ImmunoTools IT-Box-139 Award 2013

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Differentiation of Human ES/iPS-derived Medullary Thymix Epithelial Cells (mTECs) and the Expression of Promiscuous Antigens in Disease-in-a-dish Model of APECED

APECED is an autoimmune disease that affects multiple endocrine tissues. It is inherited in an autosomal recessive fashion and caused by the defect in the autoimmune regulator (AIRE) gene, located on the 21q22.3 chromosome, in the thymus. Normally, AIRE allows for the ectopic expression of tissue-specific proteins in the thymus medulla. This expression in the thymus, allows for the deletion of autoreactive thymocytes by exposing them to self-antigens during their development, a mechanism of central tolerance. This disease highlights the importance of the thymus in prevention of autoimmunity.

We hypothesize that APECED is not only a condition caused by the lack of AIRE expression in thymus epithelial cells, but rather a condition caused by the lack of AIRE expression in some cells in all three germ leyers; endo-, meso- and ectoderm. Also the disturbed development of medullary TECs in APECED might play role in Aire expression.

The aim of this study is to differentiate human embryonic stem (hES) cells *in vitro* into Aire-positive medullary thymic epithelial cells (mTECs). According to current knowledge this could be achieved step-by-step either by differentiating hES cells in the presence of critical growth factors and/or using co-cultures where *e.g.* T-cells provide suitable microenvironment to induce and direct stem cell diffentiation. When succeeded, we will proceed developing a disease-in-a-dish model for APECED by reprogramming patients` own fibroblasts into induced pluripotent stem (iPS) cells and further differentiate these cells again into mTECs. We will also differentiate control mTECs from healthy human fibroblasts and study the expression of promiscuous antigens produced by the iPS-derived mTECs of both study groups (normal controls vs. APECED patients). A long-term goal of our project is to develop a therapy for the APECED patients.

The ImmunoTools antibodies would be used to characterize the phenotypes of the various cells used in the experiments. In the FACS experiments the antibodies are used to determine the amount and phenotype of differentiated mTECs or mTEC progenitors and in sorting the right populations for further culturing.

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ImmunoTools *IT-Box-139.3* for **Pilvi Maliniemi** includes 100 antibodies

FITC - conjugated anti-human CD1a, CD2, CD3, CD4, CD5, CD6, CD7, CD8, CD9, CD11a, CD11b, CD14, CD15, CD16, CD18, CD19, CD21, CD25, CD29, CD36, CD41a, CD43, CD45, CD45RA, CD46, CD52, CD53, CD54, CD58, CD62p, CD63, CD69, CD71, CD80, CD86, CD95, CD235a, HLA-ABC, HLA-DR, IL-6, Control-IgG1, Control-IgG2a, Control-IgG2b, Annexin V

PE - conjugated anti-human CD2, CD3, CD4, CD8, CD11b, CD14, CD15, CD18, CD19, CD20, CD21, CD22, CD27, CD33, CD34, CD37, CD38, CD40, CD42b, CD45, CD45RB, CD50, CD72, CD95, CD105, CD147, CD177, Control-IgG1, Control-IgG2a, Control-IgG2b, Annexin V

PE/Dy647 -tandem conjugated anti-human CD45

APC -conjugated anti-human CD3, CD4, CD7, CD8, CD10, CD11c, CD14, CD16, CD19, CD27, CD37, CD40, CD44, CD56, CD59, CD61, CD62L, CD62P, CD69, IL-6, Control-IgG1, Control-IgG2a, Control-IgG2b, Annexin V DETAILS

plus CD45APC

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