

## **II Non-Technical Abstract**

Bone marrow transplantation remains important in the treatment of a number of malignant and inherited disorders. Generally the optimal donor is a sibling that is a tissue type match, but the majority of patients do not have a fully matched related donor. In this circumstance, the use of alternative donors such as a matched unrelated donor can prove effective therapy, but there is an increased chance of a complication termed graft-versus-host disease (GVHD), in which the donor cells become reactive against the patient. The development of GVHD can be severe and life threatening. The removal of the T cells, which are the immune related cells that cause GVHD, from the marrow can decrease the incidence and severity of GVHD. However, the risk that the new bone marrow cells will not “take” and grow adequately is increased when T cell depletion is performed. The proposed study will test a strategy in which genetic engineering of the donor T cells is performed using a “suicide gene”, that makes the donor T cells sensitive to a reagent that is otherwise non-toxic. The concept that will be explored is the potential to infuse the genetically engineered cells, obtaining the benefits of including the T cells with the transplant, and if significant GVHD occurs to have a means of eradicating the problematic cells.