# Berberine synergizes with ferroptosis inducer sensitizing NSCLC to ferroptosis in p53-dependent SLC7A11-GPX4 pathway

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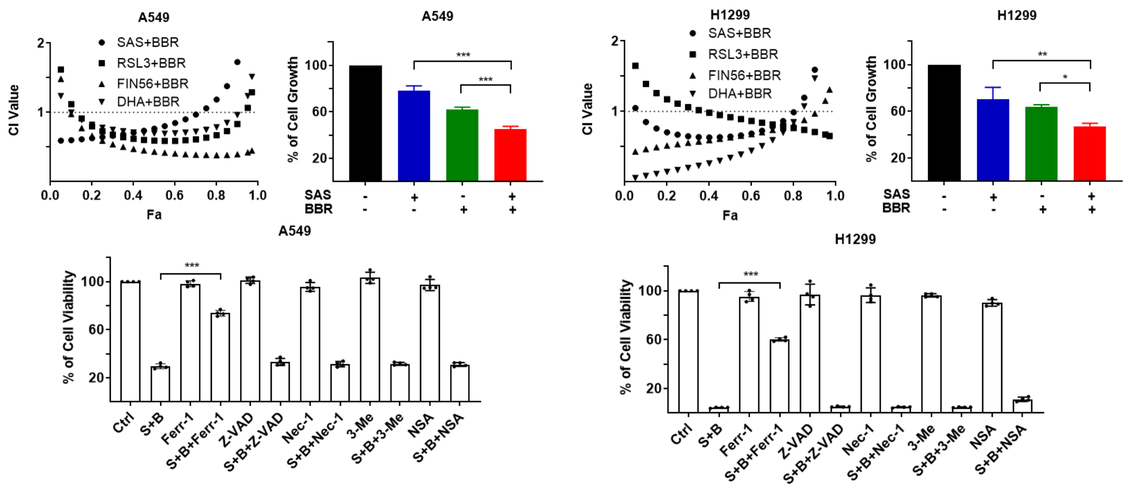
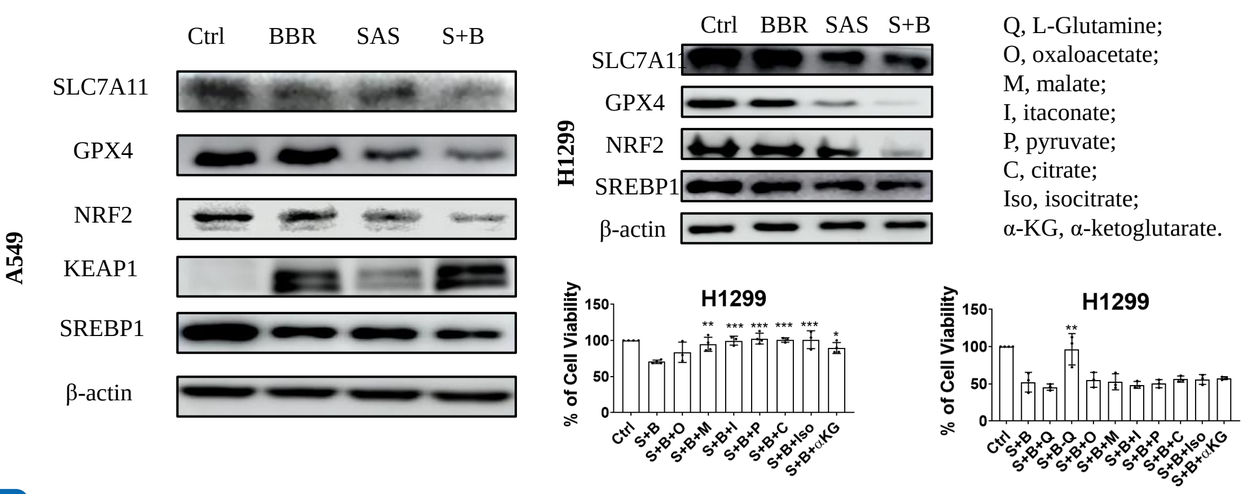
## Abstract

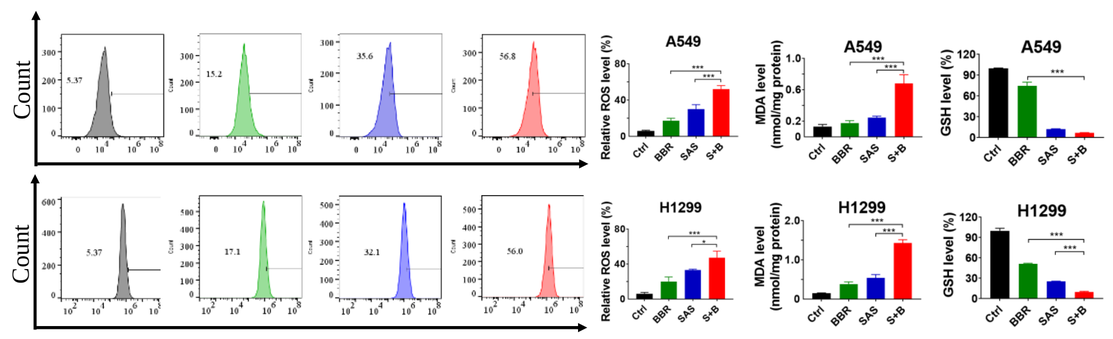
Berberine (BBR), a compound from Chinese herbal medicine, is known for anticancer properties. Research suggests BBR can inhibit tumor growth by participating in ferroptosis. (1) Studies show that berberine combined with ferroptosis inducers inhibited NSCLC by down-regulating SLC7A11, GPX4, and NRF2 expression, leading to ferroptosis. (2) This process significantly depleted GSH and increased reactive oxygen species and malondialdehyde. (3) In lung cancer models, the combination treatment showed enhanced anticancer effects compared to individual drugs. (4) The presence of p53 is critical for ferroptosis sensitivity, as the combination treatment did not show a synergistic anticancer effect in cells with a p53 mutation or with expression of mutant p53.

## Synergistic cell growth inhibition of berberine with ferroptosis inducer

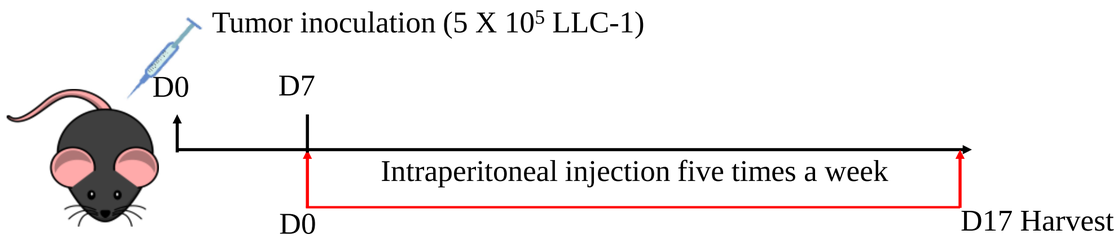


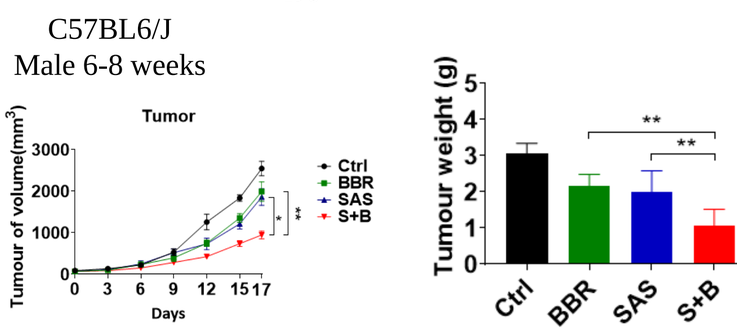

## BBR enhanced SAS-triggered ferroptosis in cell



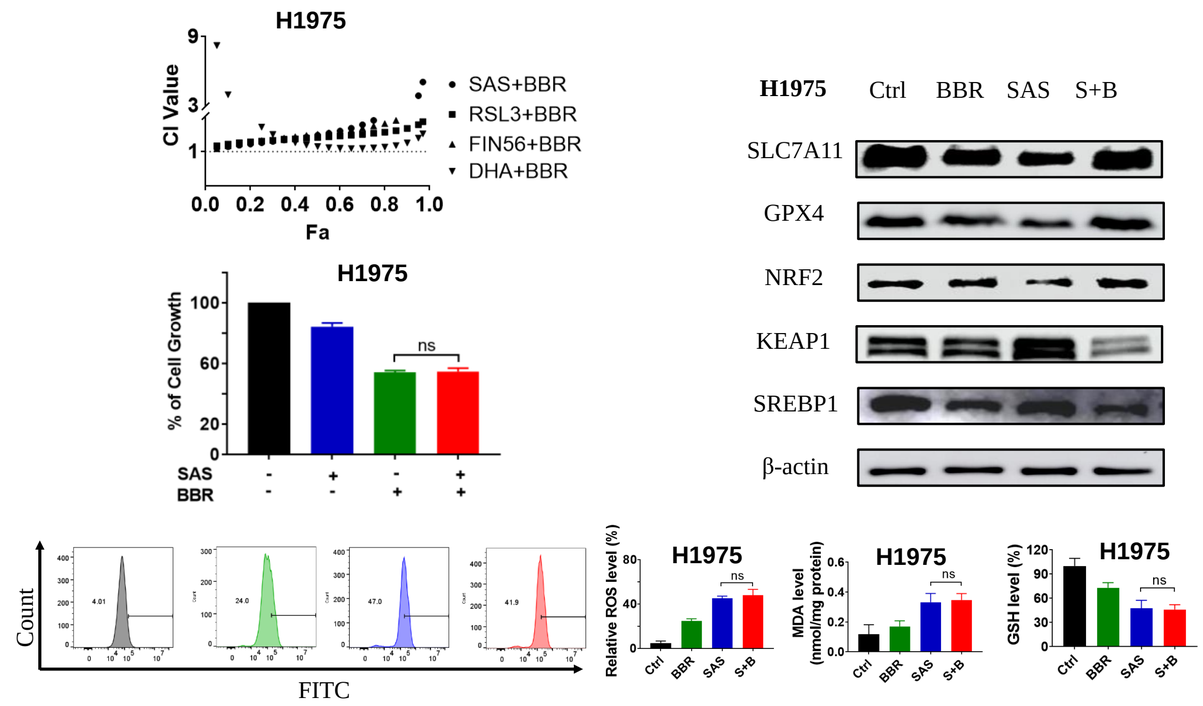




## Combination of BBR and SAS synergistically exerts its antitumor effects in vivo

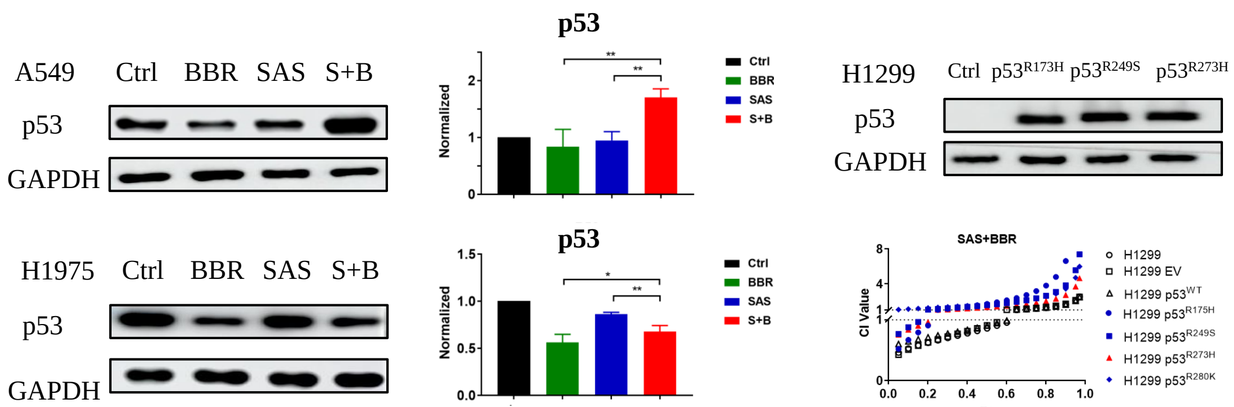


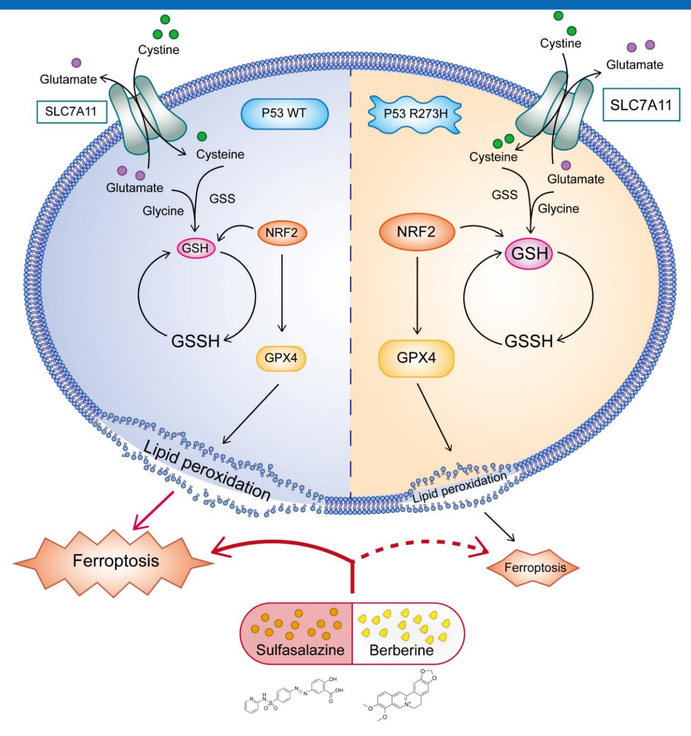

## BBR combined with SAS did not exhibit a synergistic effect in the H1975 cell



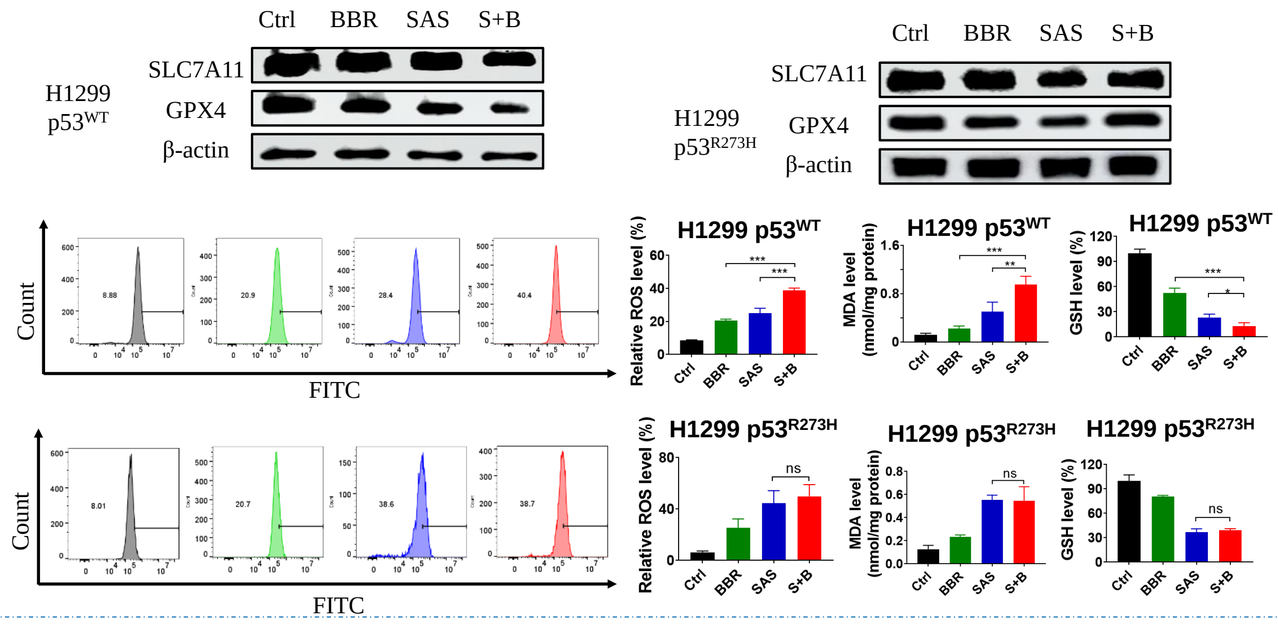

## The presence of p53 mutation in NSCLC abolishes the synergistic effect of the combination of BBR and SAS




## The mechanism of the combinative treatment of BBR and SAS in NSCLC cells




## p53 R273H disrupted combination-mediated ferroptosis signal

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