

Wendy Yang, Ph.D. Updates

Update on 4-24-17

Video Update

Update on 10-1-16

Over the past six months, I performed studies that focused on the activation of Cx43 function using a novel peptide (AAP10) that once added to cell cultures induce the phosphorylation of this connexins, and opening of Gap Junction made of Cx43, which in turn results in a greater cell-to-cell communication between adjacent cells (21,22).

Specifically, we conducted a series of experiments in which stem cells were differentiated in the presence or absence of the AAP10 peptide, and monitored for their ability to produce Definitive Endoderm, and, subsequently, pancreatic cell lineages.

The results of these studies show that addition of AAP10 to the culture media during the directed differentiation of stem cells toward pancreatic cell lineages leads to a significant increase in the number of Definitive Endoderm (DE) cells. Interestingly, when we continued the differentiation of these AAP10- treated cultures in the presence of this Gap Junction-activating peptide, we also observed a significant increase in the number Pdx1+ and Nkx6.1+ cells, as well as Pdx1+ /Sox9+ co-expressing cells. Subsequently, we also discovered that, to achieve this enhanced differentiation of stem cells toward pancreatic progenitors, the treatment with AAP10 is only required during the early stages of differentiation (i.e. up to DE stage), when Cx43 expression levels are most prominent. These results suggest that AAP10 (or increased utilization of Cx43-Gap Junctions) promote the development of a Definitive Endoderm that has a high propensity to commit toward the pancreatic cell lineage.

These are important discoveries since recent evidence indicate that without an effective early induction of Definitive Endoderm the commitment toward pancreatic endoderm and islet progenitors remain relatively low. Therefore, we believe that this is an important milestone in stem cell biology, as increasing the yields of pancreatic islet cells from undifferentiated stem-cell preparations will have significant implications for perfecting protocols for the derivation of insulin-producing cells to treat T1D.