

Conotoxin-derived biomimetic coiled cone-shaped peptide as ligand for selective nanodelivery to norepinephrine transporter-expressing neuroblastoma cells.

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Streszczenie

Selective drug delivery is an emerging powerful strategy, which promises efficient and safer neuroblastoma treatment in contrast to conventional therapeutic modalities. Herein, we present a newly designed apoferritin nanovehicle loaded with ellipticine and decorated with conotoxin-derived biomimetic peptide YKL-6 (sequence: YKLYKLYKLYKLYKLYKLC) to target the norepinephrine transporter (hNET), which is highly expressed on neuroblastoma cells membrane. The peptide forms a coiled cone-shape forming anti-parallel beta sheets in aggregation *in vitro*. Molecular docking analysis suggests electrostatic interaction mediated by lysine residues against negatively charged residues of the hNET. The assembled nanovehicles show optimal biocompatibility in healthy epithelial cells and ability to deliver ellipticine into neuroblastoma cells (UKF-NB-4 and SH-SY5Y). In our analyses, we have excluded hNET-mediated endocytosis as an uptake mechanism and demonstrated the ellipticine-triggered anti-proliferative mechanisms in neuroblastoma cells *via* downregulation of Bcl-2, survivin and N-myc. Finally, we present a selective inhibition of neuroblastoma growth and metastasis *in vivo* in an *ex ovo* and *in ovo* chicken chorioallantoic membrane assay. Overall, these findings demonstrate a great leap forward in the design of biomimetic homing peptides towards possible application in neuroblastoma nanomedicine.

Słowa kluczowe

Apoferritin, Biomimetic peptides, Drug delivery, Neuroblastoma, Norepinephrine transporter, Targeted therapy

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