Designing a Modified HAC-PD-1 to Antagonize PD-L2 for the Improvement of Cancer Immunotherapy

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PD-L1 and PD-L2 are two transmembrane proteins created by cancerous tumors that have an affinity towards PD-1, a protein receptor expressed by T Cells. I If these proteins bind to the receptor, it effectively shuts down the T Cells and stops their proliferation, therefore preventing the immune system from fighting the tumor. In order to counteract this, monoclonal antibodies have been used to block this interaction, however, they are too large to penetrate smaller tumors, and often have random effects on patients. Therefore, a High Affinity Consensus mutated form of PD-1, known as HAC-PD-1, was developed to bind to PD-L1 and interrupt the PD-1:PD-L1 reaction in order to allow the immune system to effectively fight a tumor. However, HAC-PD-1 does not effectively prohibit the PD-L2 reaction. This experiment aims to create a modified version of HAC-PD-1 that will effectively bind to and antagonize PD-L2 to block it from interrupting the immune system process. Protein data base structures and homology structures were inputed into the protein docking system GRAMM-X, and then inputed into PRODIGY to predict the binding affinity. It was discovered that mutating residues 70-79 of PD-L2 resulting in the highest binding affinity with HAC-PD-1. Therefore, if HAC-PD-1 was modified that match these residues, it may create an effective treatment against PD-L2. This way, a patient could be treated for both ligands with a method much more effective than monoclonal antibodies.

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