

chain comprises a heavy chain variable domain, the amino acid sequence of which is the sequence of SEQ ID NO:1, and in which each light chain comprises a light chain variable domain, the amino acid sequence of which is the sequence of SEQ ID NO:2.

5 A particular embodiment is antibody Ab327, which is an engineered and humanized antibody to human IL-21, the amino acid sequence of each heavy chain of which is the sequence of SEQ ID NO:3 and the amino acid sequence of each light chain of which is the sequence of SEQ ID NO:4.

The present ~~invention-disclosure~~ also provides pharmaceutical compositions comprising the antibodies of the invention and a pharmaceutically-acceptable excipient.

10 The present ~~disclosure invention~~ also includes DNA molecules encoding the heavy and light chains of the antibodies of the present ~~disclosure invention~~ for expressing the antibodies of the present ~~disclosure invention~~. In particular, according to another aspect of the present ~~invention disclosure~~ there is provided a DNA molecule comprising a polynucleotide that encodes the antibody heavy chain whose amino acid sequence is the sequence of SEQ ID NO:3. The
15 ~~invention-present disclosure~~ also provides a DNA molecule comprising a polynucleotide whose sequence is the sequence of SEQ ID NO:5. This polynucleotide sequence corresponds to the antibody heavy chain.

According to a further aspect of the present ~~disclosure invention~~ there is provided a DNA molecule comprising a polynucleotide that encodes the antibody light chain whose amino acid
20 sequence is the sequence of SEQ ID NO:4. The ~~invention-present disclosure~~ further provides a DNA molecule comprising a polynucleotide whose sequence is the sequence of SEQ ID NO:6. This polynucleotide sequence corresponds to the antibody light chain.

According to a further aspect of the present ~~disclosure invention~~, there is provided a DNA molecule comprising a polynucleotide that encodes the antibody heavy chain whose amino acid
25 sequence is the sequence of SEQ ID NO:3 and comprising a polynucleotide that encodes the antibody light chain whose amino acid sequence is the sequence of SEQ ID NO:4. The present ~~disclosure invention~~ further provides a DNA molecule comprising a polynucleotide whose sequence is the sequence of SEQ ID NO:5 and comprising a polynucleotide whose sequence is the sequence of SEQ ID NO:6.

30 The present ~~disclosure invention~~ includes mammalian cells for expressing the antibodies of the ~~invention-present disclosure~~ by recombinant means. In particular, the present ~~disclosure invention~~ provides a mammalian cell transformed with a DNA molecule of the ~~invention-present disclosure~~ described above.

In another aspect of the present disclosure, there is provided a mammalian cell transformed with the DNA molecule of the present disclosure described above and the DNA molecule of the present disclosure described above, which transformed mammalian cell is capable of expressing an antibody comprising two antibody heavy chains and two immunoglobulin light chains, in which the amino sequence of each of the two heavy chains is the sequence of SEQ ID NO:3 and the amino acid sequence of each of the two light chains is the sequence of SEQ ID NO:4.

In a further aspect of the present disclosure, there is provided a mammalian cell transformed with the DNA molecule of the present disclosure described above, which transformed mammalian cell is capable of expressing an antibody comprising two antibody heavy chains and two immunoglobulin light chains, in which the amino sequence of each of the two heavy chains is the sequence of SEQ ID NO:3 and the amino acid sequence of each of the two light chains is the sequence of SEQ ID NO:4.

Another aspect of the present ~~disclosure invention~~ includes a process for producing an antibody, which antibody comprises two antibody heavy chains and two immunoglobulin light chains, in which the amino sequence of each of the two heavy chains is the sequence of SEQ ID NO:3 and the amino acid sequence of each of the two light chains is the sequence of SEQ ID NO:4, and which process comprises: a) cultivating a mammalian cell of the ~~invention~~ present disclosure, as described above, under conditions such that the antibody is expressed, and b) recovering the expressed antibody. A further aspect of the present disclosure ~~The present invention~~ includes an antibody obtainable by the process of the ~~invention~~ present disclosure as described immediately above.

The present ~~invention~~ disclosure includes methods of using the antibodies, particularly for treating autoimmune (AI) conditions, especially primary Sjögren's syndrome (pSS), Sjögren's Syndrome (SS), Systemic Lupus Erythematosus, Grave's disease, or type 1 diabetes, methods of preparing the antibodies, polynucleotides encoding the antibodies, vectors comprising the nucleotides for transforming host cells and for expressing the antibodies, host cells for expressing the antibodies, antibodies prepared by a process of recombinant expression in mammalian host systems, and pharmaceutical compositions of the antibodies that comprise the antibody and a pharmaceutically-acceptable excipient.

Particular uses envisioned for the antibodies are the treatment of AI conditions, in particular AI conditions such as primary Sjögren's syndrome (pSS), Sjögren's Syndrome (SS), systemic lupus erythematosus, Grave's disease, or type 1 diabetes. The present ~~disclosureinvention~~ includes antibodies for use in therapy, in treating autoimmune

5 conditions, in treating primary Sjögren's syndrome (pSS), Sjögren's Syndrome (SS), Systemic Lupus Erythematosus, Grave's disease, or type 1 diabetes, and particularly in treating primary Sjögren's syndrome (pSS), Sjögren's Syndrome (SS) or Systemic Lupus Erythematosus. The present ~~disclosureinvention~~ includes use of an antibody of the ~~invention-present disclosure~~ for the manufacture of a medicament for use in treating an

10 autoimmune condition; for use in treating primary Sjögren's Syndrome (pSS), Sjögren's Syndrome (SS), Systemic Lupus Erythematosus, Grave's disease, or type 1 diabetes; for treating primary Sjögren's Syndrome (pSS), Sjögren's Syndrome (SS); or for treating Systemic Lupus Erythematosus. In particular, the present ~~disclosureinvention~~ includes the use of an antibody of the present ~~disclosureinvention~~ in the manufacture of a

15 medicament for the treatment of an autoimmune condition; primary Sjögren's Syndrome (pSS), Sjögren's Syndrome (pSS), Systemic Lupus Erythematosus,

Grave's disease, or type 1 diabetes; primary Sjögren's Syndrome (pSS), Sjögren's Syndrome (SS); or Systemic Lupus Erythematosus.

In another aspect of the present disclosure, there is provided a use of the antibody of the present disclosure described above in the manufacture of a medicament for treating an autoimmune condition in a patient.

In a further aspect of the present disclosure, there is provided the antibody of the present disclosure described above for use in therapy.

In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising the antibody of the present disclosure described above and a pharmaceutically-acceptable excipient.

Brief Description of the Figures

Figure 1. Binding of Ab327 to human IL-21 and other ligands that bind human common-gamma chain receptor by ELISA is shown.

Figure 2. Ab327 is shown to neutralize human IL-21-induced proliferation of primary human B cells *in vitro*.

Figure 3. Average percent of body weight change from baseline in severely immuno-compromised NSG mice (NOD-scid IL-2R γ null) engrafted with human peripheral blood mononuclear cells (PBMCs) treated with IL-21 antibody or isotype control antibody for 42 days. Treatments occurred at points indicated by arrows.

Symbols: -■- Ab327 (10 mg/kg); --▼-- Ab327 (1 mg/kg); --□--; Isotype control (10 mg/kg); -●- non-engraftment.

Figure 4. Average percent of body weight change from baseline in severely immuno-compromised NSG mice (NOD-scid IL-2R γ null) engrafted with human peripheral blood mononuclear cells (PBMCs) treated with IL-21 antibody or isotype control antibody. Treatments occurred at points indicated by arrows. Symbols: -■-

Ab327 (10 mg/kg); --□--; Isotype control (10 mg/kg); -●- non-engraftment.

Figures 5 and 6. Treatment with anti-mouse IL-21 antibody is shown to alleviate lymphocytic infiltration in salivary glands of NOD mice by mRNA analysis (Figure 5) and histological analysis (Figure 6, lymphocytes are outlined).

Figures 7A and 7B. Surrogate Antibody 728 is shown to prevent autoimmune diabetes development in NOD mice. Treatment starts at 7 weeks of age (A) as prevention or at 13 weeks of age (B) during pre-diabetic phase. Diabetic incidence is calculated per group as two consecutive readings over 250 mg/dl and displayed as percentage of diabetic mice per group (A: mIgG1 n=12; Ab728 n=12 and B: mIgG1 n=8; Ab728 n=11). Diabetes incidence is scored as survival curve data and is different by log-rank test (A: p=0.0007 and B: p=0.002).

- a. cultivating the mammalian cell of claim 11 or the mammalian cell of claim 12 under conditions such that the antibody is expressed, and
- b. recovering the expressed antibody.

5 14. An antibody obtainable by the process of claim 13.

10 15. ~~Use of the antibody of any one of claims 1 to 4 or 14 in the manufacture of a medicament for~~ A method of treating an autoimmune condition in a patient comprising administering an effective dose of the antibody of any one of claims 1 to 4 or 14 to the patient.

15 16. The ~~method-use~~ of claim 15 in which the autoimmune condition is primary Sjögren's Syndrome, Sjögren's Syndrome, Systemic Lupus Erythematosus, Grave's disease, or type 1 diabetes.

 17. The ~~method-use~~ of claim 16 in which the autoimmune condition is primary Sjögren's Syndrome or Sjögren's Syndrome .

20 18. The ~~method-use~~ of claim 16 in which the autoimmune condition is Systemic Lupus Erythematosus.

 19. The antibody of any one of claims 1 to 4 or 14 for use in therapy.

25 20. The antibody of Claim 19 for use in the treatment of an autoimmune condition.

 21. The antibody of Claim 19 for use in the treatment of primary Sjögren's Syndrome, Sjögren's Syndrome , Systemic Lupus Erythematosus, Grave's disease, or type 1 diabetes.

30 22. The antibody of Claim 19 for use in the treatment of primary Sjögren's Syndrome or Sjögren's Syndrome.