CLAIMS

1. A thymic cell product generated by the process of:

a) generating one or more population of thymic cells;

b) extracting and sequencing RNA from each of the population of thymic cells;

c) analyzing RNA sequenced in a) to identify sub-populations within each population of thymic cells to generate a test thymic map for each of the population of thymic cells;

d) comparing each of the test thymic maps to a reference thymic map; and

e) identifying a thymic cell product by selecting a test thymic map that has a Sub-Population Ratio (SPR) or a Relative cTEC Ratio (RCTR) of from about 0.7 to 1.4.

2. The thymic cell product of claim 1, wherein the sub-populations within each population of thymic cells comprise one or more of immature thymic epithelial cells (iTECs), cTEC-high cells, cTEC-low cells, Aire+ mTEC-high cells, mTEC-low cells, Corneocyte like mTEC cells, Ciliated cells , Myelin cells, Myoid cells, Neuroendocrine cells and Tuft/lonocyte cells.

3. The thymic cell product of any one of claims 1-2, wherein the SPR of from about 0.7 to 1.4, preferably the SPR is a iTEC SPR, a cTEC-high SPR, a cTEC-low SPR, a Aire+ mTEC-high SPR, a mTEC-low SPR, a Corneocyte like mTEC SPR, a Ciliated SPR, a Myelin SPR, a Myoid SPR, a Neuroendocrine SPR and a Tuft/lonocyte SPR.

4. The thymic cell product of claim 2, wherein the iTEC SPR, the cTEC-high SPR, the cTEC-low SPR, the Aire+ mTEC-high SPR, the mTEC-low SPR, the Corneocyte like mTEC SPR, the Ciliated SPR, the Myelin SPR, the Myoid SPR, the Neuroendocrine SPR and the Tuft/lonocyte SPR is from about 0.7 to 1.4, preferably wherein the SPR is an the iTEC SPR, and wherein the iTEC is 1.

5. The thymic cell product of claim 1, wherein the RCTR is of from about 0.7 to 1.4, preferably the RCTR is 1.

6. The thymic cell product of claim 1, wherein the one or more populations of thymic cells are prepared by differentiation of stem cells, preferably induced pluripotent stem cells.

7. The thymic cell product of claim 1, wherein the reference thymus map is prepared from one or more human thymi, preferably wherein the human thymi are selected from fetal human thymi, postnatal human thymi, adolescent thymi, adult human thymi or a combination thereof.

8. The thymic cell product of claim 2, wherein:

(i) the subpopulation comprises iTEC, and wherein iTEC comprises expression of one or more of IGKC (ENSG00000211592), ANAX2, LIMA1 (ENSG00000050405), EGFR (ENSG00000146648), ASCL1 (ENSG00000139352), HES1 (ENSG00000114315), JUND (ENSG00000130522), FOS (ENSG00000170345), ARID5B (ENSG00000150347), IRF1 (ENSG00000125347), MAFB (ENSG00000204103), IFI16 (ENSG00000163565) , FOXC1 (ENSG00000054598), STAT1 (ENSG00000115415), JUNB (ENSG00000171223), EGFR1, ZFP36 (ENSG00000128016), JUN (ENSG00000177606), FOSB (ENSG00000125740), IER2 (ENSG00000160888), PAX9 (ENSG00000198807), and/or HIF1A (ENSG00000100644); and/or

(ii) the subpopulation comprises cTEC, and wherein cTEC comprises expression of one or more of PSMA3 (ENSG00000100567), FABP5 (ENSG00000164687), APRT (ENSG00000198931), LSM6 (ENSG00000164167), CTSV (ENSG00000136943), SNRPE (ENSG00000182004), ECHS1 (ENSG00000127884), HSPE1 (ENSG00000115541), RAN (ENSG00000132341), TMA7 (ENSG00000232112), TIMM13 (ENSG00000099800), LDHB (ENSG00000111716), ECI1 (ENSG00000167969), GCSH (ENSG00000140905), NOP58 (ENSG00000055044), MRPL11 (ENSG00000174547), STOML2 (ENSG00000165283),

ING2 (ENSG00000168556), TOMM7 (ENSG00000196683), MRPS34 (ENSG00000074071), MRPL14 (ENSG00000180992), MRPL57 (ENSG00000173141), IMP3 (ENSG00000177971), MZT2A (ENSG00000173272), and/or XRCC6 (ENSG00000196419); and/or

(iii) the subpopulation comprises corneocyte-like mTEC, and wherein corneocyte-like mTEC comprises expression of one or more of CD24 (ENSG00000272398), ELF3 (ENSG00000163435), CLDN4 (ENSG00000189143), MAL2 (ENSG00000147676), ASAH1 (ENSG00000104763), TMEM123 (ENSG00000152558), TMBIM6 (ENSG00000139644), LGALS3 (ENSG00000131981-), MYL12B (ENSG00000118680), ACADVL (ENSG00000072778), KRT19 (ENSG00000171345), SAT1 (ENSG00000130066), RAB25 (ENSG00000132698), WFDC2 (ENSG00000101443), VAMP8 (ENSG00000118640), SPINT1 (ENSG00000166145), SERPINB1 (ENSG00000021355), CDH1 (ENSG00000039068), GSN (ENSG00000148180), SDC4 (ENSG00000124145), MGST2 (ENSG00000085871), CAST (ENSG00000153113), B4GALT1 (ENSG00000086062), PERP (ENSG00000112378), and/or DMKN (ENSG00000161249).

9. A method for generating a population of thymic cells *in vitro* comprising:
culturing a population of cells in the presence of a soluble factor, a mineral or a combination thereof to induce differentiation or maturation of the population of cells to thymic cells;
wherein the population of cells is optionally engineered to express a cell surface receptor or an intracellular factor; and
wherein the population of cells comprises one or more cell types selected from the group consisting of pluripotent stem cells (PSCs), definitive endodermal (DE) cells, third pharyngeal pouch endodermal (PPE) cells, and anterior foregut endodermal (AFE) cells.

10. The method of claim 9, wherein the population of thymic cells comprises subpopulations of one or more of immature thymic epithelial cells (iTECs), cTEC-high cells, cTEC-low cells, Aire+ mTEC-high cells, mTEC-low cells, Corneocyte like

mTEC cells, Ciliated cells , Myelin cells, Myoid cells, Neuroendocrine cells and Tuft/lonocyte cells.

11. The method of claim 9, wherein the population of cells is cultured in the presence of a soluble factor, wherein the soluble factor is one or more of:

(i) a growth factor, preferably the growth factor is epidermal growth factor (EGF; ENSG00000138798);
(ii) a cytokine, preferably the cytokine is macrophage inhibitory factor (MIF; ENSG00000240972);
(iii) a transporter, preferably the transporter is Lactotransferrin (LTF; ENSG00000012223); or
(iv) a hormone.

12. The method of claim 9, wherein the population of cells is cultured in the presence of a mineral, preferably the mineral is one or more of iron, magnesium, calcium, manganese, molybdenum, phosphorus, potassium, sodium, sulfur, zinc, chloride, chromium, copper, fluoride or iodine, more preferably the mineral is iron.

13. The method of claim 9, wherein the population of cells is engineered to express:

(i) a cell surface receptor, preferably the cell surface receptor is CD74 (ENSG00000019582), integrin beta 1 (ITGB1; ENSG00000150093) or epidermal growth factor receptor (EGFR; ENSG00000146648); or
(ii) an intracellular factor, preferably the intracellular factor is Enolase 1 (ENO1; ENSG00000074800).

14. A method of maintaining a population of thymic cells *in vitro* comprising one or more of:

a) culturing the population of thymic cells in the presence of a soluble factor or a mineral;
b) culturing the population of thymic cells in the presence of one or more supporting cells; and/or

engineering the population of thymic cells to express a cell surface receptor or an intracellular factor.

15. The method of claim 14, wherein the population of thymic cells is cultured in the presence of a soluble factor, wherein the soluble factor is one or more of:

    (i) a growth factor, preferably the growth factor is epidermal growth factor (EGF; ENSG00000138798);
    (ii) a cytokine, preferably the cytokine is macrophage inhibitory factor (MIF; ENSG00000240972);
    (iii) a transporter, preferably the transporter is Lactotransferrin (LTF; ENSG00000012223); or
    (iv) a hormone.

16. The method of claim 14, wherein the population of thymic cells is cultured in the presence of a mineral, preferably the mineral is one or more of iron, magnesium, calcium, manganese, molybdenum, phosphorus, potassium, sodium, sulfur, zinc, chloride, chromium, copper, fluoride or iodine, more preferably the mineral is iron.

17. The method of claim 14, wherein the population of thymic cells is engineered to express:

    (i) a cell surface receptor, preferably the cell surface receptor is CD74 (ENSG00000019582), integrin beta 1 (ITGB1; ENSG00000150093) or epidermal growth factor receptor (EGFR; ENSG00000146648); or
    (ii) an intracellular factor, preferably the intracellular factor is Enolase 1 (ENO1; ENSG00000074800).

18. The method of claim 14, wherein the population of thymic cells is cultured in the presence of one or more supporting cells, preferably the supporting cells are one or more of endothelial cells, mesenchymal stem cells, macrophages, dendritic cells

(DCs), epithelial cells, fibroblasts, stromal cells, adipocytes, fibroblasts, vascular smooth muscle cells (VSMCs), or lymphatic endothelial cells.

19. The method of claim 18, wherein the supporting cells are mesenchymal stem cells or endothelial cells.

20. The method of any one of claims 14-19, wherein the population of thymic cells comprises sub populations of one or more selected from the group consisting of thymic epithelial progenitor cell (TEPCs), immature thymic epithelial cells (iTECs), thymic epithelial cells (TECs), medullary thymic epithelial cells (mTECs) and cortical thymic epithelial cells (cTECs).