

We claim:

1. A mouse whose genome comprises:

(a) an insertion of one or more human V_L gene segments and one or more human J_L gene segments upstream of a mouse immunoglobulin light chain constant region gene, wherein the one or more human V_L gene segments and one or more human J_L gene segments are operably linked to the mouse immunoglobulin light chain constant region gene;

(b) an insertion of one or more human V_L gene segments and one or more human J_L gene segments upstream of a mouse immunoglobulin heavy chain constant region gene, wherein the one or more human V_L gene segments and one or more human J_L gene segments are operably linked to the mouse immunoglobulin heavy chain constant region gene; and

(c) an ectopic nucleic acid sequence that encodes a mouse ADAM6a protein or a functional fragment thereof and an ectopic nucleic acid sequence that encodes a mouse ADAM6b protein or a functional fragment thereof, wherein the mouse ADAM6a and ADAM6b proteins or functional fragments thereof are expressed from the ectopic nucleic acid sequences,

wherein the mouse expresses an antibody comprising (i) a polypeptide that comprises a human light chain variable domain linked to a mouse heavy chain constant domain; and (ii) a polypeptide that comprises a human light chain variable domain linked to a mouse light chain constant domain.

2. The mouse of claim 1, wherein the mouse immunoglobulin light chain constant region gene is a mouse C_k.

3. The mouse of claim 1 or 2, wherein the one or more human V_L gene segments and one or more human J_L gene segments upstream of the mouse immunoglobulin light chain constant region gene are one or more human V_k gene segments and one or more human J_k gene segments.

4. The mouse of any one of the preceding claims, wherein the one or more human V_L gene segments and one or more human J_L gene segments upstream of the mouse immunoglobulin heavy chain constant region gene are one or more human V_k gene segments and one or more human J_k gene segments.

5. The mouse of any one of claims 1-4, wherein the ectopic nucleic acid sequences are present between two of the inserted one or more human V_L gene segments and one or more human J_L gene segments of (b).
6. The mouse of claim 5, wherein the inserted one or more human V_L gene segments and one or more human J_L gene segments are human κ light chain gene segments or human λ light chain gene segments.
7. The mouse of any one of the preceding claims, wherein the inserted one or more human V_L gene segments includes Vk5-2 and Vk4-1 and the ectopic nucleic acid sequences that encode the mouse ADAM6a and ADAM6b proteins or functional fragments thereof are present between Vk5-2 and Vk4-1.
8. The mouse of any one of claims 1-6, wherein the inserted one or more human V_L gene segments includes Vk4-1 and the inserted one or more J_L gene segments include Jk1 and the ectopic nucleic acid sequences that encode the mouse ADAM6a and ADAM6b proteins or functional fragments thereof are present between Vk4-1 and Jk1.
9. The mouse of any one of the preceding claims, wherein the mouse comprises one or more endogenous V_L and/or one or more endogenous J_L gene segments that are incapable of rearranging to form an immunoglobulin light chain variable sequence in the mouse.
10. The mouse of any one of the preceding claims, wherein the mouse comprises deletion of, or replacement of, one or more endogenous immunoglobulin heavy chain gene sequences.
11. A cell derived from the mouse of claim 1.
12. The cell of claim 11, wherein the cell is a B cell.
13. A hybridoma made from the B cell of claim 12.
14. A method for making an antibody that binds to an antigen of interest, wherein the method comprises
 - (a) exposing a mouse of claim 1 to an antigen of interest;

(b) isolating one or more B cells of the mouse, wherein the one or more B cells express an antibody that binds the antigen of interest;

(c) identifying a nucleic acid sequence that encodes one of the light variable chain domains of the antibody that binds that antigen of interest, wherein the antibody comprises a human immunoglobulin κ light chain variable domain linked to a mouse light chain constant domain and a human immunoglobulin κ light chain variable domain linked to a mouse heavy chain constant domain; and

(d) employing the nucleic acid sequence of (c) with a human immunoglobulin constant region nucleic acid sequence to make a human antibody that binds the antigen of interest.