

## Fife – Lay summary of progress

If successful, this study will dramatically impact clinical care and will revolutionize how we diagnose and treat autoimmune diabetes in Minnesota. The first major advancement will be earlier diagnosis and better insulin management to preserve remaining beta cells. Current immunological biomarkers for T1D measure autoantibody titers. Their production occurs late in the disease process and is not 100% correlative with diabetes development. If successful, our tetramer reagents could be used to detect activated CD4 T cells before autoantibodies appear and extensive damage has occurred. Secondly, having a tool to track the number and activation of autoreactive T cells will be transformative in the clinic to determine disease status and therapeutic efficacy. We have observed an increase in antigen specific T cells during Type 1 diabetes (T1D). We have generated a unique biomarker reagent and successfully determined and tracked these antigen-specific T cells in patients with T1D and compared these findings to non-diabetic control patients. The next step is to target these islet-specific T cells for removal or better control. In addition to testing targeted immunotherapies, we will assess the extent of islet regeneration and the success of islet transplantation as a replacement therapy in mouse models of disease. This grant will determine if islet beta cells can regenerate, or survive better after transplantation, in the absence of T cell mediated killing, thus curing diabetes. This would transform future therapeutic design for autoimmune diabetic patients in Minnesota.