uL)	0.46	0.14	0.58	0.34	0.28	0.35
	EO (K/uL)	0.09	0.13	0.12	0.16	0.10	0.10
	BASO (K/uL)	0.00	0.00	0.01	0.01	0.02	0.01
	NEUT (%)	38.3	42.5	31.7	51.2	48.3	62.9
	LYMPH (%)	37.3	43.5	36.2	32.9	37.0	24.8
	MONO (%)	20.4	7.3	26.2	10.6	10.3	9.3
	EO (%)	4.0	6.7	5.4	5.0	3.7	2.7
BASO (%)	0.0	0.0	0.5	0.3	0.7	0.3	

RBC, red blood cell; HGB, hemoglobin concentration; HCT, hematocrit; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; RDW-SD and RDW-CV, red blood cell distribution width standard deviation and coefficient of variance; RET, reticulocyte relative and absolute counts; PLT, platelet count; PDW, platelet distribution width; MPV, mean platelet volume; WBC, white blood cell; and relative and absolute counts of NEUT, neutrophils, LYMPH, lymphocytes, MONO, monocytes, EO, eosinophils, BASO, basophils

**Table S4.** Histopathologic profiles in tumor-bearing mice

	<i>HT1080 Particle-Exposed Female</i>		<i>HT1080 Saline Vehicle Female</i>		<i>786-O Particle-Exposed Female</i>		<i>786-O Saline Vehicle Male</i>	
<b>Tumor H&amp;E</b>	SQ tumor consistent with HT1080	SQ tumor consistent with HT1080	SQ tumor consistent with HT1080	SQ tumor consistent with HT1080	SQ tumor consistent with 786-O	SQ tumor consistent with 786-O	SQ tumor consistent with 786-O	SQ tumor consistent with 786-O
<b>Tumor Mac2</b>	Marked	Marked	Mild	Mild	Marked	Marked	ND	ND
<b>Liver H&amp;E</b>	N.	Hepatitis, histiocytic and neutrophilic, 1, MFR; Extramedullary hematopoiesis, 1.	N.	N.	N.	N.	N.	N.
<b>Kidney H&amp;E</b>	Cortical tubular cyst, F, U.	N.	N.	N.	N.	N.	Cortical tubular necrosis and regeneration, 1, MF, U.	N.

SQ, subcutaneous; N, normal; Mac2, macrophage immunohistochemical marker; N: Normal, F: Focal, FE: Focally extensive, MF: Multifocal, MFR: Multifocal random, D: Diffuse, U: Unilateral, 1: Minimal, 2: Mild, 3: Moderate, 4: Marked.