Using the immune system as a cancer treatment has the potential to induce long-term, durable remissions, and perhaps even cure some patients. The T cells of the immune system are able to specifically kill the target cells they recognize. T cells are also able to persist in the body for many years, and form immune ‘memory,’ which enables the possibility of long-term protection. The Maus laboratory is interested in using genetic engineering techniques to re-direct T cells to find and kill tumor cells, while sparing healthy tissues. We aim to develop new ways to design molecular receptors to target T cells to liquid and solid tumors; use T cells as delivery vehicles for other drugs, and use drugs to help T cells work against tumors; and understand how T cells can work as “living drugs” to treat patients with cancer.

Immune therapies that engage T cells have the potential to induce long-term durable remissions of cancer. In hematologic malignancies, allogeneic hematopoietic stem cell transplant can be curative, in part due to T-cell mediated anti-tumor immunity. In solid tumors, checkpoint blockades with anti- CTLA-4 or anti-PD-1 monoclonal antibodies can mediate long-term responses by releasing T cells from tightly controlled peripheral tolerance. Our laboratory focuses on T cell biology and T cell engineering. We design chimeric antigen receptors (CARs) to re-direct T cells to specific antigens. Redirecting T cells with CARs is an alternative method of overcoming tolerance and has shown great promise in the clinical setting for B cell malignancies such leukemia and lymphoma. However, successful application of this form of therapy to other cancers is likely to require refinements in the molecular and clinical technologies.

*PhD Candidate
**MD candidate

1. Contain molecular designs to enhance specificity, potency, and safety.

Novel types of antigen receptors are in development to target multiple antigens on tumor cells, which improves elimination of heterogenous tumor cells and prevents antigen-negative relapse while also decreasing the risk of targeting healthy cells. We are also using novel techniques to improve CAR T cell safety by regulating their activation and the molecules they release when activated. In liquid tumors, the focus is on improving the safety of CAR T cells, while in solid tumors, the focus is increasing their potency.
2. Be administered in combination with other drugs to sensitize tumors to T cell mediated killing and/or potentiate T cell function.

Many of the small molecule drugs and antibodies used in the clinic exert their effects on signaling pathways in tumor cells, T cells, and other immune cells. We aim to discover synergistic drug/T cell combinations to increase safety and efficacy, and use genetic engineering tools to confer specific drug sensitivity, resistance, or enhanced molecular switches.

3. Have additional modifications that make CAR T cells (a) resistant to inhibitory mechanisms, (b) imageable, or (c) more feasible to manufacture and administer.

Control of T cell function is a complex process orchestrated by a variety of molecules, some of which deliver inhibitory signals. Tumors often express ligands or cytokines to inhibit T cell function. Using a single vector, genetically modified T cells can be re-directed not only to recognize a new antigen on tumor cells, but also to be resistant to the inhibitory tumor microenvironment.

4. Further build on the basic biology and mechanisms that drive natural and engineered T cell functions.

We aim to understand the signaling mechanisms and effector functions used by CAR T cells versus native T cells, to further improve CAR T cell efficacy and safety. By understanding how CAR T cells kill tumor cells, we can also decipher how tumors become or are intrinsically resistant to killing by CAR T cells. We can then better engineer CAR T cells to prevent resistance from occurring.