

Summary

Reported herein is a common antibody light chain variable domain that has the amino acid sequence

5 DIQMTQSPSS LSASVGDRVT ITCRASQSSIS SYLNWYQQKP
 GKAPKLLIYA ASSLQSGVPS RFSGSGSGTD FTLTISSLQP
 EDFATYYCQQ SYSTPLTFGG GTKVEIK (SEQ ID NO: 01)

or a variant thereof.

Reported herein is a common antibody light chain comprising a light chain variable domain that has the amino acid sequence

10 DIQMTQSPSS LSASVGDRVT ITCRASQSSIS SYLNWYQQKP
 GKAPKLLIYA ASSLQSGVPS RFSGSGSGTD FTLTISSLQP
 EDFATYYCQQ SYSTPLTFGG GTKVEIK (SEQ ID NO: 01)

or a variant thereof.

15 In one example the common light chain comprises up to 13 amino acid mutations.
 In one preferred example the common light chain comprises up to 13 amino acid mutations, whereof at most 11 are in the HVRs.

In one example the common light chain comprises up to 11 amino acid mutations.

20 In one example the common light chain comprises 1 to 11 amino acid mutations within the amino acid sequence of SEQ ID NO: 01. In one preferred example the common light chain comprises 1 to 13 amino acid mutations within the amino acid sequence of SEQ ID NO: 01, whereof at most 11 mutations are in the HVRs.

25 In one example a variant of the common antibody light chain as reported herein comprises a light chain variable domain that has a sequence identity to SEQ ID NO: 01 of 90 % or more (i.e. comprises up to 11 mutations). In one example the sequence identity is 95 % or more. In one example the sequence identity is 98 % or more.

Reported herein is an antibody comprising a light chain as reported herein.

Reported herein is a multispecific antibody comprising two or more different heavy chain variable domains and two or more common light chain variable domains as reported herein.

5 In one example the multispecific antibody is a bispecific full-length antibody comprising two different heavy chains and two common light chain variable domains or two common antibody light chains as reported herein.

In one example the multispecific antibody is a trispecific antibody comprising three different heavy chain variable domains and three common light chain variable domains as reported herein.

10 In one example the multispecific antibody is a tetraspecific antibody comprising four different heavy chain variable domains and four common light chain variable domains as reported herein.

Reported herein is the use of a common antibody light chain as reported herein for the generation of bispecific antibodies.

15 In one example the use is by combining two common antibody light chains with a first antibody heavy chain and a second antibody heavy chain, wherein the first antibody heavy chain together with a common antibody light chain forms a first antigen binding site and the second antibody heavy chain together with a common antibody light chain forms a second antigen binding site.

20 Reported herein is a transgenic vector comprising a humanized immunoglobulin light chain locus, wherein said humanized immunoglobulin light chain locus comprises

- (a) a V gene segment derived from human light chain V segment IGKV1-39-01,
- 25 (b) 3' proximal to said light chain gene segment a promoter, and
- (c) 5' proximal to said light chain gene segment at least a fragment of the human IGKJ4 J-element.

In one example transgenic vector comprises a humanized light chain locus, wherein said humanized light chain locus comprises

- 30 (a) as V gene segment the human light chain V segment IGKV1-39-01,

- (b) 3' proximal to said light chain gene segment a promoter, and
- (c) 5' proximal to said light chain gene segment the human IGKJ4 J-element or a functional fragment thereof.

5 Reported herein is a transgenic rabbit comprising the humanized immunoglobulin light chain locus present in the transgenic vector as reported herein. In one example the transgenic rabbit has an essentially intact endogenous regulatory and antibody production machinery.

In one example the transgenic rabbit further comprises

- 10 (1) a transgene derived from the rabbit immunoglobulin heavy chain locus, substituted with 8 human VH elements, human JH1-JH6 elements, human C μ -coding regions fused to human bcl2 coding sequence, and human C γ coding regions;
- 15 (2) a transgene derived from the rabbit immunoglobulin light chain locus, comprising the human V κ element IGKV1-39-01 and the human IgKJ4 J-element;
- (3) transgenes derived from the human CD79 α and CD79 β loci; and
- (4) loss-of-function mutations within the rabbit C μ and rabbit C κ loci.

20 Reported herein is a B-cell from the transgenic rabbit as reported herein, comprising the humanized immunoglobulin light chain locus present in the transgenic vector as reported herein.

In one aspect, reported herein is a B-cell from a transgenic rabbit comprising a humanized light chain immunoglobulin locus comprising

- (a) as V gene segment the human light chain V segment IGKV1-39-01,
- (b) 3' proximal to said light chain gene segment a promoter, and
- 25 (c) 5' proximal to said light chain gene segment the human IGKJ4 J-element, wherein the transgenic rabbit further comprises

- (1) a transgene derived from the rabbit immunoglobulin heavy chain locus, substituted with 8 human VH elements, human JH1-JH6 elements, human C μ -coding regions fused to human bcl2 coding sequence, and human C γ coding regions;
 - 5 (2) a transgene derived from the rabbit immunoglobulin light chain locus, comprising the human V κ element IGKV1-39-01 and the human IgKJ4 J-element;
 - (3) transgenes derived from the human CD79 α and CD79 β loci; and
 - (4) loss-of-function mutations within the rabbit C μ and rabbit C κ loci.
- 10 As reported herein is a method for producing a human immunoglobulin using the transgenic rabbit as reported herein.

In one example the human immunoglobulin is an antibody. In one example the human immunoglobulin is a polyclonal antibody. In one preferred example the human immunoglobulin is a monoclonal antibody.

Patent Claims

1. A B-cell from a transgenic rabbit comprising a humanized light chain immunoglobulin locus comprising
 - (a) as V gene segment the human light chain V segment IGKV1-39-01,
 - 5 (b) 3' proximal to said light chain gene segment a promoter, and
 - (c) 5' proximal to said light chain gene segment the human IGKJ4 J-element, wherein the transgenic rabbit further comprises
 - 10 (1) a transgene derived from the rabbit immunoglobulin heavy chain locus, substituted with 8 human VH elements, human JH1-JH6 elements, human C μ -coding regions fused to human bcl2 coding sequence, and human C γ coding regions;
 - (2) a transgene derived from the rabbit immunoglobulin light chain locus, comprising the human V κ element IGKV1-39-01 and the human IgKJ4 J-element;
 - 15 (3) transgenes derived from the human CD79 α and CD79 β loci; and
 - (4) loss-of-function mutations within the rabbit C μ and rabbit C κ loci.