Development of Peptide-Drug Conjugates Targeting Glioblastoma Cells

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Glioblastoma accounts for 50.1 percent of all primary malignant brain tumors. Tumor stem cells play a key role in treatment resistance and tumor recurrence, as they are capable of self-renewal, have tumor-initiating capabilities, and are adaptable to environmental stress, including chemotherapy. The aim of this study was to generate variants of an already published peptide that specifically targets the Cadherin 2 membrane proteins and receptors found on glioblastoma stem cells, which may improve diagnostics and therapeutic targeting. I synthesized the peptides, using flow technology - a method that enables faster and more accurate solid-phase peptide synthesis, uses less material, produces less environmentally harmful "waste", making it more cost-effective and environmentally friendly. The most important result of the study so far is the structure-activity relationship of the peptide – daunomycin conjugates based on the CD spectroscopy analysis and MTT assays. It was shown that the AWEFWFP sequence-based derivative -when compared to the other peptides- has a slightly more ordered structure. In contrast, the others indicate very dynamic and mobile disordered structures without a characteristic structures but they also showed a partial bend structure or even the formation of a temporary beta sheet structure. The MTT test result obtained highlighted that the conjugate containing Tyr instead of Trp in position 2 (Dau=Aoa-LRRY-AYEFYFP-NH2) showed similar activity to the original targeting peptide with additional advantages: the conjugate is easier to synthesize due to the absence of tryptophan, and is less insoluble than other conjugates, thus these properties make it more suitable for further drug development.

Awards Won:

Drug, Chemical &amp

Associated Technologies Association (DCAT): DCAT First Prize

American Chemical Society: Diploma of Recognition and $100 gift card