Technology Overview

There is a critical unmet need to provide therapies with durable and potentially curative responses to patients with pancreatic cancer. Mesothelin (Msln) as a target antigen is overexpressed in pancreatic cancer and other targets. Hutch scientists have previously demonstrated the utility of targeting Msln in murine models of pancreatic cancer. Drs. Chapuis, Schmitt, and Greenberg have identified and isolated high affinity anti-Msln specific TCRs from healthy donors. Preclinical validation of these Msln TCRs expressed in CD8 T cells has displayed strong cytotoxic activity towards tumor cells and a favorable safety profile. A clinical candidate has been chosen and the clinical research team plans to initiate a first in human Phase 1 study at Fred Hutch within the next 12 months.

Applications

- Immunotherapy target for tumors overexpressing Msln, including pancreatic, ovarian, mesothelioma, breast cancer, and other solid tumor indications

Advantages

- Msln is a target well-characterized for safety and efficacy
- Preclinical murine data supports the efficacy and safety of Msln-targeting TCRs in the treatment of pancreatic and ovarian cancer

Market Overview

The current market for pancreatic cancer therapeutics is $1.45 billion with a CAGR of 5.1% during 2016 – 2026. Several companies are developing CAR-T based Msln approaches to pancreatic cancer; however, CAR-T approaches have demonstrated limited efficacy in solid tumor settings. Msln is a questionable target for CAR-T based approaches based off the biology of the antigen, given it is shed from the tumor surface and the soluble molecule can decoy CAR based approaches. Additionally, CAR-T cells can recognize and severely injure the normal somatic cells expressing low levels of Msln. This results in severe toxicity, which has never been observed with the Msln-specific TCR-engineered T cells.