

We claim:

1. A mouse comprising in its germline, at an endogenous mouse light chain locus, a human λ light chain variable region sequence, wherein the human lambda variable region sequence is expressed in a light chain that comprises a mouse immunoglobulin constant region gene sequence.
2. The mouse of claim 1, wherein the endogenous mouse light chain locus is a λ locus.
3. The mouse of claim 1, wherein the endogenous mouse light chain locus is a κ locus.
4. The mouse of claim 1, wherein the mouse lacks an endogenous light chain variable sequence at the endogenous mouse light chain locus.
5. The mouse of claim 1, wherein all or substantially all endogenous mouse light chain variable region gene segments are replaced with one or more human λ variable region gene segments.
6. The mouse of claim 1, wherein the human λ light chain variable region sequence comprises a human J λ sequence.
7. The mouse of claim 6, wherein the human J λ sequence is selected from the group consisting of J λ 1, J λ 2, J λ 3, J λ 7, and a combination thereof.
8. The mouse of claim 1, wherein the human λ light chain variable region sequence comprises a fragment of cluster A of the human light chain locus.
9. The mouse of claim 8, wherein the fragment of cluster A of the human λ light chain locus extends from hV λ 3-27 through hV λ 3-1.
10. The mouse of claim 1, wherein the human λ light chain variable region sequence comprises a fragment of cluster B of the human light chain locus.

11. The mouse of claim 10, wherein the fragment of cluster B of the human λ light chain locus extends from hV λ 5-52 through hV λ 1-40.
12. The mouse of claim 1, wherein the human λ light chain variable region sequence comprises a genomic fragment of cluster A and a genomic fragment of cluster B.
13. The mouse of claim 12, wherein the human λ light chain variable region sequence comprises at least one gene segment of cluster A and at least one gene segment of cluster B.
14. The mouse of claim 1, wherein more than 10% of the light chain repertoire of the mouse is derived from at least two hV λ gene segments selected from 2-8, 2-23, 1-40, 5-45, and 9-49.
15. The mouse of claim 14, wherein more than 20% of the light chain repertoire of the mouse is derived from at least three hV λ gene segments selected from 2-8, 2-23, 1-40, 5-45, and 9-49.
16. The mouse of claim 15, wherein more than 30% of the light chain repertoire of the mouse is derived from at least four hV λ gene segments selected from 2-8, 2-23, 1-40, 5-45, and 9-49.
17. A mouse that expresses an immunoglobulin light chain that comprises a human lambda variable sequence fused with a mouse constant region, wherein the mouse exhibits a κ usage to λ usage ratio of about 1:1.
18. The mouse of claim 17, wherein the immunoglobulin light chain is expressed from an endogenous mouse light chain locus.
19. Use of a mouse as described in any one of the preceding claims to make an antigen-binding protein.
20. Use according to claim 19, wherein the antigen-binding protein is human.
21. A cell or tissue derived from a mouse of any one of claims 1-18.

We claim:

1. A transgenic mouse whose genome comprises an endogenous λ light chain immunoglobulin locus comprising:
 - i) a deletion of a first endogenous $V\lambda$ - $J\lambda$ - $C\lambda$ gene cluster;
and
 - ii) a replacement of a fragment of endogenous $V\lambda$ and $J\lambda$ gene segments in a second endogenous $V\lambda$ - $J\lambda$ - $C\lambda$ gene cluster with human $V\lambda$ and $J\lambda$ gene segments, wherein the human $V\lambda$ and $J\lambda$ gene segments comprise at least one human $V\lambda$ gene segment and at least one human $J\lambda$ gene segment, and wherein the human $V\lambda$ and $J\lambda$ gene segments are operably linked to a mouse $C\lambda$ gene.
2. The transgenic mouse of claim 1, wherein the human $V\lambda$ and $J\lambda$ gene segments comprise a human $J\lambda 1$ gene segment.
3. The transgenic mouse of claim 1, wherein the human $V\lambda$ and $J\lambda$ gene segments comprise four human $J\lambda$ gene segments.
4. The transgenic mouse of claim 3, wherein the four human $J\lambda$ gene segments are $J\lambda 1$, $J\lambda 2$, $J\lambda 3$ and $J\lambda 7$.
5. The transgenic mouse of claim 1, wherein the endogenous mouse $V\lambda$ gene segments of the second endogenous $V\lambda$ - $J\lambda$ - $C\lambda$ gene cluster have been replaced with a contiguous sequence of the human immunoglobulin λ light chain locus that spans from a human $V\lambda 3-12$ gene segment to a human $V\lambda 3-1$ gene segment.
6. The transgenic mouse of claim 1, wherein the replacement endogenous mouse $V\lambda$ gene segments of the second endogenous $V\lambda$ - $J\lambda$ - $C\lambda$ gene cluster have been replaced with a contiguous sequence of the human immunoglobulin λ light chain locus that spans from a human $V\lambda 3-27$ gene segment to a human $V\lambda 3-1$ gene segment.

7. The transgenic mouse of claim 1, wherein the replacement comprises endogenous mouse V λ gene segments of the second endogenous V λ -J λ -C λ gene cluster have been replaced with a contiguous sequence of the human immunoglobulin λ light chain locus that spans from a human V λ 3-27 gene segment to a human V λ 3-1 gene segment and a contiguous sequence of the human immunoglobulin λ light chain locus that spans from a human V λ 5-52 gene segment to a human V λ 1-40 segment.
8. The transgenic mouse claim 1, wherein the human V λ and J λ gene segments comprise at least 12 human V λ gene segments.
9. The transgenic mouse of claim 8, wherein the 12 human V λ gene segments include human V λ 3-1, V λ 4-3, V λ 2-8, V λ 3-9, V λ 3-10, V λ 2-11 and V λ 3-12.
10. The transgenic mouse of claim 1, wherein the human V λ and J λ gene segments comprise at least 28 human V λ gene segments.
11. The transgenic mouse of claim 10, wherein the 28 human V λ gene segments include human V λ 2-14, V λ 3-16, V λ 2-18, V λ 3-19, V λ 3-21, V λ 3-22, V λ 2-23, V λ 3-25 and V λ 3-27.
12. The transgenic mouse of claim 1, wherein the human V λ and J λ gene segments comprise at least 40 human V λ gene segments.
13. The transgenic mouse of claim 12, wherein the 40 human V λ gene segments include human V λ 5-52, V λ 1-51, V λ 9-49, V λ 1-47, V λ 7-46, V λ 5-45, V λ 1-44, V λ 1-44, V λ 7-43 and V λ 1-40.