Harnessing RNA Nanotechnology: In silico Design and Structural Modeling of RNA Aptamers Targeting BRCA1 for Early Detection of Breast and Ovarian Cancer

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BRCA1 is a tumor suppressor protein essential for DNA repair, cell cycle regulation, and the maintenance of genomic stability. Mutations in the BRCA1 gene are strongly associated with an increased risk of breast and ovarian cancer. RNA aptamers are short, single-stranded nucleic acids that fold into specific three-dimensional structures, enabling high-affinity and selective binding to target proteins. This study investigates how base mutations influence aptamer structure and binding interactions with the BRCA1 protein through molecular modeling and molecular dynamics simulations. Nine parent RNA aptamers were designed and structurally modeled, followed by molecular docking to evaluate binding affinity. Among these, Aptamer 7 (MeLW7) demonstrated the strongest interaction with the BRCA1 binding domain. To further optimize binding performance, targeted base-pair mutations were introduced to MeLW7, generating a series of mutant aptamers. These variants were analyzed using molecular dynamics simulations in GROMACS to assess structural stability and interaction behavior under solvated conditions. Results showed that mutant aptamer 5 (MA5) achieved the highest mean binding score and exhibited enhanced stability compared to the original sequence. It is hypothesized that strategic base mutations improve RNA aptamer conformational stability and binding specificity by strengthening intermolecular interactions within the BRCA1 binding region. These findings support the potential of RNA aptamers as precise biomarkers and targeted agents for the early detection and treatment of BRCA1-associated cancers.

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