

Nanocarrier Design for Enhanced Batimastat Delivery in Glioblastoma

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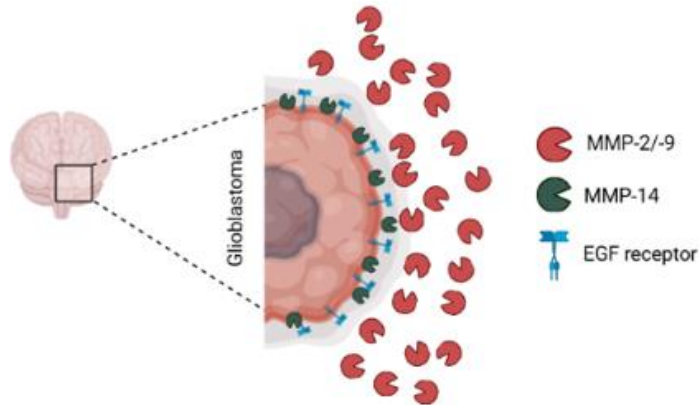


Concept

Glioblastoma invasiveness potential

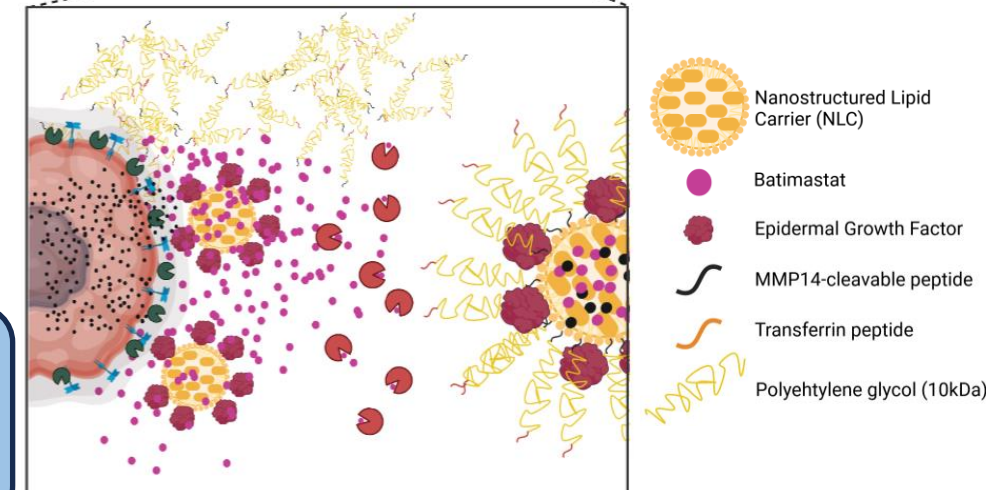
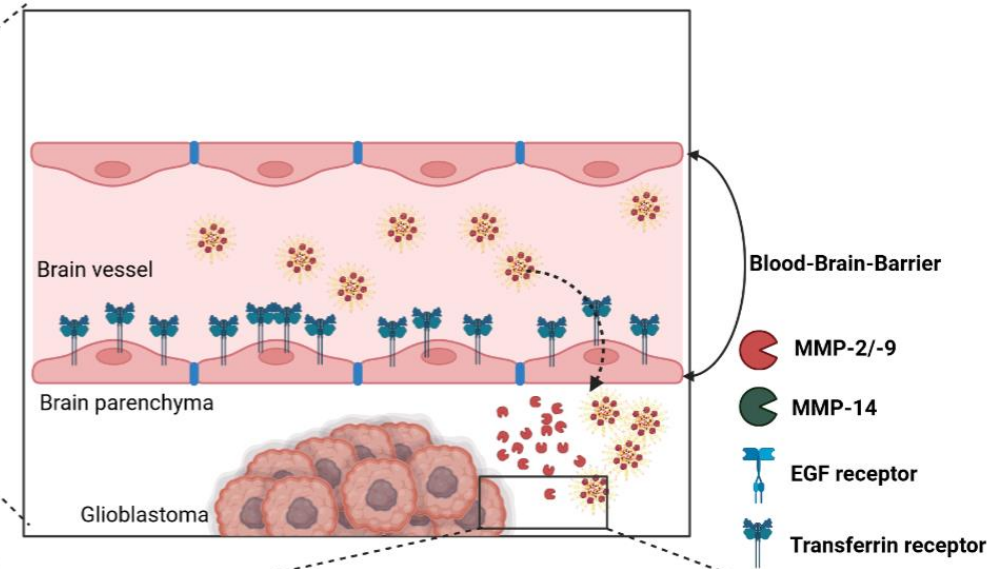
Ease of extracellular matrix remodeling

Overexpression of matrix metalloproteinases:
Secreted gelatinases (MMP-2 and MMP-9)
Transmembranar MMP-14



AIM

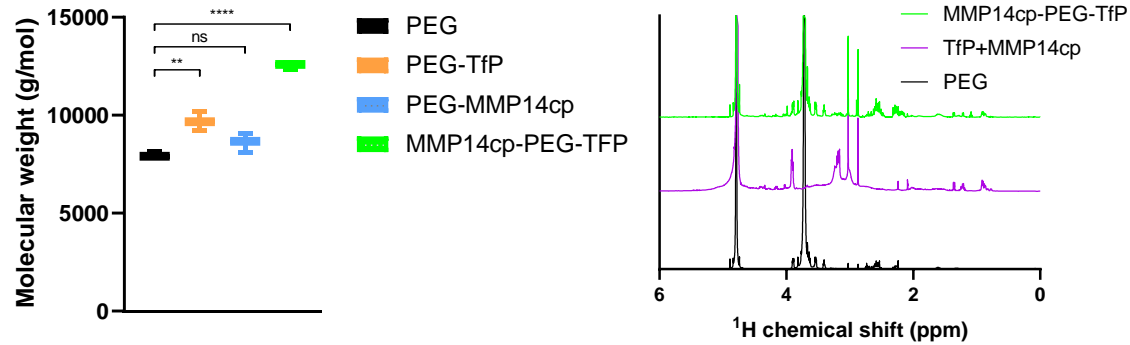
Develop a GB-specific targeted nanosystem carrying an MMP inhibitor to affect the GB's invasiveness potential



Results

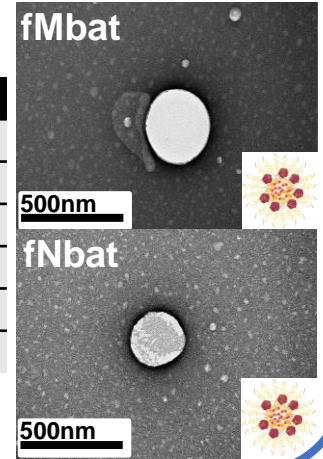
MMP14cp-PEG-TfP conjugation

81 ± 4% Conjugation Efficiency

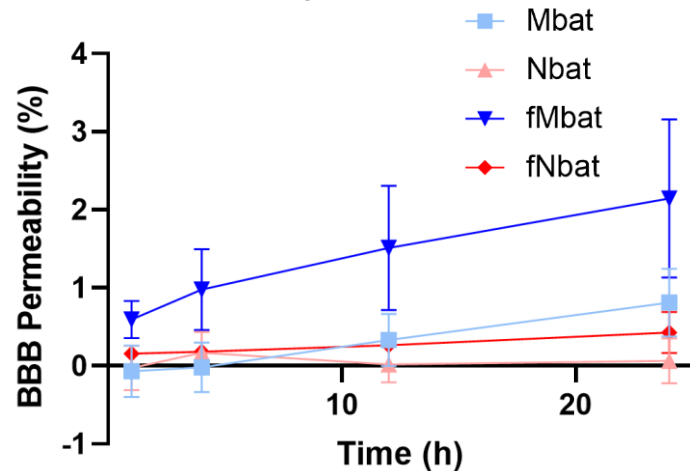


Nanostructured lipid carrier production

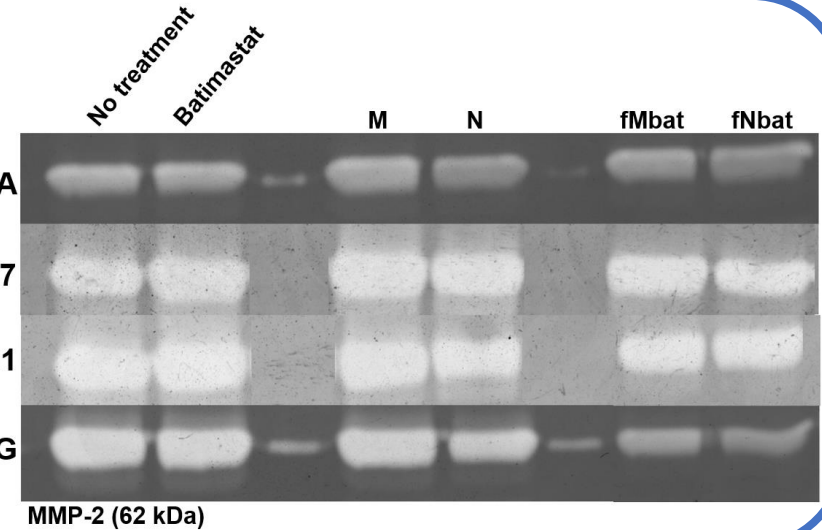
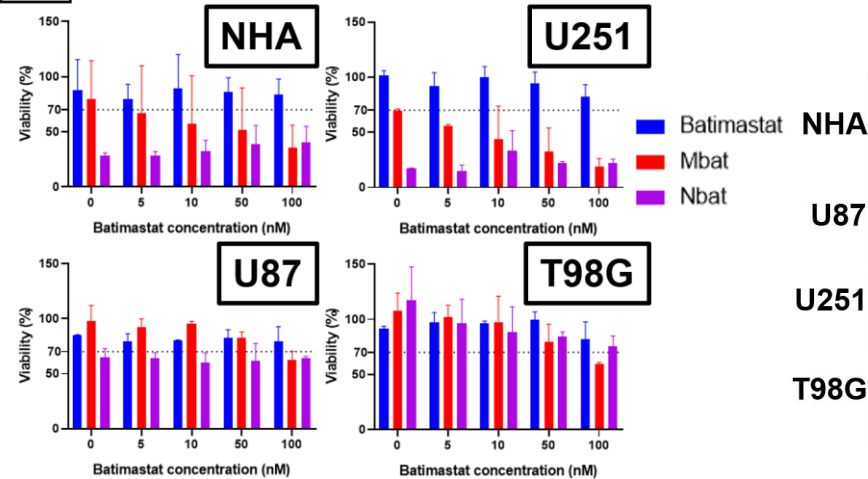
Formulation	fMbat	fNbat
Size (nm)	333.8 ± 35.3	322.2 ± 79.1
Polydispersity Index	0.335 ± 0.034	0.286 ± 0.065
ζ-potential (mV)	-23.7 ± 0.7	-21.5 ± 0.9
Encapsulation efficiency (%)	10.1 ± 0.2	10.2 ± 0.7
Drug loading (μg/mg)	0.42 ± 0.01	0.42 ± 0.02
Functionalization efficiency (%)	85 ± 15	92 ± 6



In vitro assays



48h



Conclusions and outlook

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- ✓ The functionalizing molecular construct has been successfully synthesized
 - The conjugation efficiencies of 85-92% are below the commonly published values of 90-95%.
- ✓ The complete NLC formulations, fMbat and fNbat have been synthesized and functionalized with adequate:
 - I. Average diameter
 - II. Polydispersity Index
 - III. Surface potential
 - IV. Encapsulation efficiency
 - V. Functionalization efficiency
- ✓ fNbat is more cytotoxic than fMbat, as the latter presents no cytotoxicity apart from the highest of the tested concentrations in 3 of the cell lines
 - U251, the exception, was found to be very sensitive to the nanoparticle itself
- ✓ Zymography assays showed an increase in MMP inhibition provoked by the NLC formulations
 - The free drug presented no inhibition at concentrations of 50 nM.
- ✓ MMP14cp-PEG-TfP functionalization allows the fMbat formulations allows the fMbat formulations to cross the BBB
 - DiO-labeled NLCs are physicochemically similar to the unmodified ones.

