CLAIMS

1. A bispecific antibody suitable for co-expression in a common host cell, wherein the antibody comprises
    a. a first part which is an immunoglobulin with a first variable light chain of lambda wild type (VL1) and a first variable heavy chain of wild type (VH1), that binds specifically to IL-18, and a first constant heavy chain (CH1) with a hetero-dimerization modification, and
    b. a second part which is an immunoglobulin with a second variable light chain of kappa wild type (VL2) and a second variable heavy chain of wild type (VH2), that binds specifically to IL1β, and a second constant heavy chain (CH2) with a hetero-dimerization modification which is complementary to the hetero-dimerization modification of the first constant heavy chain,

   wherein the first part and the second part, when co-expressed in a common host cell, form a bispecific antibody, wherein the first and second constant heavy chain are human IgA, IgD, IgE, IgG, or IgM, and wherein the first variable light chain is of lamba1 type, and the second variable light chain is of kappa 6 type.

2. The bispecific antibody according to claim 1, wherein the first and second constant heavy chain are selected from any one of groups (i)-(iii):
    (i) human IgD, IgE or IgG;
    (ii) human IgG1, IgG2, IgG3, or IgG4;
    (iii) IgG1.

3. The bispecific antibody according to claim 1 or 2, wherein the first and second constant heavy chain are IgG1, and wherein
    a. the first constant heavy chain has point mutations generating a knob structure and the second constant heavy has point mutations generating a hole structure, or
    b. the first constant heavy chain has point mutations generating a hole structure and the second constant heavy has point mutations generating a knob structure.

4. The bispecific antibody according to any one of claims 1-3, wherein the first and second constant heavy chains have mutations resulting in a disulfide bridge.

5. The bispecific antibody according to any one of claims 1-4, comprising a first immunoglobulin VH1 domain, a first immunoglobulin VL1 domain, a second immunoglobulin VH2 domain and a second immunoglobulin VL2 domain, wherein:
    a. the first immunoglobulin VH1 domain comprises the amino acid sequence SEQ ID NO: 85,
    b. the first immunoglobulin VL1 domain comprises the amino acid sequence SEQ ID NO: 101,
    c. the second immunoglobulin VH2 domain comprises the amino acid sequence SEQ ID NO: 53, and
    d. the second immunoglobulin VL2 domain comprises the amino acid sequence SEQ ID NO: 69.

6. The bispecific antibody according to any one of claims 1-5, comprising a first immunoglobulin heavy chain, a first immunoglobulin light chain, a second immunoglobulin heavy chain and a second immunoglobulin light chain, wherein:
    a. the first immunoglobulin heavy chain comprises the amino acid sequence SEQ ID NO: 87,
    b. the first immunoglobulin light chain comprises the amino acid sequence SEQ ID NO: 103,
    c. the second immunoglobulin heavy chain comprises the amino acid sequence SEQ ID NO: 55, and
    d. the second immunoglobulin light chain comprises the amino acid sequence SEQ ID NO: 71.

7. A method for selecting a bispecific antibody according to any one of claims 1-6, said method comprising;
    a. a first step of selecting the first part, and the second part;
    b. a second step of co-expressing the first part and the second part in a common host cell, resulting in a bispecific antibody comprising the first part and the second part;
    c. a third step of purifying the bispecific antibody by removing mismatched fragments from the correctly matched bispecific antibody.

8. The method according to claim 7, wherein the third step of purification results in a bispecific antibody which is at least 60% (mass), 70% (mass), 80% (mass), 85% (mass) pure, such as at least 90% (mass) pure, 95% (mass), 96% (mass), 97% (mass), 98% (mass), or 99% (mass) pure.

9. A method for manufacturing a bispecific antibody according to any one of claims 1-6 by co-expression in a common host cell, said method comprising;
    a. a first step of generating at least one vector encoding the first part and the second part;
    b. a second step of introducing the at least one vector into the common host cell;
    c. a third step of selecting cells specifically expressing the bispecific antibody;
    d. a forth step of culturing the selected cells under conditions wherein the cells express the bispecific antibody; and
    e. a fifth step of purifying the bispecific antibody which is at least 60% (mass), 70% (mass), 80% (mass), or 85% (mass) pure, such as at least 90% (mass) pure, 95% (mass), 96% (mass), 97% (mass), 98% (mass), or 99% (mass) pure.

10. The method according to claim 10, wherein the first step comprises generating a first vector encoding the first part and a second vector encoding the second part.

11. An expression system comprising at least one vector comprising a polynucleotide encoding the first part or the second part of the bispecific antibody according to any of claims 1-6, and a selectable marker.

12. The expression system according to claim 11 comprising:
    a. a polynucleotide encoding a first selectable marker (sm I);
    b. a polynucleotide encoding a second selectable marker (sm II), which differs from the first selectable marker (sm I).

13. The expression system according to claim 11 or 12, wherein the first selectable marker (sm I) is a folate transporter or a polynucleotide encoding a mutated folate receptor, wherein the mutated folate receptor has a decreased folate binding affinity compared to the wildtype folate receptor and the second selectable marker (sm II) is DHFR.

14. The expression system according to any one of claims 11-13, wherein the first selectable marker (sm I) is Hygromycine and the second selectable marker (sm II) is Neo/G418.

15. The expression system according to any of claims 11-14, comprising two expression vectors wherein:
    a. a first vector comprising polynucleotide encoding at least a first selectable marker (sm I) and at least polynucleotides encoding the first part; and
    b. a second vector comprising polynucleotide encoding at least a second selectable marker (sm II) and at least polynucleotides encoding the second part.

16. The expression system according to any of claims 11-15, comprising a stop codon downstream of the polynucleotides encoding the heavy chain and a polynucleotide encoding an immunoglobulin membrane anchor located downstream of the stop codon.

17. The method according to claims 9 or 10, wherein the fifth step of purifying the bispecific antibody comprises affinity chromatography and/or ion exchange chromatography.

18. The method according to claim 17, wherein the chromatography comprises
    a. a first step of capturing; and
    b. a second step of polishing.

19. The method according to claim 17 or claim 18, further comprising a third step of further polishing.

20. The method according to claim 18 or 19, wherein the first step of capturing is performed with a principle selected from the group consisting of Fc-binding affinity chromatography, such as Protein A or Protein G, lambda light chain specific affinity chromatography, such as LambdaFabSelect™, kappa light chain specific affinity chromatography, such as KappaSelect™, anti-idiotypic affinity chromatography, such as the first part or the second part, a target based affinity chromatography, such as affinity chromatography using the first target or second target, ion exchange chromatography, such as Capto™ adhere, or Fractogel™ EMD SO_3, and hydrophobic interaction chromatography.

21. The method according to any one of claims 18-20, wherein the second step of polishing is performed with a principle selected from the group consisting of Fc-binding affinity chromatography, such as Protein A or Protein G, lambda light chain specific affinity chromatography, such as LambdaFabSelect™, kappa light chain specific affinity chromatography, such as KappaSelect™, anti-idiotypic affinity chromatography, such as the first part or the second part, a target based affinity chromatography, such as affinity chromatography using the first target or second target, ion exchange chromatography, such as Capto™ adhere, or Fractogel™ EMD SO_3, hydrophobic interaction chromatography, and virus inactivation.

22. The method according to any one of claims 19-21, wherein the third step of further polishing is performed with a principle selected from the group consisting of Fc-binding affinity chromatography, such as Protein A or Protein G, lambda light chain specific affinity chromatography, such as LambdaFabSelect™, kappa light chain specific affinity chromatography, such as KappaSelect™, anti-idiotypic affinity chromatography, such as the

first part or the second part, a target based affinity chromatography, such as affinity chromatography using the first target or second target, ion exchange chromatography, such as Capto™ adhere, or Fractogel™ EMD SO_3, hydrophobic interaction chromatography, and virus inactivation, alone or in combination.

23. The method according to any one of claims 19-22, comprising steps selected from:
    a. a first step of Protein A capturing, such as MabSelect™ SuRe™, a second step of lambda light chain affinity chromatography, such as LambdaFabSelect™, and a third step of kappa light chain affinity chromatography such as KappaSelect™; or
    b. a first step of Protein A, such as MabSelect™ SuRe™, a second step of kappa light chain affinity chromatography such as KappaSelect™, and a third step of lambda light chain affinity chromatography, such as LambdaFabSelect™; or
    c. a first step of kappa light chain affinity chromatography such as KappaSelect™ and a second step of lambda light chain affinity chromatography, such as LambdaFabSelect™; or
    d. a first step of lambda light chain affinity chromatography, such as LambdaFabSelect™ and a second step of kappa light chain affinity chromatography such as KappaSelect™.

24. A pharmaceutical composition comprising the antibody according to any of claims 1-6 and a pharmaceutically acceptable carrier.

25. Use of the bispecific antibody according to any one of claims 1-6, or the pharmaceutical composition according to claim 24, in the preparation of a medicament for the treatment of an inflammasome related disease.

26. The use according to claim 25, wherein the inflammasome related disease is selected from the group consisting of sickle cell disease, vasculopathy, ischemia-reperfusion injury, cardiovascular disease, peripheral artery disease, atherosclerosis, vascular dysfunction, skeletal muscle ischemia, pulmonary sarcoidosis, fibrosis, malaria, hemodialysis-dependent, chronic kidney disease and Crohn’s disease.