Dr. Shivani Arora Final Project Update

Since patients with Type 1 diabetes actively lose their active and healthy beta-cell mass in the pancreatic islets, conserving and/or restoring the healthy beta-cell population is critical for preventing disease progression. Previous findings from our lab have established the role of senescent beta cell mass as active drivers of Type 1 Diabetes, which consummates T1D by making active beta cells senescent. This has led us to actively focus on the strategies to selectively target these cells.

Our lab has identified a unique subset of the immune population that actively and preferentially targets this SASP secreting cell mass. We have successfully established through our current work that activation of these specific types of immune cells with a small molecule not only decreases the senescent cell burden from the islets but also improves the metabolic profile.

In the preclinical settings, we are using an exogenous antigen to stimulate these cells, and we observe a significant improvement in ITT and GTT profile of the NOD mice, which correlates with the decrease in percentage of senescent cells in the islets. A brief pathway on how beta cells are rescued is shown in Figure 1.

To this date, we have very limited knowledge about the endogenous ligands for this particular subset of immune cells and as to what regulates their turnover. It is exciting and very promising to harness this endogenous immune surveillance as a therapeutic strategy, as it not only provides new treatment alternative for Type 1 Diabetes but also provides a strong supportive treatment option to deal with various other disorders that have associated auto-immune character including Rheumatoid arthritis, obesity, and pulmonary fibrosis.

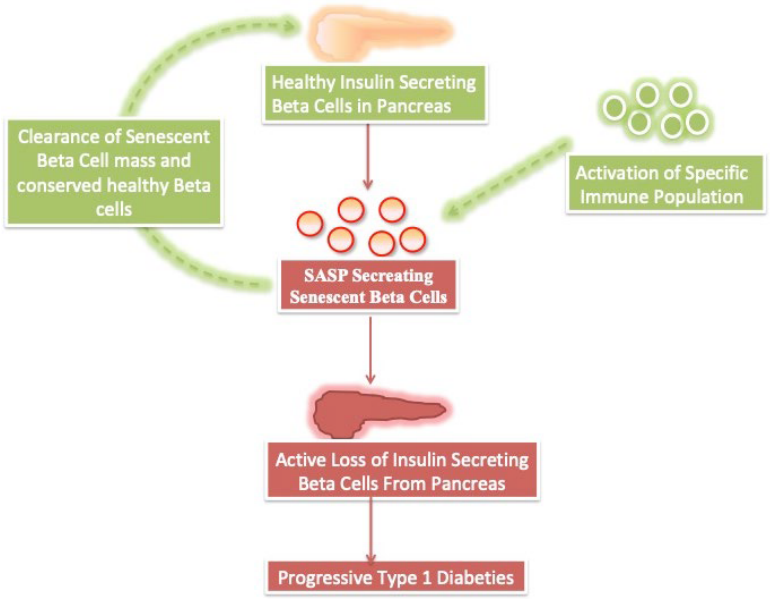

Figure 1: Activation of specific immune subset mitigates Type 1 Diabetes Progression

The current focus of my work is to delineate the effect of various immune cell populations in propagating and /or clearing out senescent cells. I am particularly interested in characterizing the cell population that plays a role in the accumulation of senescent cells by inhibiting their removal.

To this end, I harnessed our well-established high-fat diet rodent model of senescence and analyzed specific cell surface marker expression pertinent to cell survival on different immune cell populations.

From the current work, I have identified a characteristic population of B cells that decreases significantly during the development of senescence. The lab is currently focusing on targets and strategies to enhance this depleted subset and explore its therapeutic potential in preclinical settings.

The work from our lab supported by the grant entitled “iNKT cells orchestrate the removal of Senescent cells” is currently under revision for, Med, Cell Press Journal.