

MICE EXPRESSING AN IMMUNOGLOBULIN HYBRID LIGHT CHAIN

FIELD

[0001] Genetically modified mice that comprise a mouse or human lambda variable (V λ) light chain sequence operably linked with a mouse or human light chain constant region (λ or kappa(κ)). Genetically modified mice that express epitope-binding proteins that comprise an immunoglobulin light chain comprising a variable domain derived from a human lambda variable (hV λ) gene segment, a human lambda J (hJ λ) gene segment, and a mouse light chain constant (C $_L$) domain. Genetically modified mice, comprising an unrearranged immunoglobulin lambda (λ) light chain variable nucleic acid sequence at an endogenous mouse light chain locus. Mice capable of rearranging and expressing a chimeric human λ /mouse C $_L$ light chain from an endogenous light chain locus that comprises a replacement of all endogenous mouse light chain variable region gene segments with one or more hV λ gene segments and one or more hJ λ gene segments. Somatic mutated antibodies comprising hV λ domains and mouse C $_L$ domains.

BACKGROUND

[0002] Mice that express antibodies that are fully human, or partly human and partly mouse, are known in the art. For example, transgenic mice that express fully human antibodies from transgenes containing human light and heavy chain immunoglobulin variable region genes have been reported. Genetically modified mice that comprise a replacement of the endogenous mouse heavy chain variable region (HCVR) gene segments and kappa (κ) light chain variable region (LCVR) gene segments with human HCVR and LCVR gene segments and that make chimeric antibodies with a chimeric human/mouse kappa chain are known as well.

[0003] Antibody light chains are encoded by one of two separate loci: kappa (κ) and lambda (λ). Mouse antibody light chains are primarily of the κ type. The ratio of κ to λ light chain usage in humans is about 60:40, whereas in mice it is about 95:5. Biased usage of κ light chains in mice is reportedly sustained in genetically modified mice capable of expressing fully or partly human antibodies. Thus, mice that express fully or partly human antibodies appear to be constrained in lambda variable usage.

[0004] There is a need in the art to generate lambda variable regions, whether mouse or human, for use in making epitope-binding proteins. There is a need in the art for mice that express fully or partly human antibodies, wherein the mice display an increased lambda variable (V λ) usage.

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