

## Monthly Woven Spotlight:

### The Orchestra of the Pancreas

#### Cellular Neighborhood

by James LeFevre

Like an orchestra, there are a multitude of cells in the pancreatic islets playing together in a symphony to maintain glucose homeostasis—alpha, beta, delta, pancreatic polypeptide, and epsilon cells. As it turns out, we've had our ear plugs in too far and haven't been able to hear the whole beta cell section until recently. Evidence has shown that beta cells are not a homogenous population, but instead heterogeneous with four different types. So, let's turn up the volume some more and try listening to the melodies of the beta cell section.

#### Distinguishing Beta Cell Subpopulations

Dorrell and colleagues present evidence that suggests four subpopulations of beta cells rather than one homogenous population. Using monoclonal antibody collections, the researchers examined cell surface antigens to distinguish beta cell subpopulations. Here is what the researchers found:

- Four subpopulations of beta cells were found based on cell surface marker expression.
- Each subpopulation is distinguished by their expressions of ST8SIA1 and CD9.
- Each subpopulation has a diverse gene expression profile and unique basal and glucose-stimulated insulin secretion.
- Each subpopulation demonstrates different insulin release kinetics.

The researchers state that the different insulin release kinetics of each subpopulation ensures a smooth release of insulin rather than sharp changes in insulin secretion. The distinct beta cell subpopulations were named as beta 1 through beta 4, where beta 1 is the most abundant and beta 4 is the most rare.

#### What Other Evidence is there?

In a review article by Gutierrez and colleagues, the authors review evidence that supports the heterogeneous nature of beta cell populations and factors that influence their development. The article summarizes the evidence from a morphological, functional, and molecular heterogeneity perspective. The authors state that novel single cell technologies have allowed the characterization of the molecular identity of beta cells creating a new era in the beta cell field.

#### So What if Beta Cells are Heterogeneous?

At the surface, the heterogeneity of beta cells may appear insignificant, however, its implications may be monumental. Zhou and Melton discuss the therapeutic potential that beta cell populations may have. Autoimmune attack in type 1 diabetes does not uniformly affect the pancreas. Islets and lobes of the pancreas often endure beta cell attack alluding to the possibility that beta cell subpopulations may evade autoimmunity. Zhou and Melton acknowledge that it is unclear whether the evasive beta cells are

created in response to autoimmunity or are resistant to beta cell attack. The researchers suggest that further understanding of the heterogeneity of beta cells may reveal molecular targets that allow the production of insulin-secreting cells resistant to autoimmunity.

**The Takeaway:** A substantial amount of evidence has suggested that beta cells are heterogeneous. Beta cell subpopulations differ in morphological and functional characteristics. This realization could explain the nature of nonuniform beta cell attack in type 1 diabetes. Going forward, beta cell heterogeneity may be used to our advantage in treating type 1 diabetes.