

Cross Species Single Domain Antibodies Targeting PD-L1 for Treating Solid Tumors

Summary

The National Cancer Institute (NCI) seeks research co-development partners and/or licensees for single domain antibodies targeting program death ligand 1 (PD-L1) for treatment of PD-L1-expressing cancers.

NIH Reference Number

E-118-2021

Product Type

- Therapeutics

Keywords

- Programed Death-Ligand, PD-L1, Nanobody, Single Domain Antibody, Immunotherapy, Immune Checkpoint Inhibitor, ICI, Adoptive Cell Therapy, Chimeric Antigen Receptor T Cells, Phage Display, Ho

Collaboration Opportunity

This invention is available for licensing and co-development.

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Description of Technology

Programed Death-Ligand 1 (PD-L1, also known as B7-H1 or CD274) is a cell surface protein that binds to Programmed Cell Death Protein 1 (PD-1, also known as CD279). An imbalance in PD-1/PD-L1 activity contributes to cancer immune escape. PD-1 is expressed on the surface of antigen-stimulated T cells. The interaction between PD-L1 and PD-1 negatively regulates T cell-mediated immune responses. It has been suggested that disrupting the PD-L1/PD-1 signaling pathway can be used to treat cancers. The aberrant expression of PD-L1 on multiple tumor types supports this suggestion. As a result, PD-L1 represents a strong target for the development of new anti-cancer therapeutics.

Researchers at the NCI's Laboratory of Molecular Biology have isolated three anti-PD-L1

single domain antibodies (also known as nanobodies), B2, A11, and F5 that target PD-L1. These nanobodies can be used either as independent agents or as the targeting domain in chimeric antigen receptors (CARs), antibody drug conjugates (ADCs), recombinant immunotoxins (RITs), and bispecific antibodies. Significantly, CARs using these antibodies has shown potent in vitro and in vivo killing against PD-L1 positive tumors, including liver and triple-negative breast cancer, strongly supporting that these candidates may be further developed as therapeutics.

Potential Commercial Applications

- Therapeutic applications include the unconjugated antibodies and their use as a targeting moiety for CARs, RITs, ADCs, and bispecific antibodies
- Therapeutics against PD-L1-expressing cancers, including liver, bladder, pancreatic, prostate, gastric and triple-negative breast cancer
- Diagnostic agent for detection and monitoring levels of PD-L1-expressing cancers

Competitive Advantages

- These anti-PD-L1 nanobodies have an advantage, due to their small size, to potentially bind to epitopes unavailable to more conventional antibodies
- Cross-species reactivity in mouse and human
- Combination of B2 and hYP7 CARs in T cells improves lysis of liver cancer cells in mice compared to either CAR alone
- CARs using the B2 single domain antibody are available for immediate testing

Inventor(s)

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Development Stage

- Pre-clinical (in vivo)

Patent Status

- **U.S. Provisional:** U.S. Provisional Patent Application Number 63/208,755, Filed 09 Jun 2021

Related Technologies

- [E-136-2012 - High-Affinity Mouse Monoclonal Antibodies to GPC-3 for Liver Cancer Research](#)

Therapeutic Area

- Cancer/Neoplasm

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