

germline J segments, wherein the VL region is selected for its capacity to pair with at least two different human or murine VH regions, wherein the endogenous kappa and/or lambda light chain loci are inactivated, and wherein the mouse is capable of producing antibodies harboring the VL region.

In yet another aspect, there is provided a transgenic mouse, comprising a nucleic acid encoding a rearranged VL region introduced into its germline, wherein the VL region is encoded by human germline V and germline J segments, wherein the VL region is capable of pairing with at least two different human or murine VH regions, wherein the endogenous kappa and/or lambda light chain loci are inactivated, and wherein the mouse is capable of producing antibodies harboring the VL region. In yet another aspect, there is provided use of B cells obtained from the transgenic mouse as described herein after immunization of said transgenic mouse with specific antigens as a source of VH regions.

Description

In the remainder of the specification mice are typically used as examples of the non-human mammals. The transgenic non-human mammalian hosts are capable of mounting an immune response to an antigen, where the response produces antibodies having primate, particularly human, variable regions. Various transgenic hosts may be

Claims

1. A method for the production of a transgenic mouse, comprising the step of introducing by site-specific recombination an expression cassette
 5 comprising a nucleic acid encoding a rearranged human VL region of a human immunoglobulin into the mouse germline, wherein the VL region is encoded by human germline V and germline J segments,
 wherein the VL region is selected for its capacity to pair with at least two different human or murine VH regions,
 10 wherein the endogenous kappa and/or lambda light chain loci are inactivated, and
 wherein the mouse is capable of producing antibodies harboring the VL region .
- 15 2. The method of claim 1, wherein the expression cassette further encodes a murine light chain constant region.
3. The method of any of claims 1 or 2, wherein the nucleic acid encoding said VL region is targeted to the mouse Ig kappa or lambda light chain
 20 locus so as to functionally inactivate the endogenous locus.
4. The method of any of claims 1 or 2, wherein the nucleic acid encoding said VL region is targeted to the Rosa locus.
- 25 5. The method of any of claims 1 to 4, wherein the nucleic acid encoding said VL region is introduced into pronuclei of fertilized mouse oocytes or embryonic stem cells.
- 30 6. A transgenic mouse, comprising a nucleic acid encoding a rearranged VL region introduced into its germline, wherein the VL region is encoded by human germline V and germline J segments,
 wherein the VL region is capable of pairing with at least two different human or murine VH regions,

wherein the endogenous kappa and/or lambda light chain loci are inactivated, and
wherein the mouse is capable of producing antibodies harboring the VL region.

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7. The transgenic mouse of claim 6, wherein the mouse further comprises a murine light chain constant region.

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8. The transgenic mouse of any of claims 6 or 7, wherein the nucleic acid encoding said VL region is targeted to the mouse Ig kappa or lambda light chain locus so as to functionally inactivate the endogenous locus.

9. The transgenic mouse of any of claims 6 or 7, wherein the nucleic acid encoding said VL region is targeted to the Rosa locus.

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10. Use of B cells obtained from the transgenic mouse of any of claims 6 to 9 after immunization of said transgenic mouse with specific antigens as a source of VH regions.

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11. The use of claim 10, wherein the VH regions are obtained by constructing cDNA libraries or by PCR amplification using primers for human VH regions.