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.
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 cells become or are intrinsically resistant to killing by CAR T cells. We can then better engineer CAR T cells to prevent resistance from occurring.