Multifunctional biomimetic nanoparticles-induced hyperthermia improves survival in a human glioblastoma multiforme orthotopic mice model: A pilot study

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Glioblastoma multiforme (GBM) is the most common and deadliest form of brain cancer.[1] Current standard-of-care for GBM includes maximal safe surgical resection, radiation, and chemotherapy with temozolomide (TMZ). However, the highly invasive and resistant GBM nature prevents an effective tumor regression after therapy, causing significant neurologic morbidity and mortality, resulting into a mortality rate close to 100%:[2] just these data describe the urgent need for current treatment improvement and for new complementary therapies.

In light of this, applying magnetically-responsive nanoparticles to formulate anti-GBM therapies can be a powerful tool to both increase the bioavailability and the selectivity of pharmacological agents targeting the brain tumor microenvironment and to perform hyperthermia treatments.[3] In particular, superparamagnetic iron oxide nanoparticles (SPIONs) can be exploited in the development of smart drug delivery systems, as "bio-magnetics switches", owing to their capability to produce heat under the exposure to an external alternating magnetic field (AMF).[4]

In this work, lipid-based magnetic nanovectors functionalized with the peptide angiopep-2 encapsulating TMZ and SPIONs (Ang-LMNVs@TMZ) have been efficiently exploited in an *in vivo* approach to promote a cytotoxicity effect to human glioblastoma by the synergistic action of the chemotherapeutic drug loaded into the nanocarrier ([LMNVs]=24 mg/[TMZ]=0.98mg /kg weight mice; injection volume = 3 µL) and the cell sensibilization in response to the local heating ($H \times f$ = $4.2 \cdot 10^9$ A/ms, t = 30 min, 3 consecutive days, 24 h after Ang-LMNVsTMZ intratumoral administration). Obtained data on orthotopic U87MG human glioblastoma tumor-bearing nude mice evidenced an effective suppression of the tumor growth, and a significantly improved medium survival time after Ang-LMNVs@TMZ + AFM treatment (75% of the subjects are still alive at the end of the study), suggesting the suitability of the proposed nanoplatform for the GBM treatment.

References

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Figures

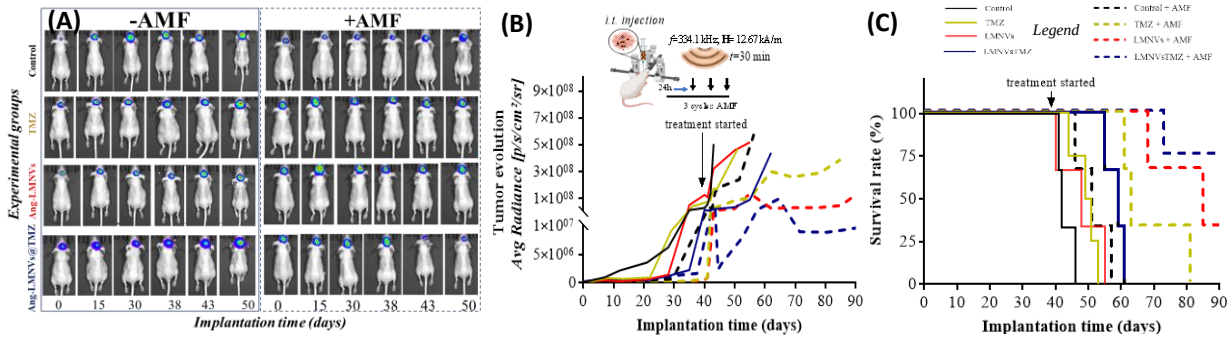

Figure 1: (A) *In vivo* bioluminescence images of orthotopic U87MG-Luc human glioblastoma tumor-bearing nude mice at different time points following tumor implantation. (B) Tumor evolution measurement by quantification of the luminescence levels of mice in each group using the IVIS system. Data are presented as mean (n = 3-4 mice/group). (C) Mice survival rate for each experimental group (n = 3-4 mice/group). Treatment schedule is also shown; data are expressed as % survival *vs.* time.