

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.

5 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.

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.

10 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.

15 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.

20 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,

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 embodiment 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 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.

One aspect as reported herein is a transgenic rabbit, comprising a humanized light chain immunoglobulin locus comprising

- 10 (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,

further comprising

- 15 (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;
- (3) transgenes derived from the human CD79 α and CD79 β loci; and
- 5 (4) loss-of-function mutations within the rabbit C μ and rabbit C κ loci.

In one embodiment 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;
- (3) transgenes derived from the human CD79 α and CD79 β loci; and
- 15 (4) loss-of-function mutations within the rabbit C μ and rabbit C κ 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.

20 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.

Patent Claims

1. 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,

further comprising

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.