

WHAT WE CLAIM IS:

1. A method of selecting pigs suitable as donors for xenotransplantation of tissues and/or cells, or as foundation pigs for further manipulation, said method comprising the step:
 - 5 a) providing a designated pathogen-free (DPF) pig herd having a low PERV copy number of between 4 and 40;
 - b) testing the PERV status of individual pigs of the herd using complete genome sequencing (CGS);
 - c) identifying individual pigs that have PERV-C and PERV-A/C negative status; and
 - 10 d) selecting said PERV-C and PERV-A/C negative pigs as donor pigs for xenotransplantation, or as foundation pigs for further manipulation.
2. The method of claim 1 further comprising identifying the PERV-A and PERV-B status of the PERV-C negative pigs of step d) and further selecting pigs that have a very low number of functioning PERV-A and PERV-B sequences of between 1-10,
15 preferably between 1-5, and most preferably between 1-2.
3. The method of claim 1 or 2 wherein the pigs are Auckland Island (AI) pigs.
4. The method of any one of claims 1-3, wherein the pigs are PERV-null.
5. Pigs selected by the method of any one of claims 1-4.
6. A method of breeding a herd of pigs that have no functional PERV genomic
20 sequences suitable as donors for xenotransplantation, or as foundation pigs for further manipulation, said method comprising the steps:
 - a) selecting PERV-C and PERV-A/C negative male and female pigs using the CGS selection method of any one of claims 1-4;
 - b) analysing the chromosomal location of any functioning PERV-A and PERV-B
25 gene sequences in the male pigs of step a);
 - c) selecting male pigs that have functioning PERV-A and/or PERV-B present in the Y-chromosome only;

- d) breeding the male pigs of step c) with the female pigs of step a) to produce progeny; and
 - e) selecting female progeny that will lack the paternal functional PERV-A and/or PERV-B as future breeding stock to produce a herd of pigs that have no functional PERV genomic sequences and that are suitable as donors of tissues and/or cells for xenotransplantation, or as foundation pigs for further manipulation.
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7. A pig herd bred by the method of claim 6.
8. A method of providing donor pigs suitable for xenotransplantation of whole organs, tissues and/or cells into a human recipient comprising the steps:
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- (a) selecting PERV-C and PERV-A/C negative donor pigs using the CGS method of any one of claims 1-4,
 - (b) establishing a PERV-C and PERV-A/C negative cell line from the pigs of step (a);
 - 15 (c) gene editing cells of said cells of step (b) to eliminate or deactivate one or more xenoantigen genes;
 - (d) optionally gene editing selected isolated cells of step (c) to express one or more human genes selected from A20, CD39, CD46, CD47, CD55, CD59, hemoxygenase-1 (HO-1), HLA-E, HLA-G, thrombomodulin (TM), CTLA4-Ig, and LEA29Y;
 - 20 (e) establishing a gene-edited cell line from the pig cells of step (c) or (d);
 - (f) carrying out somatic cell nuclear transfer from one or more of said gene edited cells of step (e) into an oocyte from a PERV-C and PERV-A/C negative pig in vitro;
 - 25 (g) culturing to blastocyst stage;
 - (h) transferring said blastocyst(s) to a female PERV-C and PERV-A/C negative pig and growing to full term; and
 - (i) providing donor pigs that are PERV-C and PERV-A/C negative and gene edited for one or more xenoantigens.

9. The method of claim 8, wherein the one or more xenoantigen genes is selected from GGTA1, CAMH, B4GalNT2, Neu5Gc, ASGR1 and SLA.
10. A pig cell line that is PERV-C and PERV-A/C negative and gene edited for inactivation or deletion of one or more xenoantigens and optionally for insertion of one or more human genes, produced by the method of claim 8(a)-(d) or 9.
11. Donor pigs that are PERV-C and PERV-A/C negative and gene edited for inactivation or deletion of one or more xenoantigens and optionally gene edited for expression of one or more human genes, produced by the method of claim 8 or 9.
12. Organs, tissues and/or cells from the pigs of any one of claims 5, 7 and 11 for use in xenotransplantation.
13. The organs, tissues and/or cells for use in xenotransplantation of claim 12, selected from the group consisting of kidney, liver, lung, heart, brain, pancreas, muscle, blood, bone, testes and ovary.
14. The tissue and/or cells for use in xenotransplantation of claim 12 or 13, selected from pancreatic islets, hepatocytes, non-parenchymal liver cells, gall bladder epithelial cells, gall bladder endothelial cells, bile duct epithelial cells, bile duct endothelial cells, hepatic vessel epithelial cells, hepatic vessel endothelial cells, sinusoid cells, choroid plexus cells, fibroblasts, Sertoli cells, adrenal chromaffin cells and muscle cells.
15. A method of treating a patient suffering from or predisposed to a disease, disorder or condition associated with a deficiency in or absence of organ function, said method comprising transplanting an organ, tissue and/or cells of any one of claims 11-14 to a patient in need thereof.