ENHANCING RADIOTHERAPEUTIC EFFECTS VIA NANOPARTICLE-MEDIATED RADIOSENSITIZER DELIVERY GUIDED BY FOCUSED GAMMA RAYS IN LEWIS LUNG CARCINOMA–BEARING MOUSE BRAIN TUMOR MODELS

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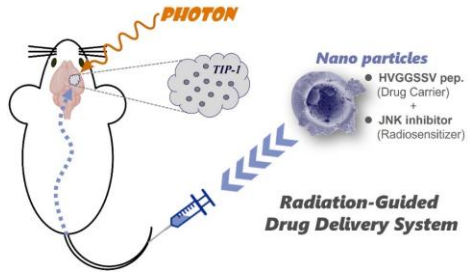
Background

For improved radiotherapeutic efficacy and safety, this study aimed to enhance the tumor-specific delivery and bioavailability of a nanoparticle-mediated radiosensitizer in mouse brain tumor models.

Methods

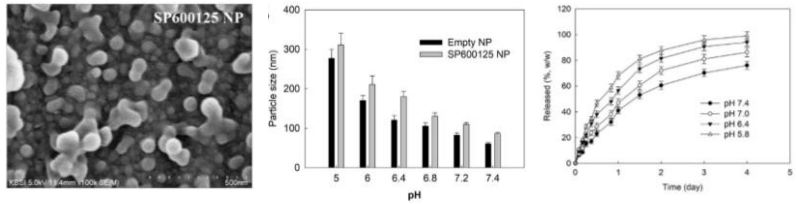
The pH-sensitive nanoradiosensitizer HVSP-NP was developed by conjugating TIP-1-targeting peptide (HVGGSSV) and JNK inhibitor (SP600125) onto chitoPEGAcHIS nanoparticles.



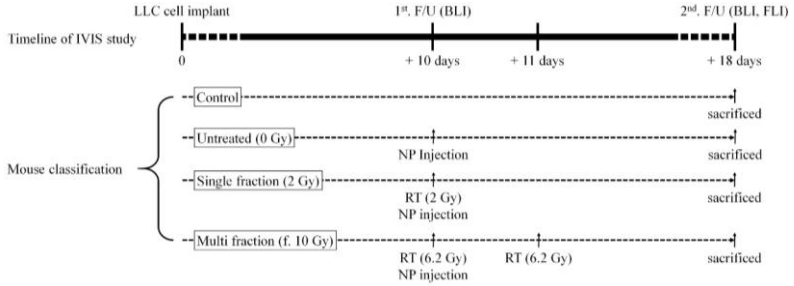
Results

The JNK inhibitor SP600125 effectively reduced DNA damage repair in irradiated LLC cells. The pH-sensitivity assay demonstrated that HVSP-NP swelled and increased in diameter under acidic conditions, leading to a gradual increase in the drug-release rate. Radiation therapy combined with HVSP-NP induced greater apoptosis and significantly suppressed tumor growth compared with radiation alone.

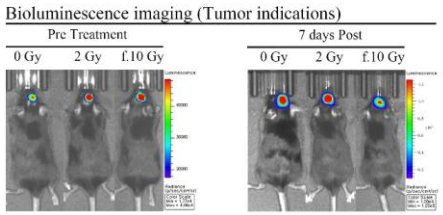
Characterization of nano-sensitizer

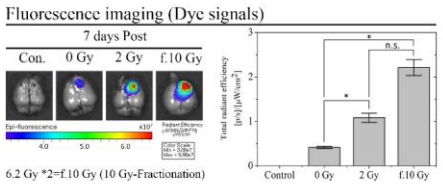


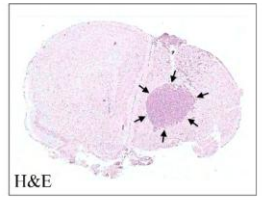
Radiation-inducible TIP-1 receptor targeting studies

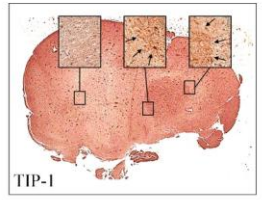


[Timeline of IVIS study to identify tumor targetability of HVSP-NP]

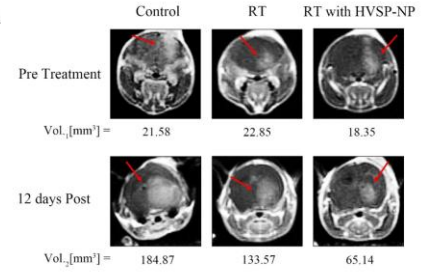


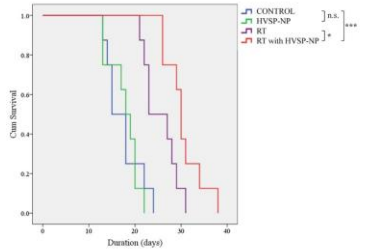


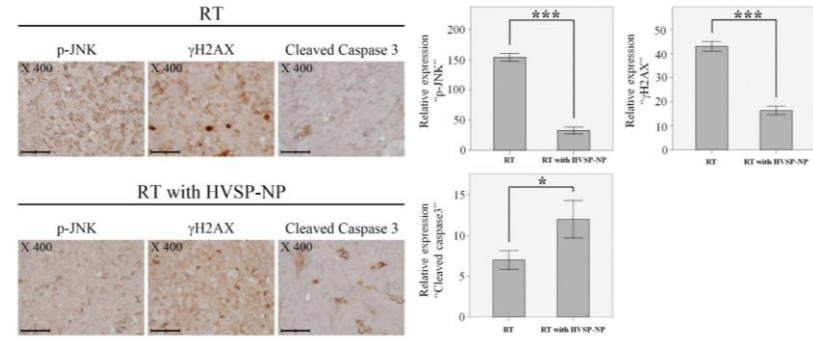




Survival studies for mice receiving various treatments







Conclusion

HVSP-NP, a novel nanoradiosensitizer, selectively targeted irradiated tumors and substantially enhanced tumor growth delay in LLC-bearing mouse brain tumor models. These findings demonstrate that delivering a pH-responsive nanoradiosensitizer to brain tumors with radiation-induced TIP-1 expression can improve radiosensitizer release within the acidic tumor microenvironment and produce synergistic therapeutic effects when combined with radiation treatment.