The thymus is a lymphoid organ found in the neck region of vertebrates that produces T-cells critical for the adaptive immune system. However, thymus involution relatively early in the aging process leads to a deterioration in immune function. Models in regenerative medicine have the prospect of replacing lost cells and combating the problem. This experiment is a preliminary step geared towards achieving the overarching goal of boosting long-term maintenance of adaptive immunity over the typical aging process or following therapeutic immune depletion. Specifically, the objective is to show that disparate cell lineages can be reprogrammed—both morphologically and physiologically—using the forced expression of a transgene into components of a functional thymus and that these induced components can perform normal thymic duties, such as facilitating the maturation of T-cell progenitors into Helper and Cytoxic T-cells.

The methodology of the experiment includes successfully reprograming a line of mouse embryonic fibroblast cells (MEFs) into induced thymic epithelial cells (iTECs) using plasmid transfection to force the expression of transcription factor Foxn1, a master regulator of TEC development. A co-culture of the iTECs with early T-cell progenitors (ETPs) was generated, and after six days flow cytometry was employed to observe if any of the ETPs differentiated into mature T-cells, as would be expected of an in vivo system. Although the MEFs were successfully transformed into iTECs and partially-matured T-cells developed after co-culture, the cell line was not robust enough to support significant generation of fully-developed T cells. Additional experiments are underway to refine the process and further investigate the therapeutic functionality and gene expression profiles of the system.