

What is claimed is:

1. A genetically modified non-human animal comprising in its germline an immunoglobulin light chain locus comprising two unrearranged human Vk gene segments and one or more unrearranged human Jk gene segment(s) operably linked to an immunoglobulin light chain constant region sequence,

wherein the two unrearranged human Vk gene segments are human Vk1-39 and Vk3-20 gene segments each comprising one or more substitutions of a non-histidine codon with a histidine codon, and

wherein the human Vk and Jk gene segments are capable of rearranging and the human Vk and Jk gene segments encode a human light chain variable domain comprising one or more histidines at a position selected from the group consisting of 105, 106, 107, 108, 109, 111 (according to IMGT numbering), and a combination thereof, wherein the one or more histidines are derived from the one or more substitutions.

2. The animal of claim 1, wherein the animal does not comprise an endogenous κ light chain variable region gene segment that is capable of rearranging to form an immunoglobulin light chain.

3. The animal of claim 1, wherein the immunoglobulin light chain constant region sequence is a non-human immunoglobulin light chain constant region sequence.

4. The animal of claim 3, wherein the non-human immunoglobulin light chain constant region sequence is a mouse or a rat sequence.

5. The animal of claim 3, wherein the non-human immunoglobulin light chain constant region sequence is an endogenous immunoglobulin light chain constant region sequence.

6. The animal of claim 1, further comprising in its germline an immunoglobulin heavy

chain locus that comprises an unrearranged immunoglobulin heavy chain variable region sequence comprising human V_H, D_H, and J_H gene segments operably linked to an immunoglobulin heavy chain constant region sequence.

7. The animal of claim 6, wherein the immunoglobulin heavy chain constant region sequence is a non-human immunoglobulin heavy chain constant region sequence.

8. The animal of claim 7, wherein the non-human immunoglobulin heavy chain constant region sequence is a mouse or a rat sequence.

9. The animal of claim 7, wherein the non-human immunoglobulin heavy chain constant region sequence is an endogenous non-human immunoglobulin heavy chain constant region sequence.

10. The animal of claim 1, wherein the two unrearranged human V_k gene segments and the one or more unrearranged human J_k gene segment(s) are present at the endogenous immunoglobulin light chain locus.

11. The animal of claim 1, wherein the immunoglobulin light chain constant region is a C_k region.

12. The animal of claim 1, wherein the animal is a rodent.

13. The rodent of claim 12, wherein the rodent is a rat or a mouse.

14. The rodent of claim 13, wherein the rodent is a mouse.

15. The animal of claim 1, wherein the animal comprises a population of B cells in response to an antigen of interest that is enriched for antibodies that exhibit a decrease in dissociative half-life ($t_{1/2}$) at an acidic pH as compared to neutral pH of at least about 2-fold, at least about 3-fold, at least about 4-fold, at least about 5-fold, at least about 10-

fold, at least about 15-fold, at least about 20-fold, at least about 25-fold, or at least about 30-fold.

16. The animal of claim 15, wherein the enrichment in antibodies that exhibit a decrease in $t_{1/2}$ is at least about 2 fold.

17. The animal of claim 1, wherein the animal comprises five human Jk segments, and the five human Jk segments are human Jk1, Jk2, Jk3, Jk4, and Jk5 segments.

18. The animal of claim 1, wherein the immunoglobulin light chain locus comprises no more than the human Vk1-39 and Vk3-20 gene segments and the one or more unrearranged human Jk gene segment operably linked to an immunoglobulin light chain constant region sequence.

19. The animal of claim 18, wherein either or both of the unrearranged human Vk1-39 and Vk3-20 gene segments comprise a substitution of three or four non-histidine codons with the histidine codons.

20. The animal of claim 19, wherein the substitution is of three non-histidine codons of the human Vk1-39 gene segment, and the substitution is designed to express histidines at positions 106, 108, and 111 of the human Vk1-39 gene segment.

21. The animal of claim 19, wherein the substitution is of four non-histidine codons of the human Vk1-39 gene segment, and the substitution is designed to express histidines at positions 105, 106, 108, and 111 of the human Vk1-39 gene segment.

22. The animal of claim 19, wherein the substitution is of three non-histidine codons of the human Vk3-20 gene segment, and the substitution is designed to express histidines at positions 105, 106, and 109 of the human Vk3-20 gene segment.

23. The animal of claim 19, wherein the substitution is of four non-histidine codons of

the human Vk3-20 gene segment, and the substitution is designed to express histidines at positions 105, 106, 107, and 109 of the human Vk3-20 gene segment.

24. The animal of claim 1, wherein the animal expresses a population of antigen-specific antibodies in response to an antigen wherein all antibodies in the population comprise:

immunoglobulin light chain variable domains derived from a rearrangement of the unrearranged human Vk1-39 and Vk3-20 gene segments and the one or more unrearranged human Jk gene segment(s), and

immunoglobulin heavy chains comprising human heavy chain variable domains derived from a repertoire of human heavy V, D, and J segments.

25. A method of making a non-human animal that comprises a genetically modified immunoglobulin light chain locus in its germline, the method comprising:

modifying a germline genome of the non-human animal to delete or render non-functional endogenous immunoglobulin light chain Vk and Jk gene segments in an immunoglobulin light chain locus, and

placing in the germline genome of the non-human animal an immunoglobulin light chain variable region comprising two unrearranged human Vk gene segments and at least one unrearranged human Jk gene segment, such that the immunoglobulin light chain variable region sequence is operably linked to an immunoglobulin constant region sequence,

wherein the two unrearranged human Vk gene segments are human Vk1-39 and Vk3-20 gene segments each comprising one or more substitutions of a non-histidine codon with a histidine codon, and

wherein the unrearranged human Vk and Jk gene segments are capable of rearranging and the unrearranged human Vk and Jk gene segments encode a human light chain variable domain comprising one or more histidines at a position selected from the group consisting of 105, 106, 107, 108, 109, 111 (according to IMGT

numbering) and a combination thereof, wherein the one or more histidines are derived from the one or more substitutions.

26. The method of claim 25, wherein the immunoglobulin light chain variable region is at the endogenous non-human immunoglobulin light chain locus.

27. The method of claim 25, wherein the animal is a rodent.

28. The method of claim 27, wherein the rodent is a mouse or a rat.

29. A method of generating an antibody that exhibits pH-dependent binding to an antigen of interest comprising: immunizing the animal of claim 1 with an antigen of interest.

30. The method of claim 29, further comprising selecting an antibody that binds to the antigen of interest with a desired affinity at a neutral pH while displaying reduced binding to the antigen of interest at an acidic pH.