AI-Augmented Computational Modeling of Bispecific Antibody Targeting B7H4+ Cancer Cells and CD3e+ CAR T-Cells for Targeted Therapy in Solid Tumors

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A solid tumor is an abnormal mass of uncontrolled cell growth, typically originating in the breast, lung, or prostate. Its physiological features make treatment by traditional methods difficult. In solid tumors, the B7H4 receptor is overexpressed on the surface of the cancer cells. This makes it an essential target for cancer diagnosis and targeted therapy. A DuoBody is a bispecific antibody with two halves of antibodies designed to target two specific receptors and enhance therapeutic effects by bringing T cells to cancer cells, resulting in cancer cell apoptosis. In this research, I am working on the B7H4 receptor, which is highly expressed in solid tumors, and the CD3e receptor, which plays a role in activating T-cell response. I hypothesize that these DuoBody antibodies can be used to target the B7H4+ solid cancer cells by inducing the CAR T-cells toward the cancer cells. I have performed computational modeling to design a DuoBody antibody targeting cancer (B7H4 receptor) and CAR T cells (CD3e receptor). Initially, I got the 3D structures of the receptors by using the AlphaFold 3 web server. The 3D structure of antibodies was downloaded from the protein data bank. The downloaded antibodies were docked on the predicted receptor structures using the HDOCK2.0 software. The docking results were validated using GrASP. The antibodies were selected based on visual inspection, binding energy, and hydrogen bond interactions of the output obtained from the molecular docking simulations. The Binding energies calculated by the PRODIGY software showed that antibody 4a6y strongly bond to the CD3e receptor and that 1il1 strongly bond to the B7H4 receptor. This research can be used in pharmaceutical drug development to engineer Duobodys that target cancer cells.

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