

Designing Ligand Functionalized Synthetic Exosomes for Targeted CRISPR-Cas9 Delivery: A Multistep Computational Approach to Cancer Treatment

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CRISPR Cas9 is a gene-editing tool that holds immense importance for precision medicine, yet off-target effects remain as a major challenge. This project aims to design ligand-functionalized exosomes for targeted CRISPR delivery, minimizing unintended modifications. By screening a range of ligands for their binding affinity, this project seems to identify an optimal ligand for cancer cell targeting. The computational screening approach was used to evaluate multiple ligands capable of functionalizing the exosome surface for enhanced targeting. The molecular docking simulations were conducted to assess various ligand-receptor interactions. The optimal ligand was also docked with a few healthy cell receptors to understand the chances of off-targets. The selected ligand is conjugated to exosome surfaces, enhancing their affinity for cancer cells while minimizing systemic exposure. These exosomes encapsulate CRISPR-Cas9 as an mRNA payload, promoting efficient gene editing within malignant cells. The design is supported by thorough and proper research as incorporated functionalization and loading techniques into my design. An additional part of my design is to be adding pH-sensitive linkers to ensure the therapeutic molecules are specifically being delivered to the target cells. Computational validation helps validate the accuracy of targeting and delivery. By addressing the limitations of current CRISPR delivery systems, this research aims to improve the safety and efficacy of gene therapy, offering a transformative step toward precision oncology.

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