SYNTHESIS AND *IN VITRO* BIOLOGICAL EVALUATION OF DRUG-PEPTIDE CONJUGATES AGAINST GLIOBLASTOMA

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Glioblastoma (glioblastoma multiforme, GBM, a type of astrocytomas) is the most aggressive form of primary brain tumors. Drug delivery is challenging because the blood-brain barrier (BBB) prevents small molecule transport. Our goal is to achieve enhanced cellular uptake and activity of antitumor compounds on glioma cell cultures using drug-peptide conjugates.

As carrier peptides derivatives of SynB3 and tuftsin were used. SynB3 is a cell penetrating peptide that can facilitate the transport of drug molecules through the BBB.[1] Tuftsin is a naturally occurring peptide that can bind to neuropilin-1 receptors that are over-expressed on angiogenic tumor blood vessels (including brain endothelial cells) and on tumor cells.[2] Tandem peptides composed of SynB3 and tuftsin derivatives were also used as carriers. Daunomycin and salicylanilide derivatives as antitumor agents were conjugated to the peptides. The *in vitro* cellular uptake and cytostatic/cytotoxic activity of the compounds and conjugates were evaluated on human U87 glioblastoma and on HUVEC umbilical vein endothelial cells.

SynB3 derivatives have higher uptake rate on U87 cells than tuftsin derivatives. Salicylanilide derivatives have high cytostatic activity on U87; antitumor activity of the conjugable salicylanilide and daunomycin is preserved in the peptide-drug conjugates. Tandem peptide derivatives showed slightly lower uptake and antitumor activity than the SynB3 peptide derivatives. In contrast with the free drugs, most conjugates are selective towards glioma cells since they have no cytotoxic effect on HUVECs.

Conjugates containing SynB3-tuftsin tandem peptides could be used to exploit the advantages of both types of peptides to achieve enhanced cellular uptake and to create a more selective delivery system for glioblastoma treatment (Fig. 1).

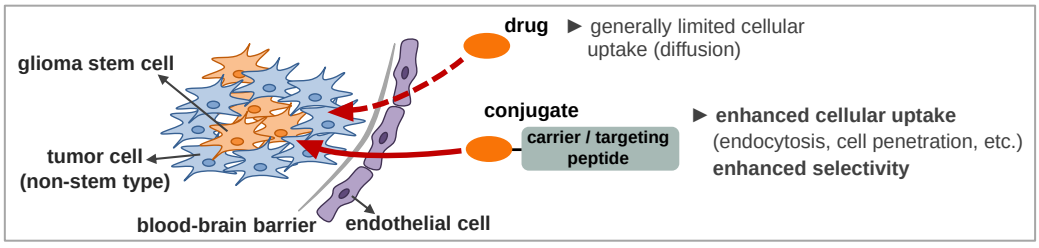

Fig. 1: Enhanced cellular uptake of drugs against glioblastoma

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