

**Supplementary Table S1. Drugs described in this paper that exploit GSH to promote cell death.**

Experimental Model	Tumor Types	Cell Lines	Drugs or Reagents	Effect on GSH	Mechanism Related to GSH	Reference
4T1 tumor-bearing mice	Breast cancer	4T1, MCF-7, ADR, L02	LPOgener (FAC + Phosphatidylcholine)	GSH oxidation coupled to Fe <sup>3+</sup> reduction.	GSH-responsive metal reduction triggers lipid peroxidation for ferroptosis.	191
Murine orthotopic breast cancer model	Breast cancer	4T1, HC11	VTPA (MnO <sub>2</sub> -spiked organosilica)	GSH oxidation coupled to high-valence Mn reduction; cleaves disulfide bonds.	GSH-responsive degradation releases Mn and Fe, generating ROS storm and activating NLRP3 inflammasome for pyroptosis.	186
4T1 tumor-bearing BALB/c mice	Breast cancer	4T1, A549, U87	TPEN-loaded disulfide-linked poly(acrylic acid) shell	Cleaves disulfide shell; GSH oxidation coupled to Cu <sup>2+</sup> reduction.	GSH-responsive degradation releases TPEN, and GSH contributes to TPEN-Cu <sup>2+</sup> to TPEN-Cu <sup>+</sup> reduction, inducing Fenton-like reaction and following cell death.	185
4T1 xenograft model	Breast cancer	4T1	PNM (GSH-activatable prodrug nanomicelles)	GSH-responsive crosslinker activation	GSH-responsive disassembly releases prodrugs, triggering GSDME-mediated pyroptosis.	220
Athymic mice bearing 5637 tumors	Bladder cancer	5637, MCF-7, MCF-10A, SV-HUC-1	GOx@[Cu(tz)] (glucose oxidase (GOx)-engineered nonporous Cu <sup>+</sup> 1,2,4-triazolate coordination polymer nanoplatfom)	Consumes ~80% of GSH via a coordination reaction; GSH-responsive biodegradation of GOx@[Cu(tz)].	GSH-responsive degradation releases Cu <sup>+</sup> for cuproptosis (DLAT aggregation) and activates GOx for starvation therapy.	216
Orthotopic glioblastoma model	Glioblastoma	U87, U251	HF <sub>n</sub> -Cu-REGO (heavy-ferritin-Cu <sup>2+</sup> -regorafenib) nanoplatfom	Decreases GSH and increases GSSG/GSH ratio; GSH oxidation coupled to Cu <sup>2+</sup> reduction.	GSH-responsive degradation releases Cu <sup>2+</sup> , GSH-mediated reduction generates Cu <sup>+</sup> , and GSH depletion impairs GPX4 pathway, causing lipid peroxidation-mediated ferroptosis and cuproptosis.	221
H22 tumor-bearing mice	Hepatocellular carcinoma	HepG2, H22	Au nanoclusters-Cu <sup>2+</sup> @SA-HA platform (nanoclusters with Cu <sup>2+</sup> an in situ cross-linking composite gel of sodium alginate /hyaluronic acid)	GSH oxidation coupled to Cu <sup>2+</sup> reduction.	GSH contributes to Cu <sup>2+</sup> to Cu <sup>+</sup> reduction; and depletes GSH enabling ROS-mediated cell death and cuproptosis.	194
4T1 tumor-bearing BALB/c mice	Breast cancer	4T1, CT26	Cu-TBB (Copper-Bacteriochlorin)	GSH-mediated nanosheet disassembly; GSH oxidation coupled to Cu <sup>2+</sup> reduction.	GSH-responsive degradation releases Cu <sup>2+</sup> and GSH-mediated reduction generates Cu <sup>+</sup> , generating •OH and O <sub>2</sub> • <sup>-</sup> for GSDMD-mediated pyroptosis.	222
A549 xenograft model	Lung cancer	A549, LLC	Na <sub>2</sub> S <sub>2</sub> O <sub>8</sub> liquid nanoparticles	Cleaves disulfide bonds for activation.	GSH-responsive disassembly releases persulfate to generate •SO <sub>4</sub> <sup>-</sup> / <sup>-</sup> •OH radicals, inducing ferroptosis and pyroptosis.	219
Pancreatic cancer mouse model	Pancreatic cancer	Miapaca-2, Pan02, Panc-1	Pt-In NP (PHDT-Pt-In polymer)	Cleaves disulfide bonds and reduces Pt <sup>4+</sup> to Pt <sup>2+</sup> .	GSH-responsive degradation releases Pt <sup>4+</sup> and GSH-mediated reduction generates Pt <sup>2+</sup> , amplifying CASP3/GSDME-mediated pyroptosis.	218
4T1 tumor-bearing BALB/c mice	Breast cancer	4T1	GOx + Cu-based yolk-shell nanoplatfom	GSH oxidation coupled to Cu <sup>2+</sup> reduction.	GSH contributes to Cu <sup>2+</sup> to Cu <sup>+</sup> reduction, causing DLAT aggregation-mediated cuproptosis and amplifying ROS-mediated pyroptosis.	187

Experimental Model	Tumor Types	Cell Lines	Drugs or Reagents	Effect on GSH	Mechanism Related to GSH	Reference
Human NSCLC xenografts	Non-small cell lung cancer	H1299, H2009, PC9, A549	Cysteine starvation	CHAC1 catabolizes GSH to mobilize cysteine.	GSH-derived cysteine sustains mitochondrial Fe-S cluster synthesis, which potentiates lipid peroxidation for ferroptosis.	210
4T1 and CT26 tumor models	Breast and colorectal cancer	4T1, CT26	Platelet membrane-coated nanosystem and radiotherapy	GSH oxidation coupled to Cu <sup>2+</sup> reduction.	GSH contributes to Cu <sup>2+</sup> to Cu <sup>+</sup> reduction, causing DLAT aggregation and cuproptosis.	193
HeLa tumor-bearing nude mice	Cervical carcinoma	HeLa, A549, MCF-7	tumor microenvironment-responsive photosensitizer (BODIPY)	GSH replaces nitrophenol via S <sub>N</sub> Ar reaction.	High GSH-triggered chemical transformation from OFF to ON state triggers ROS generation, inducing CASP1/GSDMD-mediated pyroptosis.	223
CT26 tumor-bearing BALB/c mice	Colorectal cancer	CT26, L02	F127-MOF-199 NPs	Depletes GSH in TME; GSH oxidation coupled to Cu <sup>2+</sup> reduction.	GSH-responsive degradation releases Cu <sup>2+</sup> and GSH contributes to Cu <sup>2+</sup> to Cu <sup>+</sup> reduction, inducing pyroptosis and cuproptosis	189
4T1 tumor-bearing BALB/c mice	Breast cancer	4T1	Cu-NC@PEG (DSPE-PEG2000modified copper-nitrogen-doped carbon-based photocatalysts)	GSH-dependent radical generation.	GSH-mediated Cu redox promotes ROS and cuproptosis coupled with pyroptosis (CASP1/IL-1β).	188
Hepa1-6 tumor-bearing C57BL/6J mice	Hepatocellular carcinoma	Hepa1-6, NIH-3T3	D@LADFe (encapsulating doxorubicin and coordinating Fe <sup>3+</sup> into chimeric peptide nanoparticles)	GSH oxidation coupled to Fe <sup>3+</sup> reduction.	GSH-mediated reduction generates Fe <sup>2+</sup> , causing Fenton reactions and driving ferroptosis.	190
4T1 tumor-bearing BALB/c mice	Triple negative breast cancer	MDA-MB-231, MCF-7, 4T1, A549	Cu <sup>2+</sup> dipyrrophenazine complex	Degrades and depletes GSH.	GSH contributes to Cu <sup>2+</sup> to Cu <sup>+</sup> reduction, triggering ROS storm, causing cuproptosis and apoptosis.	184
CT26/4T1 tumor-bearing BALB/c mice	Colon and breast cancer	CT26, 4T1	Es@CuTCPP (Elesclomol-loaded Cu-nanosheets)	GSH oxidation coupled to Cu <sup>2+</sup> reduction.	GSH contributes to TCPP-Cu <sup>2+</sup> to TCPP-Cu <sup>+</sup> reduction, leading to ROS-dependent cell death and cuproptosis.	192