Engineering PD-L1 Specific Diabodies for PET Imaging

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Programmed Death Ligand 1, or PD-L1, is a transmembrane protein upregulated in numerous tumors. By binding to the PD-1 receptors on CD8+ T-cells, these tumors can evade T-cells' cytotoxic effect, thus continuing to proliferate. Immunotherapies that block both PD-L1 and PD-1 have had great success in treatment, however, have not worked for all patients. The differences in patients may be due to the inaccurate assessment of PD-L1 expression levels, which have been positively correlated with patient responses. To accurately assess the levels in tumors, we are engineering PD-L1 specific diabodies to be used in conjunction with PET imaging. They offer great potential as PET imaging agents due to their high affinity, stability, specificity, and short circulation times. Therefore, the goal of this project is to develop a PD-L1 specific diabody PET imaging agent to correctly identify PD-L1 expression levels in cancer patients. Based on sequencing results, we have successfully engineered diabodies from all three clones with both 5 and 8 AA linkers. Western blot analysis shows the correct molecular weight of the diabody and that both a monomer and dimer form exist. Our preliminary results, using SPR, show little binding to the PD-L1 ligand. Based on these results, it can be concluded that Diabody 2c9 with a 5 amino acid linker does not have the potential to be used as a PET imaging agent to accurately measure the expression levels of PD-L1 in tumors. More analysis is needed to assess the use of the remaining diabodies as PET imaging agents.

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