

Claims

1. An ICOS binding protein or antigen binding portion thereof comprising CDRH1 as set forth in SEQ ID NO:1; CDRH2 as set forth in SEQ ID NO:2; CDRH3 as set forth in SEQ ID NO:3; CDRL1 as set forth in SEQ ID NO:4; CDRL2 as set forth in SEQ ID NO:5 and CDRL3 as set forth in SEQ ID NO:6.
2. The ICOS binding protein or antigen binding portion thereof of claim 1 comprising a V_H domain comprising an amino acid sequence at least 90% identical to the amino acid sequence set forth in SEQ ID NO:7 and a V_L domain comprising an amino acid sequence at least 90% identical to the amino acid sequence as set forth in SEQ ID NO:8 wherein said ICOS binding protein or antigen binding portion thereof specifically binds to human ICOS.
3. The ICOS binding protein or antigen binding portion thereof of claim 1 or 2, wherein said ICOS binding protein or antigen binding portion thereof is an ICOS agonist.
4. The ICOS binding protein or antigen binding portion thereof any one of claims 1 to 3 wherein said ICOS binding protein binds to human ICOS with
 - (i) an association rate constant (k_{on}) of at least $1 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$; and a dissociation rate constant (k_{off}) of less than $6 \times 10^{-5} \text{ s}^{-1}$; or
 - (ii) a dissociation constant (K_D) of less than about 100 nM,
 wherein the affinity is measured by BIAcore.
5. The ICOS binding protein or antigen binding portion thereof of any one of claims 1 to 4 comprising a V_H domain comprising the amino acid sequence set forth in SEQ ID NO:7 and a V_L domain comprising the amino acid sequence as set forth in SEQ ID NO:8.
6. The ICOS binding protein or antigen binding portion thereof of any one of claims 1 to 5 comprising a heavy chain amino acid sequence comprising at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO: 23 and a light chain amino acid sequence comprising at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO: 24.

7. The ICOS binding protein or antigen binding portion thereof of any one of claims 1 to 6 comprising a heavy chain amino acid sequence as set forth in SEQ ID NO: 23 and a light chain amino acid sequence as set forth in SEQ ID NO: 24.
8. The ICOS binding protein or antigen binding portion thereof of any one of claims 1 to 7 wherein said ICOS binding protein or antigen binding portion thereof comprises a scaffold selected from human IgG1 isotype or variant thereof and human IgG4 isotype or variant thereof.
9. The ICOS binding protein or antigen binding portion thereof of any one of claims 1 to 8 wherein said ICOS binding protein or antigen binding portion thereof comprises an hIgG4PE scaffold.
10. The ICOS binding protein or antigen binding portion thereof of any one of claims 1 to 9 wherein said ICOS binding protein is a monoclonal antibody.
11. The ICOS binding protein or antigen binding portion thereof of claim 10 wherein the monoclonal antibody is humanized.
12. The ICOS binding protein or antigen binding portion thereof of claim 10 wherein the monoclonal antibody is fully human.
13. The ICOS binding protein or antigen binding portion thereof of any one of claims 10 to 12 wherein the monoclonal antibody is an agonist to human ICOS and comprises an IgG4 isotype scaffold or a variant thereof.
14. The ICOS binding protein or antigen binding portion thereof of claim 13 wherein said monoclonal antibody comprises a hIgG4PE scaffold.
15. A nucleic acid sequence encoding an ICOS binding protein or antigen binding portion thereof as defined in any one of claims 1 to 14.
16. An expression vector comprising a nucleic acid sequence as defined in claim 15.
17. A recombinant host cell comprising the nucleic acid sequenced of claim 15 or the expression vector of claim 16.

18. An ICOS binding protein or antigen binding portion thereof expressed by the recombinant host cell of claim 17.
19. A method for the production of an ICOS binding protein or antigen binding portion thereof as defined in any one of claims 1 to 14 or 18, comprising the steps of
 - a) culturing a recombinant host cell as defined in claim 17 under suitable conditions to express said ICOS binding protein or antigen binding protein thereof; and
 - b) isolating said ICOS binding protein or antigen binding portion thereof, whereby a polypeptide comprising the ICOS binding protein or antigen binding portion thereof is produced.
20. A pharmaceutical composition comprising an ICOS binding protein or antigen binding portion thereof of any one of claims 1 to 14 or 18 and a pharmaceutically acceptable carrier.
21. The ICOS binding protein or antigen binding portion thereof as defined in any one of claims 1 to 14 or 18, or the pharmaceutical composition of claim 20 for use in the treatment of cancer, infectious disease and/or sepsis in a human in need thereof.
22. The ICOS binding protein or antigen binding portion thereof or the pharmaceutical composition for use according to claim 21, wherein the ICOS binding protein or antigen binding portion thereof is used in combination or co-administered with at least one anti-neoplastic agent, at least one second immuno-modulatory agent, and/or at least one immunostimulatory adjuvant to said human.
23. The ICOS binding protein or antigen binding portion thereof or the pharmaceutical composition for use according to claim 22, wherein said at least one anti-neoplastic agent is a chemotherapeutic agent.
24. The ICOS binding protein or antigen binding portion thereof or the pharmaceutical composition for use according to claim 22, wherein the at least one anti-neoplastic agent is selected from: docetaxel, methotrexate, paclitaxel, gemcitabine, fluorouracil, carboplatin and cisplatin.
25. The ICOS binding protein or antigen binding portion thereof or the pharmaceutical composition for use according to claim 22, wherein said at least one second immuno-modulatory agent is selected from: an anti-CTLA4 antibody, an anti-PD-1 antibody, an anti-PDL1 antibody and an anti-OX40 antibody.

26. The ICOS binding protein or antigen binding portion thereof or the pharmaceutical composition for use according to claim 22, wherein the at least one immunostimulatory adjuvant is a TLR4 agonist, optionally CRX-601.27. Use of the ICOS binding protein or antigen binding portion thereof of any one of claims 1 to 14 or 18 in the manufacture of a medicament for the treatment of a disease selected from cancer, infectious disease, or sepsis in a human in need thereof.