GAVALAS LAB : Description of available projects

Human pluripotent stem cell (hPSC) derived therapies for diabetes are in the forefront of the battle against this disease that has reached epidemic proportions. While it has been convincingly shown that hPSCs can be differentiated into functional pancreas endocrine cells (SC-islet cells), including insulin producing beta cells, several limitations remain. Among these are full and efficient conversion as well as functional maturation of beta cells. Endothelial cells and pericytes form the islet microvasculature and participate in beta cell maturation but they have not so far employed in this process.

To address these limitations, we have developed several hPSC reporter lines, a robust pancreatic progenitor expansion procedure and a method to generate SC-islets that include functional beta cells. MAFA is a key transcription factor mediating the maturation of human beta cells and, to understand this process, we have generated *MAFA* inducible hPSC lines. Additionally, we can now differentiate hPSCs into endothelial cells and pericytes which we are co-culturing with hPSC derived pancreas progenitors to enhance their differentiation. We are using these tools in combination with gene expression and chromatin studies at the SC-islet and single cell level as well as functional analyses to understand the human beta cell maturation mechanisms and generate SC-islets suitable for diabetes cell therapies. We are collaborating with the lab of Professor Ludwig to assess the potential of the SC-islets after transplantation with or without macroencapsulation.

PROJECT 1 : **Mechanisms of human beta cell maturation**
We will use the *MAFA* inducible hPSC lines to promote beta cell maturation and understand the function of this transcription factor in this process. The findings will be employed in the generation of mature SC-islets from hPSCs for diabetes cell therapies.

PROJECT 2 : **Pancreatic islet mini organs for diabetes cell therapy**
Generate islet mini organs by combining pancreas progenitors with endothelial cells and pericytes to promote beta cell maturation. Assess the effects by advanced imaging, molecular analyses, functional analyses in vitro and following transplantation.

BACKGROUND : Cell culture experience, preferably with human pluripotent stem cells, molecular biology and imaging.

NO OF STUDENTS : 2

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