

We claim:

1. A mouse whose genome comprises a replacement of exons 2, 3 and 4 of a mouse SIRP α gene at an endogenous mouse SIRP α locus with exons 2, 3 and 4 of a human SIRP α gene to form a humanized SIRP α gene, wherein said humanized SIRP α gene is operably linked to a mouse SIRP α promoter at said endogenous mouse SIRP α locus, and expresses in said mouse a humanized SIRP α protein comprising an extracellular portion of the human SIRP α protein encoded by said human SIRP α gene and an intracellular portion of the mouse SIRP α protein encoded by said mouse SIRP α gene.
2. The mouse of claim 1, wherein the humanized SIRP α gene comprises exons 1, 5, 6, 7 and 8 of said mouse SIRP α gene.
3. The mouse of claim 1 or 2, wherein said human SIRP α protein comprises the amino acid sequence as set forth in SEQ ID NO: 4.
4. The mouse of claim 3, wherein said humanized SIRP α protein comprises the amino acid sequence as set forth in SEQ ID NO: 5.
5. The mouse of any one of claims 1-4, wherein the mouse does not express a mouse SIRP α protein.
6. The mouse of any one of claims 1-5, wherein said humanized SIRP α protein is expressed on the cell surface in said mouse and supports the engraftment of human CD34⁺ hematopoietic stem cells.
7. An isolated mouse cell or tissue whose genome comprises a replacement of exons 2, 3 and 4 of a mouse SIRP α gene at an endogenous mouse SIRP α locus with exons 2, 3 and 4 of a human SIRP α gene to form a humanized SIRP α gene, wherein said humanized SIRP α gene is operably linked to a mouse SIRP α promoter at said endogenous mouse SIRP α locus, and encodes a humanized SIRP α protein comprising an extracellular portion of the human SIRP α protein encoded by said human SIRP α gene and an intracellular portion of the mouse SIRP α protein encoded by said mouse SIRP α gene.

8. The isolated cell or tissue of claim 7, wherein the humanized SIRP α gene comprises exons 1, 5, 6, 7 and 8 of said mouse SIRP α gene.
9. The isolated cell or tissue of claim 7 or 8, wherein the cell or tissue does not express a mouse SIRP α protein.
10. A method of making a mouse, comprising:
(a) replacing exons 2, 3 and 4 of a mouse SIRP α gene at an endogenous mouse SIRP α locus in a mouse ES cell with exons 2, 3 and 4 of a human SIRP α gene to form a humanized SIRP α gene, wherein said humanized SIRP α gene is operably linked to a mouse SIRP α promoter at said endogenous mouse SIRP α locus, and encodes a humanized SIRP α protein comprising an extracellular portion of the human SIRP α protein encoded by said human SIRP α gene and an intracellular portion of the mouse SIRP α protein encoded by said mouse SIRP α gene, thereby obtaining a modified mouse ES cell comprising said humanized SIRP α gene; and
(b) creating a mouse using the modified ES cell obtained in (a).
11. A method of providing a transgenic mouse, whereas one or more human cells are transplanted into a mouse according to any one of claims 1-6.
12. The method of claim 11, wherein the human cells are human hematopoietic stem cells.
13. A method of measuring phagocytosis of a labeled substrate by one or more mouse cells, comprising:
(a) providing one or more mouse cells whose genome comprises a replacement of exons 2, 3 and 4 of a mouse SIRP α gene at an endogenous mouse SIRP α locus with exons 2, 3 and 4 of a human SIRP α gene to form a humanized SIRP α gene, wherein said humanized SIRP α gene is operably linked to a mouse SIRP α promoter at said endogenous mouse SIRP α locus, and encodes a humanized SIRP α protein comprising an extracellular portion of the human SIRP α protein encoded by said human SIRP α gene and an intracellular portion of the mouse SIRP α protein encoded by said mouse SIRP α gene;
(b) incubating the one or more cells of step (a) with the labeled substrate; and
(c) measuring phagocytosis of the labeled substrate by the one or more cells of step (b).
14. A method of measuring phagocytosis of an antigen by one or more cells of a mouse comprising:
(a) providing a mouse according to any one of claims 1-6;

- (b) exposing the mouse to the antigen; and
- (c) measuring phagocytosis of the antigen by one or more cells of the mouse.

15. A method of assessing the therapeutic efficacy of a drug targeting human cells,
5 comprising:
- (a) providing a mouse according to any one of claims 1-6 into which one or more human cells have been transplanted;
 - (b) administering a drug candidate to said mouse; and
 - (c) monitoring the human cells in the mouse to determine the therapeutic efficacy of the
10 drug candidate.