Evaluating CD44–Aptamer Binding Energetics Using Membrane-Embedded Molecular Dynamics

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Glioma is a brain tumor with a high mortality rate, partly because symptoms such as cognitive changes often emerge only after substantial tumor growth. CD44, a transmembrane protein overexpressed in glioma and glioma-like cells, represents a promising molecular target for precision drug delivery. This study presents a fully computational framework to design, simulate, and evaluate DNA origami functionalized with CD44-specific aptamers for targeted anticancer delivery, enabling efficient candidate screening before biological validation. The CD44 structure was retrieved from the Protein Data Bank (UniProt ID: P16070) and prepared for docking. DNA origami scaffolds were designed in SCADnano v0.20.1, visualized in OxView v2.0, and validated for structural stability using oxDNA v3.0.7 at 20°C over 10,000 simulation steps, confirming structural compactness without strand dissociation. Molecular docking was conducted in HADDOCK v3.0 across eight runs clustered into six complexes; Cluster 2 produced the most favorable HADDOCK score (-69.1) and buried surface area (1,479.1 Å²), indicating strong receptor–aptamer interaction. Short-timescale molecular dynamics simulations were performed in GROMACS v2026.0 using the CHARMM36 force field within a solvated periodic boundary system embedded in a lipid bilayer membrane. Over 10,000 steps, RMSD stabilization, consistent radius of gyration, and minimal SASA variation collectively confirmed structural integrity of the complex under membrane conditions. By integrating docking with membrane-embedded dynamics, this framework advances beyond static modeling approaches and demonstrates the computational feasibility of CD44-targeted DNA origami systems, while experimental validation and blood–brain barrier modeling remain future directions.

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