

Literature Report

Reporter: Wang Guangying

Date: 2020-03-31

A bioorthogonal system reveals antitumour immune function of pyroptosis

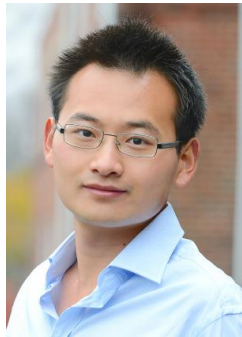
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刘志博（北京大学 特聘研究员）

主要的研究方向如下：

1. 以B-F键为基础的¹⁸F通用标记法
2. 以三氟化硼（-BF₃-）与羧酸根（-COO⁻）的相似性为基础的化学生物学研究
3. 以炎症特异性的放射性探针为基础，采用PET影像支持临床中癌症与炎症的鉴别
4. 以硼中子捕获治疗（BNCT）为基础的癌症诊疗一体化平台



邵峰（北京生命科学研究所研究员、副所长）

研究兴趣集中在病原细菌感染宿主和宿主先天性免疫防御的分子机制。

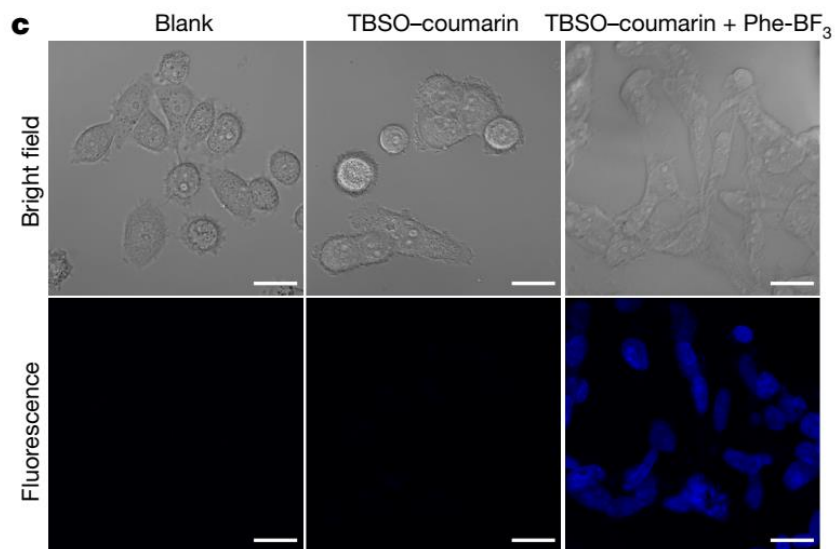
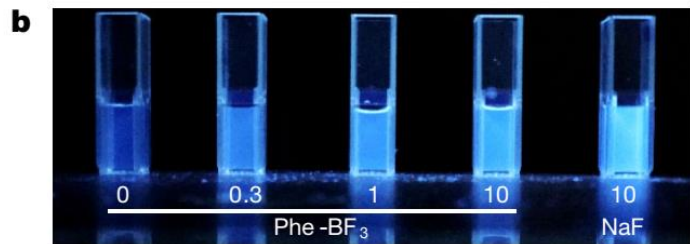
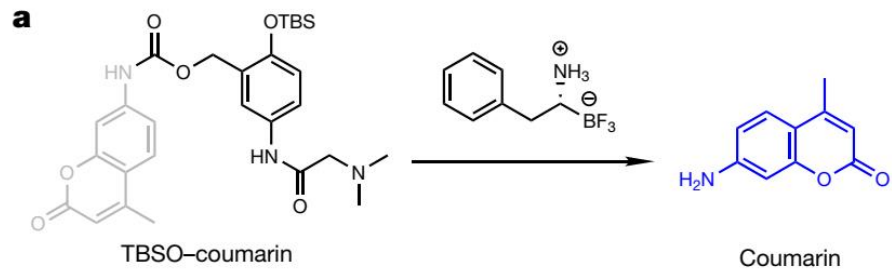
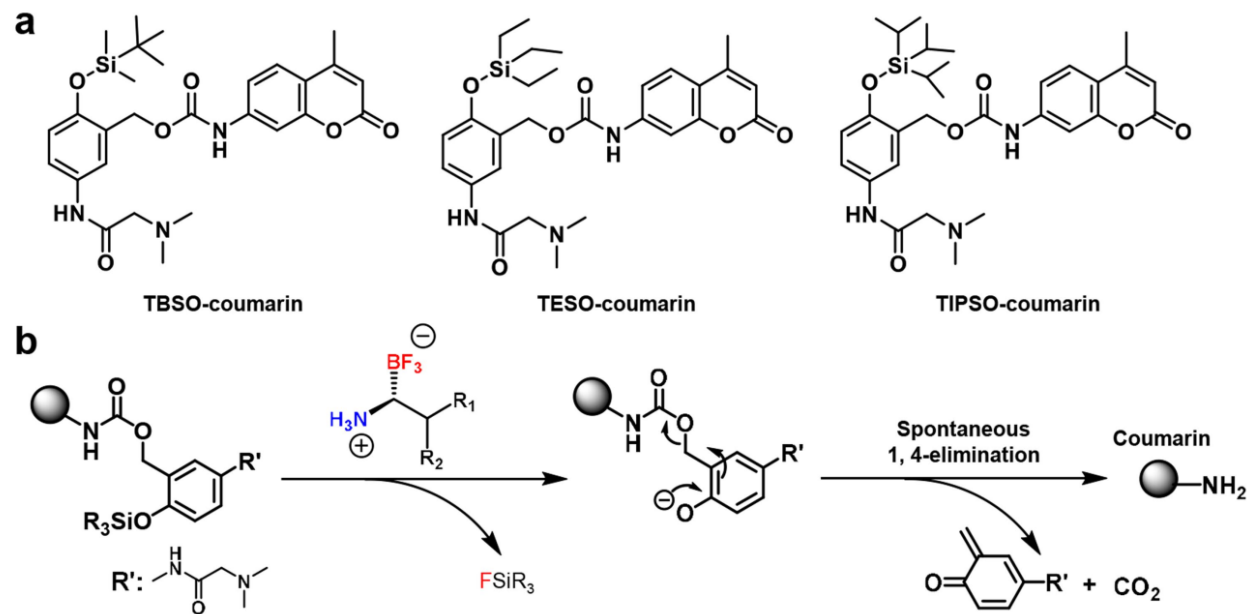
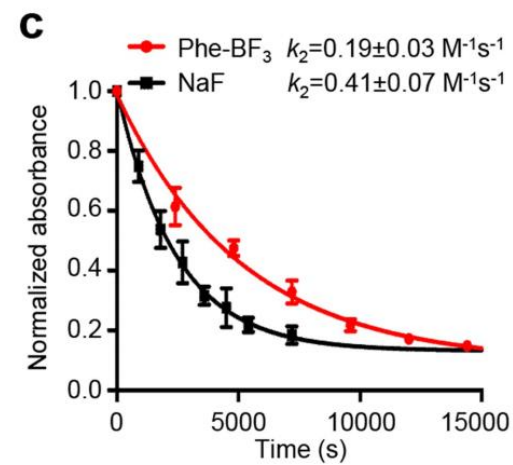


Fig. 1 (a, b, c)

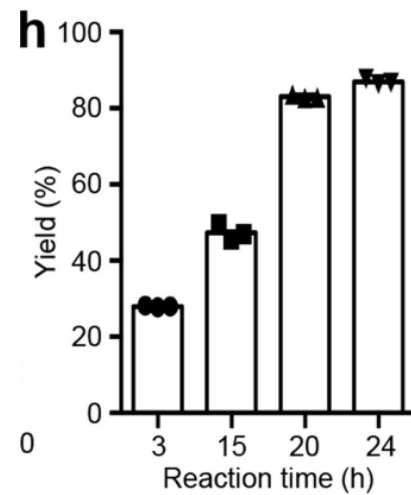
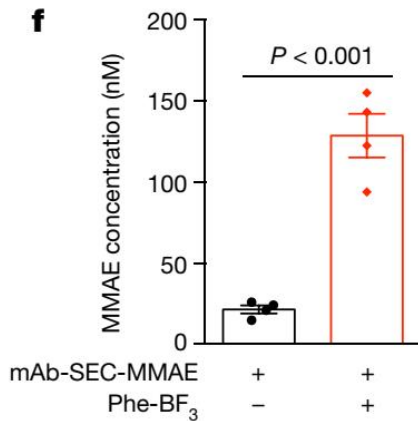
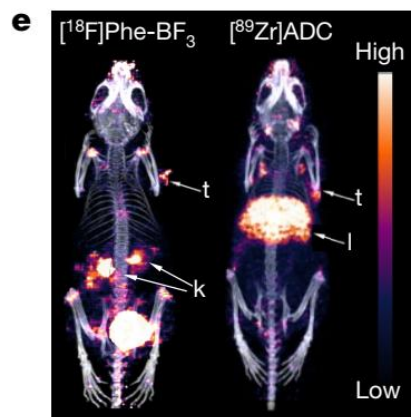
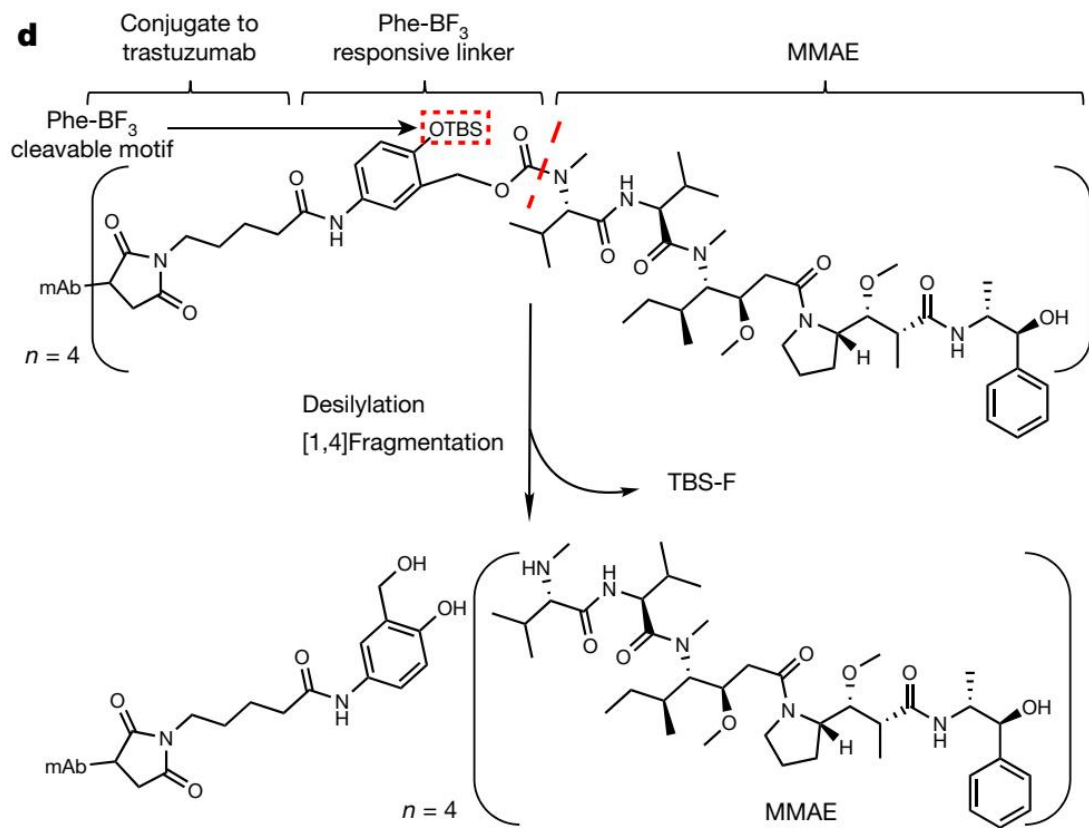
Human BGC823 cell



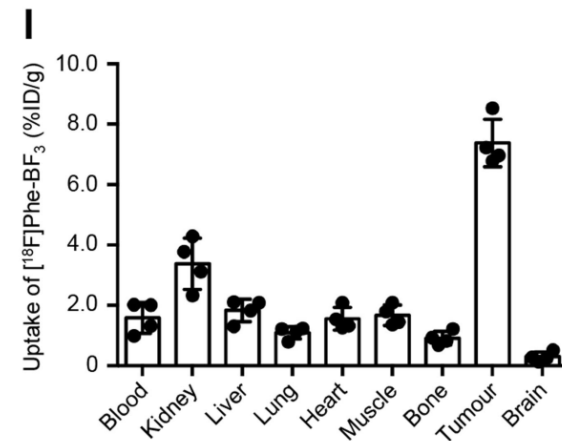
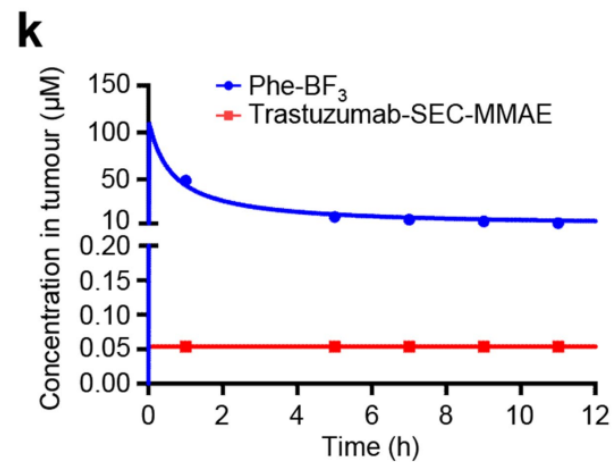
Extended Data Fig. 1 (a, b)



Extended Data Fig. 2c

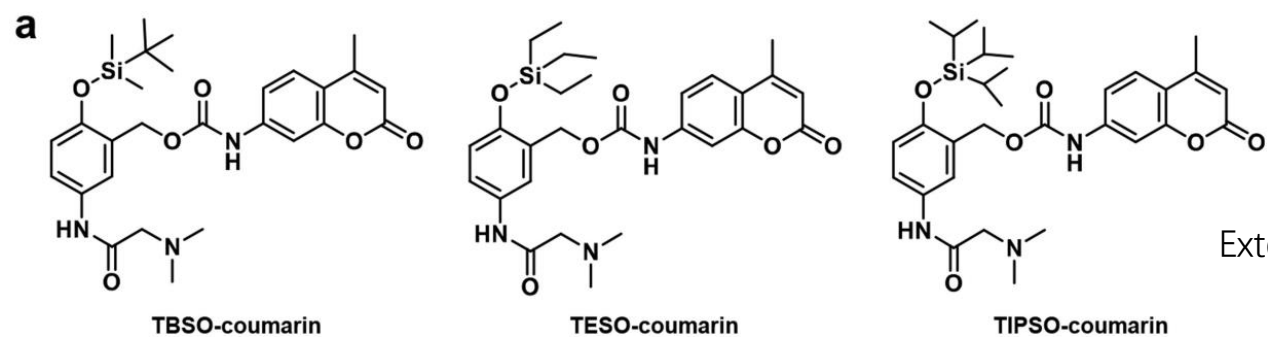
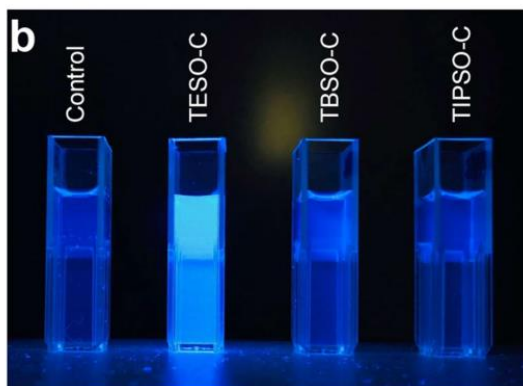
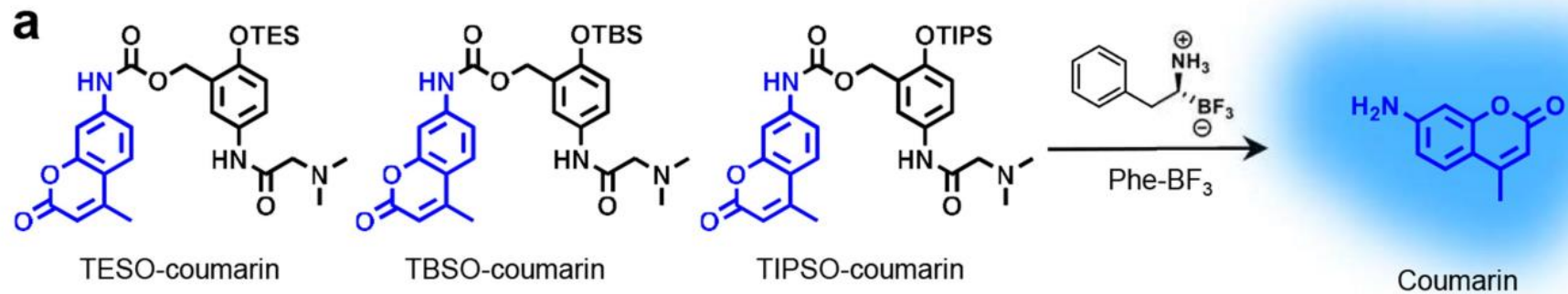


Extended Data Fig. 2h



Extended Data Fig. 2(k, l)

Fig. 1 (d, e, f)



Extended Data Fig. 1a

e

	TESO-coumarin	TBSO-coumarin	TIPSO-coumarin
	98%	19%	ND
NaF	100%	100%	ND
PBS	ND	ND	ND

g

Organofluorines					
Name	Phe-BF ₃	FDG	Leflunomide	5-FU	Capecitabine
Yield	95%	ND	ND	ND	ND

Extended Data Fig. 3 (a, b, e, g)

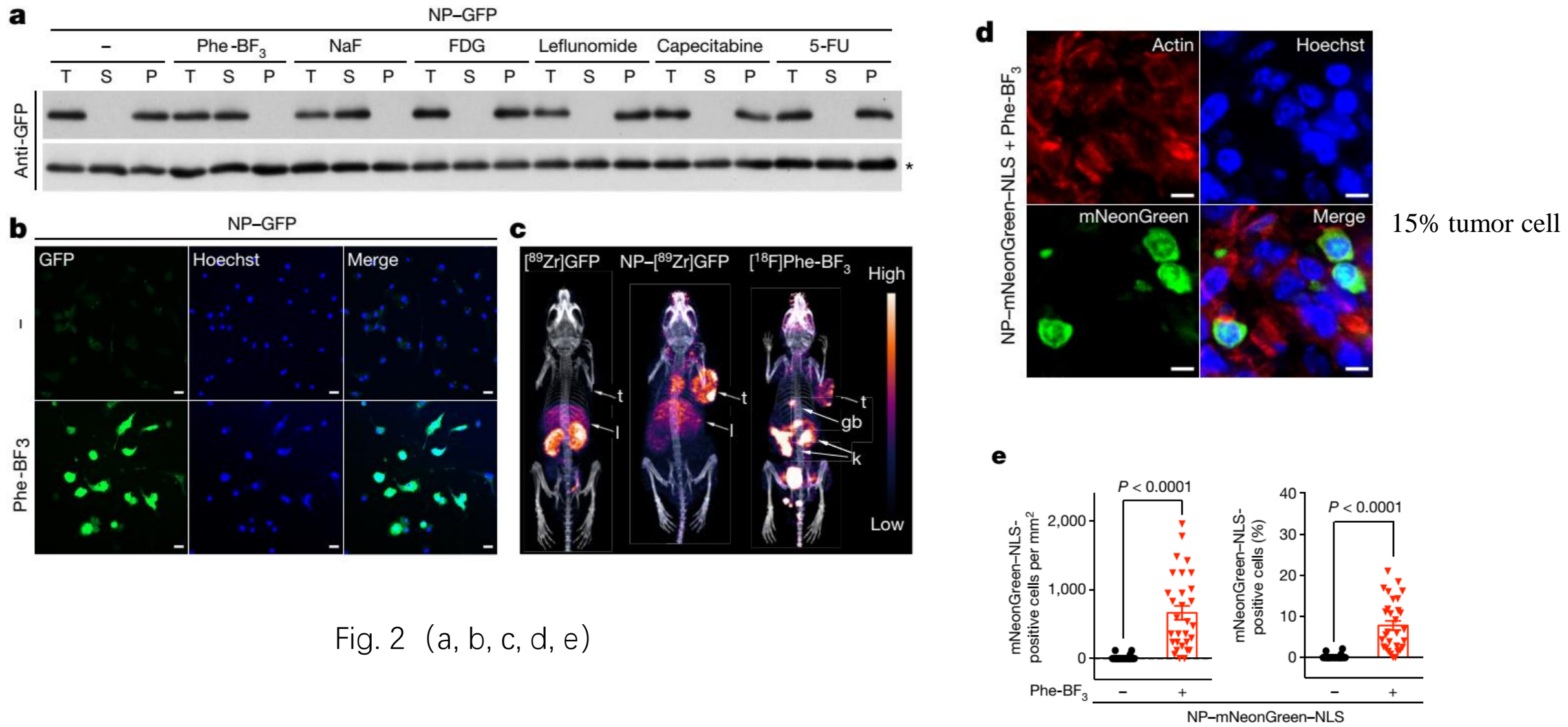


Fig. 2 (a, b, c, d, e)

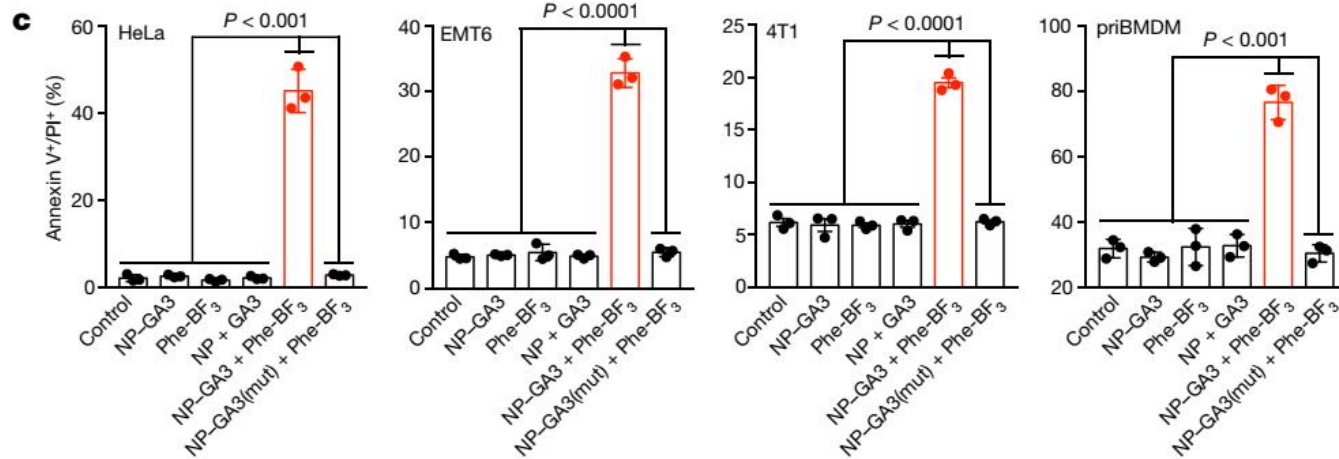
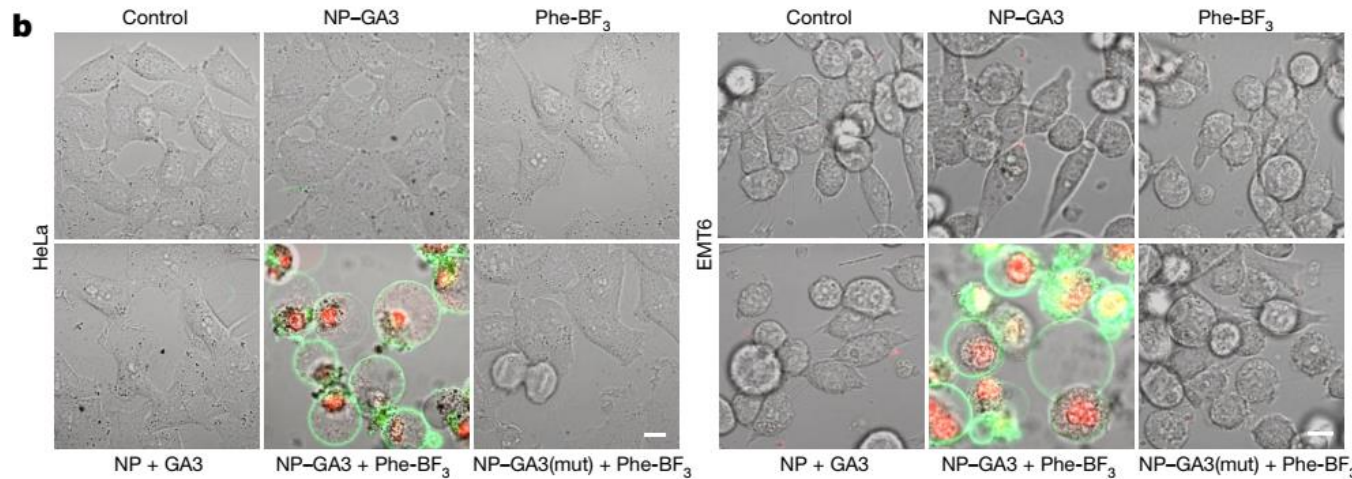
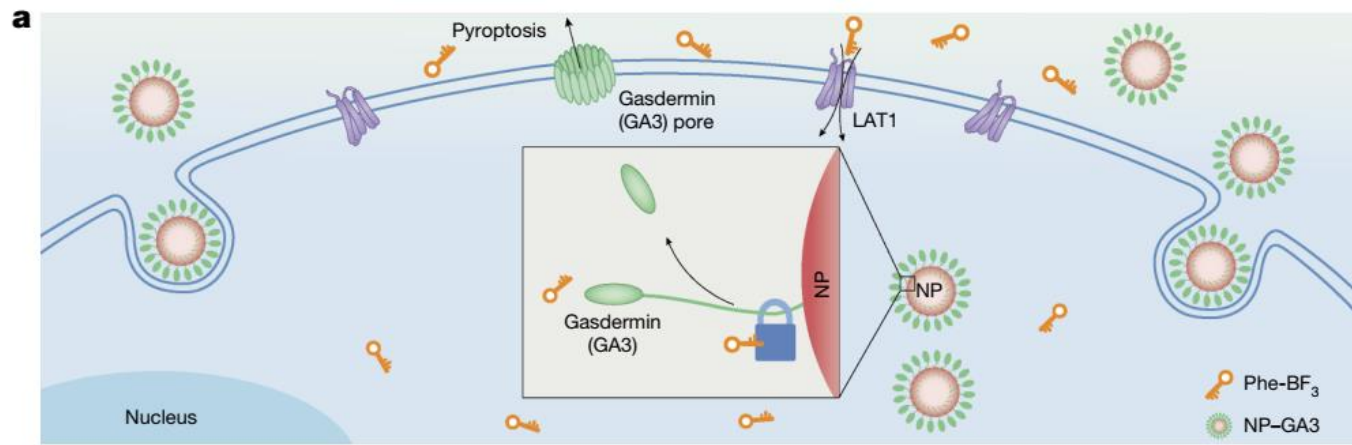


Fig. 3 | Phe-BF₃ desilylation releases gasdermin from NP-GSDMA3 to induce pyroptosis.

a, Cartoon of the experimental design. Purified GSDMA3(N + C) was conjugated to a nanoparticle to obtain NP-GSDMA3. **b**, **c**, HeLa, EMT6 or 4T1 cells, or primary BMDMs, were treated as indicated. NP + GSDMA3, nanoparticles mixed with the GSDMA3(N + C) complex. **b**, Confocal images of the treated HeLa and EMT6 cells. Scale bars, 20 μ m. **Propidium iodide (PI)** and **annexin V-fluorescein isothiocyanate (FITC)** were added to the cells 15 min before imaging. **c**, Flow-cytometry measurements of cells positive for propidium iodide and annexin V. priBMDM, primary BMDM

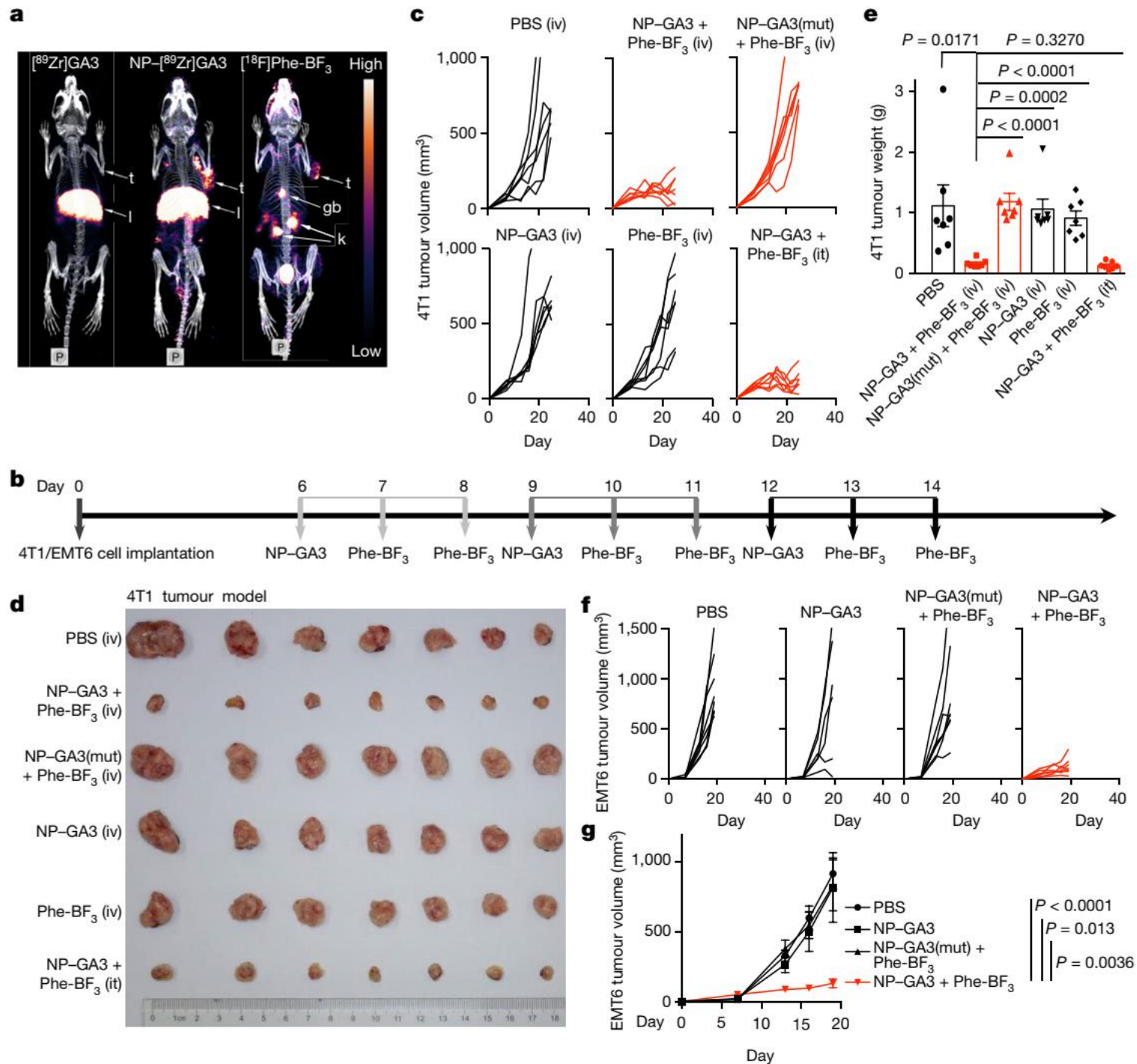


Fig. 4 | Treatment with NP-GSDMA3 and Phe-BF3 causes tumour regression in mice.

a, PET-computed tomography images of mice bearing 4T1 tumours that intravenously injected with $[^{89}\text{Zr}]$ GSDMA3, NP- $[^{89}\text{Zr}]$ GSDMA3 or $[^{18}\text{F}]$ PheBF3. **b-g**, BALB/c mice were implanted subcutaneously with 4T1 (**c-e**) or EMT6 (**f, g**) cells, followed by **intravenous (iv)** or **intratumoural (it)** injection of NP-GSDMA3 or Phe-BF3 alone, or in combination. **b**, Treatment scheme. In **c-e**, $n = 7$ mice per group. In **f, g**, $n = 8$ mice for PBS and NP-GSDMA3 and 7 mice for NP-GSDMA3 + Phe-BF3. **c, f**, Tumour volume of an individual mouse. **d**, Photographs of representative tumours on day 26. **e, g**, Average tumour weight or volume. Mean \pm s.e.m., two-tailed unpaired Student's t -test. GA3, GSDMA3(N + C).

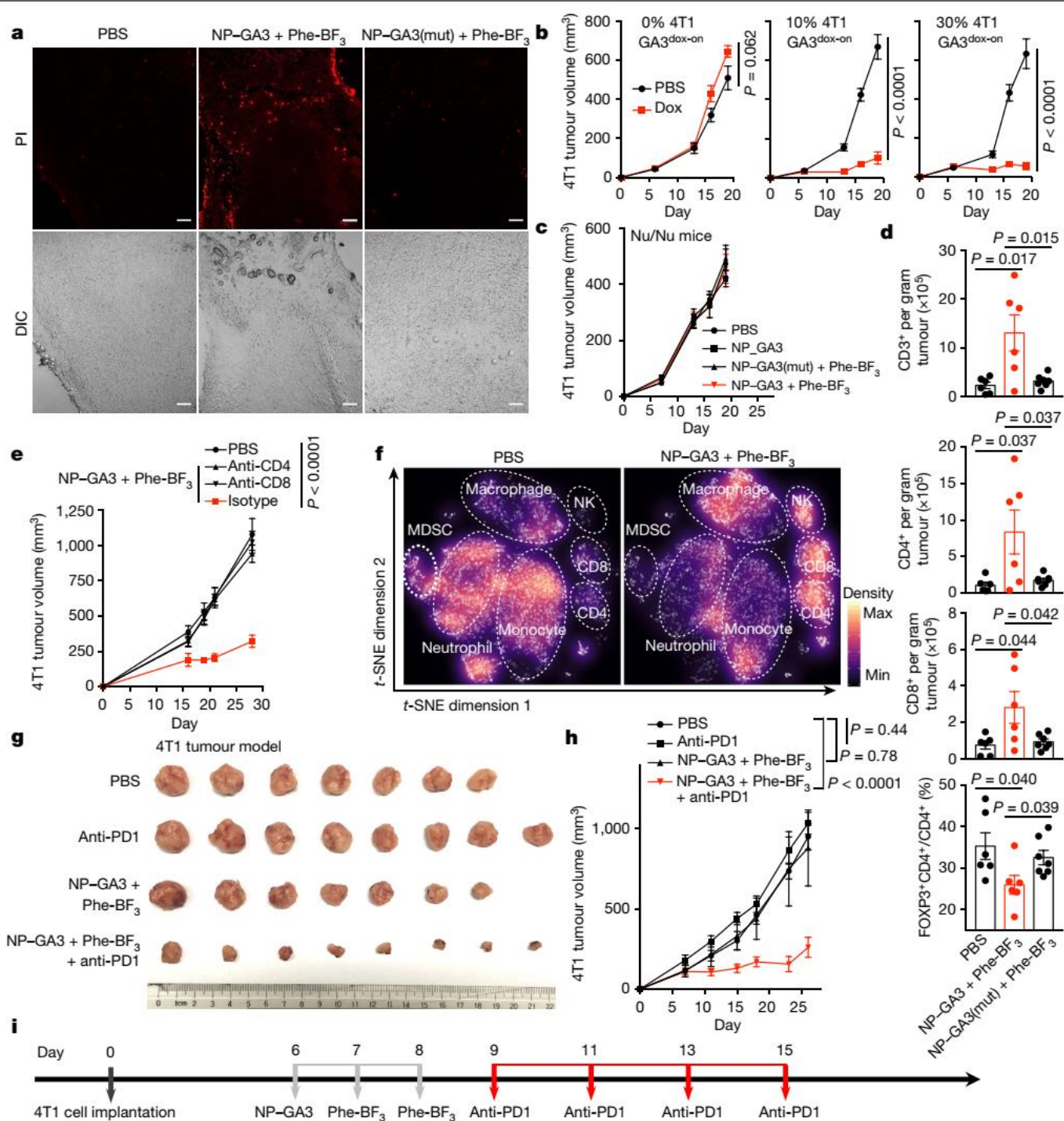


Fig. 5 | A low level of tumour-cell pyroptosis induces effective antitumour immunity and synergizes with anti-PD1 blockade.

Thanks !