

WE CLAIM:

1. A rodent whose genome comprises a humanized Programmed cell death 1 (Pdc1) gene at an endogenous Pdc1 locus,
wherein said rodent expresses a humanized Programmed cell death 1 (PD-1) polypeptide from said humanized Pdc1 gene,
which humanized PD-1 polypeptide comprises a human portion and an endogenous portion,
wherein the human portion comprises an extracellular portion of a human PD-1 polypeptide and the endogenous portion comprises the intracellular portion of an endogenous rodent PD-1 polypeptide,
wherein said extracellular portion is encoded by exon 2 and a portion of exon 3 of a human Pdc1 gene, and
wherein said rodent is a mouse or a rat.
2. The rodent of claim 1, wherein the humanized PD-1 polypeptide is translated in a cell of the rodent with a rodent signal peptide.
3. The rodent of claim 1 or 2, wherein the humanized PD-1 polypeptide further comprises the transmembrane portion of the endogenous PD-1 polypeptide.
4. The rodent according to any one of claims 1-3, wherein the human portion comprises amino acids 26-169 of a human PD-1 polypeptide.
5. The rodent according to any one of claims 1-4, wherein the humanized Pdc1 gene comprises endogenous Pdc1 exons 1, 4 and 5.
6. The rodent according to claim 5, wherein the humanized Pdc1 gene further comprises a portion of an endogenous Pdc1 exon 3.
7. The rodent according to any one of claims 1-6, wherein the humanized Pdc1 gene is operably linked to a rodent Pdc1 promoter.

8. The rodent of claim 7, wherein the Pdccl1 promoter is an endogenous rodent Pdccl1 promoter.
9. The rodent according to any one of claims 1-8, wherein the humanized Pdccl1 gene results from a replacement of a genomic fragment of the endogenous Pdccl1 gene with a genomic fragment of a human Pdccl1 gene.
10. The rodent of claim 9, wherein the humanized Pdccl1 gene comprises exon 1 of the endogenous Pdccl1 gene, exon 2 and a part of exon 3 of the human Pdccl1 gene, a part of exon 3 of the endogenous Pdccl1 gene, and exons 4-5 of the endogenous Pdccl1 gene.
11. An isolated rodent cell or tissue whose genome comprises a humanized Pdccl1 gene at an endogenous Pdccl1 locus,
wherein said humanized Pdccl1 gene encodes a humanized PD-1 polypeptide, which humanized PD-1 polypeptide comprises a human portion and an endogenous portion,
wherein said human portion comprises an extracellular portion of a human PD-1 polypeptide and the endogenous portion comprises the intracellular portion of an endogenous rodent PD-1 polypeptide,
wherein said extracellular portion is encoded by exon 2 and a portion of exon 3 of a human Pdccl1 gene, and
wherein said rodent is a mouse or a rat, wherein the rodent cell is optionally a rodent embryonic stem cell.
12. A rodent embryo generated from a rodent embryonic stem cell according to claim 11.
13. A method of making a rodent whose genome comprises a Pdccl1 gene that encodes a PD-1 polypeptide having a human portion and an endogenous portion, which portions are operably linked to a rodent Pdccl1 promoter, the method comprising

modifying a rodent genome so that the modified genome comprises a humanized Pdccl1 gene at an endogenous Pdccl1 locus, and obtaining a rodent comprising the modified genome,

wherein said rodent expresses a humanized PD-1 polypeptide from said humanized Pdccl1 gene, which humanized PD-1 polypeptide comprises a human portion and an endogenous portion,

wherein said human portion comprises an extracellular portion of a human PD-1 polypeptide and the endogenous portion comprises the intracellular portion of an endogenous rodent PD-1 polypeptide,

wherein said extracellular portion is encoded by exon 2 and a portion of exon 3 of a human Pdccl1 gene, and

wherein said rodent is a mouse or a rat.

14. A method of making a rodent that expresses a PD-1 polypeptide from an endogenous Pdccl1 gene, wherein the PD-1 polypeptide comprises a human sequence, the method comprising

(a) inserting a human genomic fragment into an endogenous rodent Pdccl1 gene at an endogenous Pdccl1 locus in a rodent embryonic stem cell to form a humanized Pdccl1 gene that encodes a humanized PD-1 polypeptide,

wherein said humanized PD-1 polypeptide comprises a human portion and an endogenous portion,

wherein said human portion comprises an extracellular portion of a human PD-1 polypeptide and the endogenous portion comprises the intracellular portion of an endogenous rodent PD-1 polypeptide,

wherein said extracellular portion is encoded by exon 2 and a portion of exon 3 of a human Pdccl1 gene, and

wherein said rodent is a mouse or a rat,;

(b) obtaining the rodent embryonic stem cell generated in (a); and,

(c) creating a rodent using the rodent embryonic stem cell of (b).

15. The method of claim 13 or 14, wherein the humanized PD-1 polypeptide is translated in a cell of the rodent with a rodent signal peptide.

16. The method according to any one of claims 13-15, wherein the humanized PD-1 polypeptide further comprises the transmembrane portion of the endogenous PD-1 polypeptide.
17. The method according to any one of claims 13-16, wherein the human portion comprises amino acids 26-169 of a human PD-1 polypeptide.
18. The method according to any one of claims 13-17, wherein the humanized Pdccl1 gene comprises endogenous Pdccl1 exons 1, 4 and 5.
19. The method of claim 18, wherein the humanized Pdccl1 gene further comprises a portion of an endogenous Pdccl1 exon 3.
20. The method according to any one of claims 13-19, wherein the humanized Pdccl1 gene is operably linked to a rodent Pdccl1 promoter.
21. The method of claim 20, wherein the Pdccl1 promoter is an endogenous rodent Pdccl1 promoter.
22. The method according to any one of claims 13-21, wherein the humanized Pdccl1 gene results from a replacement of a genomic fragment of the endogenous Pdccl1 gene with the human genomic fragment.
23. The method of claim 22, wherein the humanized Pdccl1 gene comprises exon 1 of the endogenous Pdccl1 gene, exon 2 and a part of exon 3 of the human Pdccl1 gene, a part of exon 3 of the endogenous Pdccl1 gene, and exons 4-5 of the endogenous Pdccl1 gene.