

CLAIMS

1. A rodent, whose genome comprises a replacement of a genomic fragment of a rodent Dpp4 gene at an endogenous rodent Dpp4 locus with a genomic fragment of a human DPP4 gene to form a modified DPP4 gene, wherein the modified DPP4 gene encodes a human DPP4 protein, wherein expression of the modified DPP4 gene is under control of rodent regulatory elements at the endogenous rodent Dpp4 locus, wherein the rodent is a mouse or a rat, and wherein the rodent exhibits lung inflammation when infected with Middle East respiratory syndrome coronavirus (MERS-CoV).
2. The rodent of claim 1, wherein the genomic fragment of the human DPP4 gene comprises exon 2 through exon 26 of the human DPP4 gene.
3. The rodent of claim 2, wherein the genomic fragment of the rodent Dpp4 gene being replaced comprises exon 2 through exon 26 of the rodent Dpp4 gene.
4. The rodent of claim 2, wherein the rodent is a mouse, and wherein the modified DPP4 gene comprises endogenous mouse Dpp4 exon 1, operably linked to the genomic fragment of the human DPP4 gene.
5. The rodent of any one of claims 1-4, wherein the rodent is a mouse that is incapable of expressing a mouse Dpp4 protein.
6. The rodent of any one of claims 1-5, wherein the rodent is heterozygous for the modified DPP4 gene.
7. The rodent of any one of claims 1-5, wherein the rodent is homozygous for the modified DPP4 gene.
8. A method for making a humanized rodent, comprising replacing a genomic fragment of a rodent Dpp4 gene at an endogenous rodent Dpp4 locus with a genomic fragment of a human DPP4 gene to form a modified DPP4 gene, wherein the modified DPP4 gene encodes a human DPP4 protein, wherein expression of the modified DPP4 gene is under control of rodent regulatory elements at the endogenous rodent Dpp4

locus, wherein the rodent is a mouse or a rat, and wherein the rodent exhibits lung inflammation when infected with MERS-CoV.

9. A method for making a humanized rodent, comprising

(i) replacing a genomic fragment of a rodent *Dpp4* gene at an endogenous rodent *Dpp4* locus in a rodent embryonic stem cell with a genomic fragment of a human *DPP4* gene to form a modified *DPP4* gene, wherein the modified *DPP4* gene encodes a human *DPP4* protein, wherein expression of the modified *DPP4* gene is under control of rodent regulatory elements at the endogenous rodent *Dpp4* locus, and wherein the rodent is a mouse or a rat; and

(ii) generating a rodent from the rodent embryonic stem cell from step (i), wherein the rodent exhibits lung inflammation when infected with MERS-CoV.

10. The method of claim 8 or 9, wherein the genomic fragment of the human *DPP4* gene comprises exon 2 through exon 26 of the human *DPP4* gene.

11. The method of claim 10, wherein the genomic fragment of the rodent *Dpp4* gene being replaced comprises exon 2 through exon 26 of the rodent *Dpp4* gene

12. The method of any one of claims 8-11, wherein the rodent is a mouse, and wherein the modified *DPP4* gene comprises endogenous mouse *Dpp4* exon 1, operably linked to the genomic fragment of the human *DPP4* gene.

13. The method of any one of claims 8-12, wherein the rodent is a mouse that is incapable of expressing a mouse *Dpp4* protein.

14. The method of any one of claims 8-13, wherein the rodent is heterozygous for the modified *DPP4* gene.

15. The method of any one of claims 8-13, wherein the rodent is homozygous for the modified *DPP4* gene.

16. A method for determining the *in vivo* therapeutic efficacy of a human-specific *DPP4* antagonist in a rodent, the method comprising:

determining if a human-specific DPP4 antagonist treats or prevents one or more symptoms of MERS-CoV infection in a rodent according to any one of claims 1-7 which has been administered the DPP4 antagonist, as compared to control rodents infected with MERS-CoV but not administered the DPP4 antagonist.

17. The method of claim 16, wherein the DPP4 antagonist is selected from the group consisting of small molecules, peptides and antibodies.

18. The method of claims 16, wherein the DPP4 antagonist is an antibody to a MERS-CoV protein.

19. The method of claim 18, wherein the MERS-CoV protein is MERS-CoV spike protein.

20. The method of any one of claims 16-19, wherein the determining comprises measuring viral titer or RNA level.

21. The method of any one of claims 16-20, wherein the one or more symptoms of MERS-CoV infection comprise lung inflammation.

22. The method of any one of claims 16-21, wherein the one or more symptoms of MERS-CoV infection comprise weight loss.