

Congratulations to IMCB's latest PhD graduate – Larry LOO

Tuesday, 26 May 2020



Thesis Title: Dynamics of BCL-2 Family of Proteins in Early Pancreatic Progenitors and β -CELLS

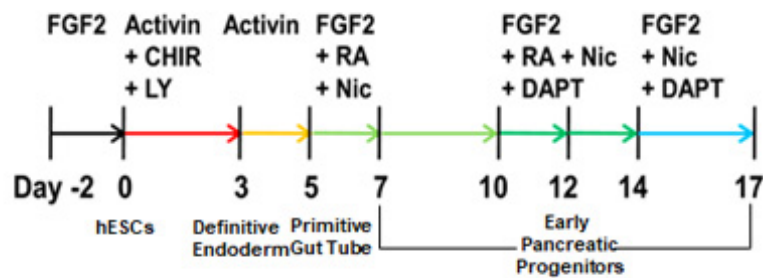
BCL-2 family of proteins play an important role in the regulation of cell survival and death. However, there are also certain members that exhibit tissue- and developmental stage-specific expression and function. Here, I report a unique reciprocal relationship between BCL-xL (not BCL2) and BAK during early human pancreatic differentiation.

The association of BCL-xL but not BCL2 with BAK has also been reported to keep apoptosis in check, albeit not specifically during pancreatic development. This is consistent with our findings that the compensatory increase in BCL2 protein expression upon BCL-xL inhibition with WEHI-539 is insufficient to curb the BAK mediated increase in cleaved caspase 3 and the triggering of the caspase cascade.

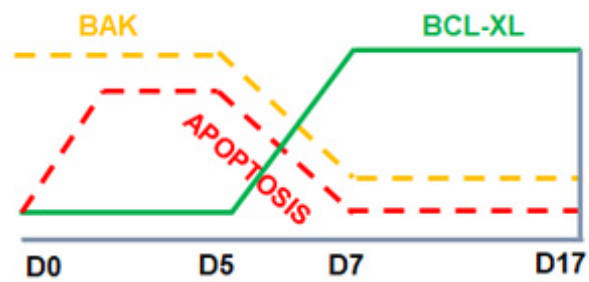
I also found that the downregulation of BCL2L1/BCL-xL expression and function resulted in a decrease in early pancreatic gene and protein expression. However, BCL-xL is known to be dispensable during rodent beta cell development but rather is important for protection against apoptotic stimuli in mature beta cells (Carrington et al., 2009). Therefore, I propose that BCL-xL might be indirectly involved in human pancreatic specification that is ultimately crucial for proper beta cell function.

Supervisor

Dr Adrian Teo Kee Keong



Differentiation of human embryonic stem cells into early pancreatic progenitors using 17D protocol



Schematics of BCL-xL and BAK expression levels contributing to pancreatic specification

Publications

- Lau H.H., Ng N.H.J., **Loo L.S.W**, Jasmen J.B., Teo K.K.A. (2017).
The molecular functions of hepatocyte nuclear factors in and beyond the liver.
J Hepatol, S0168-8278(17)32451-0
- **Loo, S.W.L, et al., 2017.**
An arduous journey from human pluripotent stem cells to functional pancreatic β -cells.
Diabetes, Obesity and Metabolism. Jan;20(1):3-13
- **Loo, S.W.L, et al., 2019.**
Dynamic proteome profiling of human pluripotent stem cell-derived pancreatic progenitors.
Stem Cells. Apr;38(4):542-555
- **Loo, S.W.L, et al., 2020.**
BCL-xL/BCL2L1 is a critical anti-apoptotic protein that promotes the survival of differentiating pancreatic cells from human pluripotent stem cells.
Cell Death and Disease. (Accepted).

Awards and Honors

- 1st Prize (NTU-Quintiles Challenge 2016)
- 2nd Prize – Most Original Idea Award (A*STAR-P&G Biotechnology Young Entrepreneur Scheme Competition 2016)
- Selected as one of the 100 leaders of tomorrow (LoT) in the Global Biotech Revolution GapSummit 2017 held in Washington D.C
- Selected for Finalist presentation at NTU Falling Walls Lab 2018 “Breaking the wall of insulin therapy for diabetes treatment”

