I am happy to inform you that this project has been funded and I will begin working on it soon. The first part of the project will determine whether a modified islet extracellular matrix (ECM) that contains large amounts of hyaluronan (HA) is formed in human islets in the early stages of type 1 diabetes (T1D). To answer this question, we will examine a large set of pancreas tissues from individuals at high risk for the disease. We will first identify the pancreas tissues from these individuals, which contain islets with HA deposits. Then we will measure these deposits and will relate their size to the number of islet cell autoantibodies that develop in these individuals. In follow-up work, we will determine whether insulitis starts prior to or after the accumulation of HA in islets. Our work will determine when the ECM abnormalities first occur in the disease, and then how the abnormal ECM results in T1D. Together these determinations will inform whether, when, and how the ECM could be a therapeutic target in T1D to stop or prevent T1D.