CLAIMS

1. A transgenic swine, comprising: (a) one or more nucleotide sequences encoding one or more HLA II polypeptides or (b) one or more nucleotide sequences encoding one or more HLA I polypeptides and 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 encoding the one or more HLA I polypeptides are inserted downstream a native SLA I promoter, and the one or more nucleotide sequences encoding the one or more HLA II polypeptides are inserted downstream a native SLA II promoter.

2. The transgenic swine of claim 1, comprising one or more nucleotide sequences encoding one or more HLA I polypeptides and 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 encoding the one or more HLA I polypeptides are inserted downstream a native SLA I promoter, and the one or more nucleotide sequences encoding the one or more HLA II polypeptides are inserted downstream a native SLA II promoter.

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

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

5. The transgenic swine of claim 3, wherein the HLA I polypeptides comprise HLA-A2 fused to human beta-2 microglobulin (B2M).

6. The transgenic swine of claim 3-5, wherein the one or more nucleotide sequences are inserted at the intron 1/exon 2 junction of the SLA I locus.

7. The transgenic swine of claims 3-6, wherein the one or more nucleotide sequences further encode HLA II polypeptides inserted into the native SLA-DQα locus.

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

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

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

12. The transgenic swine of claims 8-11, wherein the one or more nucleotide sequences encoding the HLA II polypeptides are inserted downstream the native SLA DQα promoter.

13. The transgenic swine of claims 8-11, 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. The transgenic swine of claim 1 or 2, 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. Use of thymic tissue from the transgenic swine according to any of claims 1-14 in the manufacture of a medicament for xenotransplantation of thymic tissue into a subject in need thereof.

16. Use of thymic tissue from the transgenic swine according to any of claims 1-14 in the manufacture of a medicament to recover or restore impairment of the function of the thymus in a subject in need thereof.

17. Use of thymic tissue from the transgenic swine according to any of claims 1-14 in the manufacture of a medicament to reconstitute T cells in a subject in need thereof.

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

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

20. A method of producing a transgenic swine of any of claims 1-14, 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. The method of claim 20, 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. A method of generating a human immune system (HIS) mouse, comprising:

(a) thymectomizing the mouse and

(b) introducing:

(i) swine fetal thymic tissue and

(ii) human CD34+ cells into the mouse,

wherein the fetal thymic tissue is derived from the transgenic swine of claims 1-14.

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

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