Computational Modeling of Bispecific T-Cell Engager Targeting B7H3 (CD276) for Immunotherapy in Medulloblastoma

Gude, Monica (School: Fort Mill High School)

Medulloblastoma is the most prevalent malignant brain tumor in children, and 75% of children that have it are under the age of ten. However, its current treatments are surgery, chemotherapy, and radiation and they often lead to severe neurodevelopmental side effects that impair brain growth. To explore safer therapeutic alternatives, this study investigates the feasibility of Bispecific T-cell Engager immunotherapy targeting the B7H3 (CD276) receptor in medulloblastoma. Humanized scFv antibodies were downloaded from the SabDAB database. Phylogenetic tree analysis and K-means clustering were performed to categorize the 360 antibodies into 10 clusters, which were then selected for further analysis. Furthermore, using an integrated computational pipeline, protein structures were modeled, docked, and dynamically simulated to assess molecular interactions between the T-cell receptor and B7H3. Among the tested single-chain variable fragments (scFvs), 9B6T and 9EHL exhibited the strongest binding affinities and interaction stability, with binding energies reaching up to -15.0 kcal/mol. As for the number of interactions between the scFvs and proteins, 9B6T and 9U4W displayed the most hydrogen bonds. These results highlight the potential of BiTE constructs as targeted immunotherapies capable of selectively engaging T-cells to medulloblastoma cells while minimizing off-target toxicity. Finally, the AlphaFold-modeled molecule exhibited strong thermal and structural stability, making it a promising alternative to conventional antibodies. Future in vitro and in vivo validation is required to confirm the predicted efficacy and optimize the stability for clinical translation.

Awards Won: