

CLAIMS

1. A rodent whose genome comprises a replacement of a rodent C3 gene sequence at an endogenous rodent C3 locus with a human C3 gene sequence to form a modified C3 gene, wherein the rodent C3 gene sequence comprises an exon of the endogenous rodent C3 gene and the human C3 gene sequence comprises exon 2 through exon 41 of the human C3 gene, and wherein expression of the modified C3 gene is under control of rodent regulatory elements at the endogenous rodent C3 locus.
2. The rodent of claim 1, wherein the rodent is a mouse or a rat.
3. The rodent of claim 1 or claim 2, wherein the human C3 gene encoding sequence comprises exon 1 through exon 41 of the human C3 gene.
4. The rodent of any one of claims 1-3, wherein the rodent is a mouse and the modified C3 gene comprises exon 1 of the mouse C3 gene and exon 2 through exon 41 of the human C3 gene.
5. The rodent of any one of claims 1-4, wherein the rodent is a mouse that is incapable of expressing a mouse C3 protein.
6. The rodent of any one of claims 1-5, wherein the rodent is a mouse that expresses a mouse C5 protein encoded by an endogenous mouse C5 gene.
7. The rodent of claim 5, wherein the mouse expresses a human or humanized C5 protein.
8. The rodent of claim 7, wherein the mouse comprises a replacement of a mouse C5 gene sequence at an endogenous mouse C5 locus with a human C5 gene sequence to form a modified C5 gene.
9. The rodent of claim 7 or claim 8, wherein expression of the modified C5 gene is under

control of mouse regulatory elements at the endogenous mouse C5 locus.

10. The rodent of any one of claims 1-9, wherein the rodent is a mouse that expresses human C3 protein in serum at a concentration of at least about 10% of the level of mouse C3 protein present in the serum of an age-matched mouse that expresses functional endogenous mouse C3 protein, but does not comprise said replacement.

11. The rodent of any one of claims 1-10, wherein the rodent is a mouse that expresses human C3 protein in serum at a concentration of between about 10% and about 200% of the level of mouse C3 protein present in the serum of an age-matched mouse that expresses functional endogenous mouse C3 protein, but does not comprise said replacement.

12. The rodent of any one of claims 1-11, wherein the rodent is a mouse that expresses human C3 protein in serum at a concentration of between about 100 $\mu\text{g/ml}$ and about 1500 $\mu\text{g/ml}$.

13. The rodent of any one of claims 1-12, wherein the rodent is a mouse that expresses human C3 protein in serum at a concentration of at least about 100 $\mu\text{g/ml}$.

14. A method for making a humanized rodent, comprising replacing a rodent C3 gene sequence at an endogenous rodent C3 locus with a human C3 gene sequence to form a modified C3 gene, wherein the human C3 gene sequence comprises exon 2 through exon 41 of the human C3 gene and expression of the modified C3 gene is under control of rodent regulatory elements or sequences at the endogenous rodent C3 locus.

15. The method of claim 14, wherein the rodent is a mouse or a rat.

16. The method of claim 14 or 15, wherein the human C3 gene sequence replacing the rodent C3 gene sequence comprises all 41 exons of the human C3 gene sequence.

17. The method of any one of claims 14-16, wherein the rodent is a mouse and the

modified C3 gene comprises exon 1 of the mouse C3 gene and exon 2 through exon 41 of the human C3 gene.

18. A rodent whose genome comprises a replacement of a rodent C5 gene sequence at an endogenous rodent C5 locus with a human C5 gene sequence to form a modified C5 gene, wherein the human C5 gene sequence comprises exon 2 through exon 41 of the human C5 gene and expression of the modified C5 gene is under control of rodent regulatory elements or sequences at the endogenous rodent C5 locus, and wherein the rodent further comprises a replacement of a rodent C3 gene sequence at an endogenous rodent C3 locus with a human C3 gene sequence to form a modified C3 gene, wherein the human C3 gene sequence comprises exon 2 through exon 41 of the human C3 gene, and wherein expression of the modified C3 gene is under control of rodent regulatory elements or sequences at the endogenous rodent C3 locus.

19. The rodent of claim 18, wherein the rodent is a mouse or a rat.

20. The rodent of claim 19, wherein the rodent is a mouse that is incapable of expressing a mouse C5 protein and incapable of expressing a mouse C3 protein.

21. A method for identifying a compound capable of modulating complement activation comprising:

assaying whether complement activation in a rodent according to any one of claims 1-13 or 18-20 which has been administered with a compound is modulated, thereby identifying a compound capable of modulating complement activation.

22. The method of claim 21, wherein the compound is a small molecule chemical compound.

23. The method of claim 21, wherein the compound is a protein.

24. The method of claim 23, wherein the protein is an antibody.

25. The method of claim 21, wherein the compound is an inhibitory nucleic acid.
26. The method of any one of claims 21-25, wherein the serum of the rodent is assayed to determine if complement activation in the rodent is modulated.
27. The method of claim 26, wherein the assay is the CH₅₀ complement screening assay.