CLAIMS

1. A transgenic swine, comprising one or more nucleotide sequences encoding one or more HLA I polypeptides and/or one or more HLA II polypeptides inserted into one or more native SLA loci of the pig genome,

wherein the one or more nucleotide sequences are inserted downstream a native SLA I promoter.

2. The transgenic swine of claim 1, wherein the one or more nucleotide sequences encode HLA I polypeptides inserted into a native SLA I locus.

3. The transgenic swine of claim 2, wherein the SLA I locus is selected from the group consisting of SLA-1 and SLA-2.

4. The transgenic swine of claim 2, wherein the HLA I polypeptides comprise HLA-A2 fused to human beta-2 microglobulin (B2M).

~~5. The transgenic swine of claim 2-4, wherein the one or more nucleotide sequences are inserted behind a native SLA I promoter.~~

~~6~~5. The transgenic swine of claim 2-4, wherein the one or more nucleotide sequences are inserted at the intron 1/exon 2 junction of the SLA I locus.

~~7~~6. The transgenic swine of claims 2-~~6~~5, wherein the one or more nucleotide sequences further encode HLA II polypeptides inserted into the native SLA-DQα locus.

~~8~~7. The transgenic swine of claim 1, wherein the one or more nucleotide sequences encode HLA II polypeptides inserted into the native SLA-DQα locus.

~~9~~8. The transgenic swine of claims ~~7-8~~6-7, wherein the HLA II polypeptides comprise ~~the~~ HLA-DQ8 polypeptides.

~~10~~9. The transgenic pig of claim ~~10~~8, wherein the HLA-DQ8 polypeptides are targeted to the native SLA-DQα locus through a bicistronic vector encoding HLA-DQ8 (HLA-DQA1:03:01:01 and HLA-DQB1:03:02:01).

~~11~~10. The transgenic swine of claim ~~10~~9, wherein the bicistronic vector further comprises a high-efficiency IRES element.

~~12~~11. The transgenic swine of claims 7-~~11~~10, wherein the one or more nucleotide sequences encoding the HLA II polypeptides are inserted ~~behind~~ downstream the native SLA DQα promoter.

~~13~~12. The transgenic swine of claims 7-~~11~~10, wherein the one or more nucleotide sequences encoding the HLA II polypeptides are inserted at the intron 1/exon 2 junction of the SLA DQα locus.

~~14~~13. The transgenic swine of claim 1, wherein the HLA I polypeptides are selected from the group consisting of HLA-A, HLA-A2, HLA-B, HLA-C, HLA-E, HLA-F and HLA-G, and wherein the HLA II polypeptides are selected from the group consisting of HLA-DP, HLA-DM, HLA-DO, HLA-DQ, and HLA-DR.

~~15~~14. ~~A method of xenotransplantation of thymic tissue into a subject in need thereof, comprising the introduction of thymic tissue from the transgenic swine according to any of claims 1-14 into the subject.~~ Use of thymic tissue from the transgenic swine according to any of claims 1-13 in the manufacture of a medicament for xenotransplantation of thymic tissue into a subject in need thereof.

~~16~~15. ~~A method of recovering or restoring impairment of the function of the thymus in a subject in need thereof, comprising the introduction of thymic tissue from the transgenic swine according to any of claims 1-13 into the subject.~~ Use of thymic tissue from the transgenic swine according to any of claims 1-13 in the manufacture of a medicament to recover or restore impairment of the function of the thymus in a subject in need thereof.

~~17~~16. ~~A method of reconstituting T cells in a subject in need thereof, comprising the introduction of thymic tissue from the transgenic swine according to any of claims 1-13 into the subject.~~ Use of thymic tissue from the transgenic swine according to any of claims 1-13 in the manufacture of a medicament to reconstitute T cells in a subject in need thereof.

~~18~~17. The ~~method~~ use of claims ~~15-17~~14-16, wherein the subject is a human.

~~19~~18. The ~~methods~~ use of claims ~~15-18~~14-17, wherein the transgenic swine comprises HLA polypeptides derived from the subject.

~~20~~19. A method of producing a transgenic swine of any of claims 1-~~14~~13, comprising administering at least one targeting vector and at least one CRISPR-Cas9 plasmid into a

swine cell, wherein the targeting vector comprises one or more nucleotide sequences encoding one or more HLA I polypeptides and/or one or more HLA II polypeptides.

~~21~~20. The method of claim ~~20~~19, wherein the one or more nucleotide sequences encoding one or more HLA I polypeptides and/or one or more HLA II polypeptides derive from a specific individual subject.

~~22~~21. A method of generating a human immune system (HIS) mouse, comprising thymectomizing the mouse and introducing swine fetal thymic tissue and human CD34+ cells into the mouse.

~~23~~22. The method of claim ~~22~~21, wherein the human CD34+ cells are fetal or adult.

~~24~~23. The method of claim ~~22~~21, wherein the human CD34+ cells are derived from cord blood.

~~25~~24. A method of generating a human immune system (HIS) mouse, comprising thymectomizing the mouse and introducing swine fetal thymic tissue, wherein the fetal thymic tissue is derived from the transgenic swine of claims 1-~~14~~13.