rheumatoid arthritis affect a large percentage of the population (for example, rheumatoid arthritis affects approximately 1% of the adult population worldwide), there is a need to provide alternative biologics for the treatment of immune-mediated diseases which overcome, or at least ameliorate, one or more of the disadvantages described above.

## SUMMARY OF THE INVENTION

[8] In a first aspect, there is provided use of an isolated antibody or an antigen-binding fragment thereof, wherein the isolated antibody or antigen-binding fragment thereof is capable of binding to a muramyl peptide, or a derivative or an analog or a salt thereof, wherein the muramyl peptide comprises muramic acid and an amino acid selected from the group consisting of alanine, isoglutamine, glutamic acid, and a salt thereof, in the manufacture of a medicament for prophylactically or therapeutically treating an autoimmune or inflammatory disease, wherein the medicament is to be administered with one or more therapeutic agents, wherein said one or more therapeutic agents are selected from the group consisting of nonsteroidal anti-inflammatory drugs (NSAIDs), non-biologic and biologic disease-modifying anti-rheumatic drugs (DMARDs), and corticosteroids.

[9] Disclosed is an isolated antibody or an antigen-binding fragment thereof as defined in the first aspect, for use in the prophylactic or therapeutic treatment of an autoimmune or inflammatory disease.

[10] Also disclosed is a method of prophylactically or therapeutically treating an autoimmune or inflammatory disease comprising administering an isolated antibody or an antigen-binding fragment thereof as defined in the first aspect.

[11] In a second aspect, there is provided a composition comprising an isolated antibody or an antigen-binding fragment thereof as defined in the first aspect, one or more therapeutic agents selected from the group consisting of NSAIDs, non-biologic and biologic DMARDs, and corticosteroids, and optionally a pharmaceutically acceptable carrier.

[12] Disclosed is a method of prophylactically or therapeutically treating an autoimmune or inflammatory disease comprising administering a composition of the second aspect.

[13] Also disclosed is a composition of the second aspect for use in the prophylactic or therapeutic treatment of an autoimmune or inflammatory disease.

[14] In a third aspect, there is provided use of the composition of the second aspect in the manufacture of a medicament for prophylactically or therapeutically treating an autoimmune or inflammatory disease.

[14a] In a fourth aspect, there is provided use of an isolated antibody or an antigen-binding fragment thereof, wherein said isolated antibody or antigen-binding fragment thereof is capable of binding to a muramyl peptide, or a derivative or an analog or a salt thereof, wherein said muramyl peptide comprises muramic acid and an amino acid selected from the group consisting of alanine, isoglutamine, glutamic acid, and a salt thereof, in the manufacture of a medicament for prophylactically or therapeutically treating an autoimmune or inflammatory disease in a patient that responds poorly to TNFα inhibitory biologics.

## BRIEF DESCRIPTION OF THE DRAWINGS

**Claims**

1. Use of an isolated antibody or an antigen-binding fragment thereof, wherein said isolated antibody or antigen-binding fragment thereof is capable of binding to a muramyl peptide, or a derivative or an analog or a salt thereof, wherein said muramyl peptide comprises muramic acid and an amino acid selected from the group consisting of alanine, isoglutamine, glutamic acid, and a salt thereof, in the manufacture of a medicament for prophylactically or therapeutically treating an autoimmune or inflammatory disease, wherein the medicament is to be administered with one or more therapeutic agents, wherein said one or more therapeutic agents are selected from the group consisting of nonsteroidal anti-inflammatory drugs (NSAIDs), non-biologic and biologic disease-modifying anti-rheumatic drugs (DMARDs), and corticosteroids.

2. The use according to claim 1, wherein said muramic acid comprises an N-acetyl group.

3. The use according to claim 1, wherein said muramic acid does not comprise an N-acetyl group.

4. The use according to any one of claims 1 to 3, wherein said alanine is L-alanine, or a salt thereof.

5. The use according to any one of claims 1 to 4, wherein said isoglutamine is D-isoglutamine, or a salt thereof.

6. The use according to any one of claims 1 to 5, wherein said glutamic acid is D-glutamic acid, or a salt thereof.

7. The use according to any one of claims 1 to 6, wherein said amino acid comprises L-alanine or a salt thereof, and D-isoglutamine or a salt thereof.

8. The use according to any one of claims 1 to 7, wherein said amino acid comprises L-alanine or a salt thereof, and D-glutamic acid or a salt thereof.

9. The use according to any one of claims 1 to 8, wherein said muramyl peptide, or derivative or analog or salt thereof, is selected from the group consisting of N-acetylmuramyl-L-alanyl-D-isoglutamine, muramyl-L-alanyl-D-isoglutamine, N-acetylmuramyl-L-alanyl-D-glutamate, and muramyl-L-alanyl-D-glutamate.

10. The use according to any one of claims 1 to 9, wherein said muramyl peptide, or derivative or analog or salt thereof, is part of a peptidoglycan or fragment thereof.

11. The use according to any one of claims 1 to 10, wherein said isolated antibody or antigen-binding fragment thereof comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 1.

12. The use according to any one of claims 1 to 11, wherein said isolated antibody or antigen-binding fragment thereof comprises a light chain encoded by the nucleotide sequence of SEQ ID NO: 2.

13. The use according to any one of claims 1 to 12, wherein said isolated antibody or antigen-binding fragment thereof comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 1 and a light chain encoded by the nucleotide sequence of SEQ ID NO: 2.

14. The use according to any one of claims 1 to 13, wherein said isolated antibody or antigen-binding fragment thereof comprises a heavy chain variable domain comprising the amino acid sequence as set forth in SEQ ID NO: 3.

15. The use according to any one of claims 1 to 14, wherein said isolated antibody or antigen-binding fragment thereof comprises a light chain variable domain comprising the amino acid sequence as set forth in SEQ ID NO: 4.

16. The use according to any one of claims 1 to 15, wherein said isolated antibody or antigen-binding fragment thereof comprises a heavy chain variable domain comprising the

amino acid sequence as set forth in SEQ ID NO: 3, and a light chain variable domain comprising the amino acid sequence as set forth in SEQ ID NO: 4.

17. The use according to any one of claims 1 to 16, wherein said isolated antibody or antigen binding fragment thereof is monoclonal.

18. The use according to claim 17, wherein said monoclonal antibody is of the subtype IgG1.

19. The use according to claim 17 or 18, wherein said monoclonal antibody is selected from the group consisting of a humanized antibody and a chimeric antibody.

20. The use according to any one of claims 1 to 19, wherein said antigen-binding fragment is selected from the group consisting of Fab, Fab', (Fab')2, Fv, sFV, and scFv.

21. The use according to any one of claims 1 to 20, wherein said isolated antibody or antigen-binding fragment binds to said muramyl peptide, or a derivative or an analog or a salt thereof, with a Kd value selected from the group consisting of less than about 1 nM, less than about 900 pM, less than about 800 pM, less than about 700 pM, less than about 600 pM, less than about 500 pM, less than about 400 pM, less than about 300 pM, less than about 200 pM, less than about 100 pM, less than about 90 pM, less than about 80 pM, less than about 70 pM, less than about 60 pM, less than about 50 pM, less than about 40 pM, less than about 30 pM, less than about 20 pM, and less than about 10 pM.

22. The use according to any one of claims 1-21, wherein the autoimmune or inflammatory disease is selected from the group consisting of sepsis, septic shock, Crohn's disease, rheumatoid arthritis, asthma, allergy, atopic disorders, multiple sclerosis, pertussis, gonorrhea, inflammatory bowel disease, and antibiotic-associated disorder.

23. The use according to claim 22, wherein the autoimmune or inflammatory disease is rheumatoid arthritis.

24. The use according to claim 22, wherein the autoimmune or inflammatory disease is multiple sclerosis.

25. The use according to claim 1, wherein said DMARD is selected from the group consisting of methotrexate, hydroxychloroquine, sulfasalazine, leflunomide, Tumor Necrosis Factor (TNF) inhibitors, T-cell costimulatory blocking agents, B cell depleting agents, Interleukin-6 (IL-6) inhibitors and Interleukin-1 (IL-1) receptor antagonists.

26. The use according to claim 25, wherein said TNF inhibitor is selected from the group consisting of etanercept, adalimumab, infliximab, certolizumab pegol and golimumab.

27. A composition comprising an isolated antibody or an antigen-binding fragment thereof as defined in any one of claims 1 to 21, one or more therapeutic agents selected from the group consisting of NSAIDs, non-biologic and biologic DMARDs, and corticosteroids, and optionally a pharmaceutically acceptable carrier.

28. The composition according to claim 27, wherein said DMARD is selected from the group consisting of methotrexate, hydroxychloroquine, sulfasalazine, leflunomide, TNF inhibitors, T-cell costimulatory blocking agents, B cell depleting agents, IL-6 inhibitors and IL-1 receptor antagonists.

29. The composition according to claim 28, wherein said TNF inhibitor is selected from the group consisting of etanercept, adalimumab, infliximab, certolizumab pegol and golimumab.

30. Use of the composition of any one of claims 27 to 29 in the manufacture of a medicament for prophylactically or therapeutically treating an autoimmune or inflammatory disease.

31. The use according to claim 30, wherein the autoimmune or inflammatory disease is selected from the group consisting of sepsis, septic shock, Crohn's disease, rheumatoid arthritis, asthma, allergy, atopic disorders, multiple sclerosis, pertussis, gonorrhea, inflammatory bowel disease, and antibiotic-associated disorder.

32. The use according to claim 31, wherein the autoimmune or inflammatory disease is rheumatoid arthritis.

33. The use according to claim 32, wherein the autoimmune or inflammatory disease is multiple sclerosis.

34. Use of an isolated antibody or an antigen-binding fragment thereof, wherein said isolated antibody or antigen-binding fragment thereof is capable of binding to a muramyl peptide, or a derivative or an analog or a salt thereof, wherein said muramyl peptide comprises muramic acid and an amino acid selected from the group consisting of alanine, isoglutamine, glutamic acid, and a salt thereof, in the manufacture of a medicament for prophylactically or therapeutically treating an autoimmune or inflammatory disease in a patient that responds poorly to TNFα inhibitory biologics.