Summary

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

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

or a variant thereof.

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

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

or a variant thereof.

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

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

In one embodiment the common light chain comprises 1 to 11 amino acid mutations within the amino acid sequence of SEQ ID NO: 01. In one preferred embodiment 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.

In one embodiment 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 embodiment the sequence identity is 95 % or more. In one embodiment the sequence identity is 98 % or more.

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

As 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.

In one embodiment 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.

One aspect as reported herein is a bispecific full-length antibody comprising two heavy chains and two common light chains each comprising a variable domain that has the amino acid sequence of SEQ ID NO: 01 or is a variant thereof.

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

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

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

One aspect as reported herein is use of a common antibody light chain comprising a variable domain that has the amino acid sequence of SEQ ID NO: 01 or is a variant thereof for the generation of bispecific antibodies.

In one embodiment 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.

As 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,

(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.

One aspect as reported herein is a transgenic vector comprising a humanized light chain locus, wherein said humanized light chain locus comprises

(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.

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

(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.

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

In one embodiment 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 Cμ-coding regions fused to human bcl2 coding sequence, and human Cγ coding regions;

(2) a transgene derived from the rabbit immunoglobulin light chain locus, comprising the human Vκ element IGKV1-39-01 and the human IgKJ4 J-element;

(3) transgenes derived from the human CD79α and CD79β loci; and

(4) loss-of-function mutations within the rabbit Cμ and rabbit Cκ loci.

As 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.

One aspect as reported herein is a B-cell from the transgenic rabbit as reported herein, comprising the humanized immunoglobulin locus present in the transgenic vector as reported herein.

One aspect as reported herein is a method for producing a human immunoglobulin using the transgenic rabbit as reported herein.

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