Claims:

1) An isolated monoclonal antibody that binds to and neutralizes a biological activity of a human interferon omega (IFN-ω) and at least three, four, five, six, seven, eight, nine, ten or eleven human interferon alpha (IFN-α) subtypes, wherein the antibody comprises a heavy chain variable region and a light chain variable region wherein the antibody comprises a heavy chain variable region and a light chain variable region, the antibody being selected from:

A. an antibody wherein the heavy chain variable region comprises heavy chain complementarity determining region (HCDR) amino acid sequences - HCDR1, HCDR2 and HCDR3 and the light chain variable region comprises light chain complementarity determining region (LCDR) amino acid sequences - LCDR1, LCDR2 and LCDR3, the antibody comprising:

the HCDR1 amino acid sequence of SEQ ID NO: 109;

the HCDR2 amino acid sequences of SEQ ID NOs: 111, 112 or 113;

the HCDR3 amino acid sequences of SEQ ID NOs: 115 or 116;

the LCDR1 amino acid sequences of SEQ ID NOs: 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90 or 91;

the LCDR2 amino acid sequences of SEQ ID NOs: 93, 94 or 95; and

the LCDR3 amino acid sequences of SEQ ID NOs: 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106 or 107;

B. an antibody wherein the heavy chain variable region comprises heavy chain complementarity determining region (HCDR) amino acid sequences - HCDR1, HCDR2 and HCDR3 of SEQ ID NOs: 109, 113 and 116, respectively, and the light chain variable region comprises light chain complementarity determining region (LCDR) amino acid sequences - LCDR1, LCDR2 and LCDR3, of SEQ ID NOs: 82, 94 and 99, respectively.

C. an antibody wherein the heavy chain variable region comprises heavy chain complementarity determining region (HCDR) amino acid sequences - HCDR1, HCDR2 and HCDR3 of SEQ ID NOs: 109, 114 and 121, respectively, and the light chain variable region comprises light chain complementarity determining region (LCDR) amino acid sequences - LCDR1, LCDR2 and LCDR3 of SEQ ID NOs: 118, 119 and 120, respectively;

D. an antibody wherein the heavy chain variable region comprises heavy chain complementarity determining region (HCDR) amino acid sequences - HCDR1, HCDR2 and HCDR3 of SEQ ID NOs: 109, 114, 121, respectively, and the light chain variable region comprises light chain complementarity determining region (LCDR) amino acid sequences - LCDR1, LCDR2 and LCDR3 of SEQ ID Nos: 159, 119 and 160, respectively;

E. an antibody wherein the heavy chain variable region comprises heavy chain complementarity determining region (HCDR) amino acid sequences - HCDR1, HCDR2 and HCDR3 of SEQ ID NOs: 109, 114, 121, respectively, and the light chain variable region comprises light chain complementarity determining region (LCDR) amino acid sequences - LCDR1, LCDR2 and LCDR3 of SEQ ID Nos: 161, 119 and 162, respectively;

F. an antibody which comprises a heavy chain variable region (VH) amino acid sequence of SEQ ID NO: 28 and a light chain variable region (VL) amino acid sequence of SEQ ID NO: 150;

G. an antibody wherein the heavy chain variable region comprises heavy chain complementarity determining region (HCDR) amino acid sequences - HCDR1, HCDR2 and HCDR3 and the light chain variable region comprises light chain complementarity determining region (LCDR) amino acid sequences - LCDR1, LCDR2 and LCDR3, the antibody comprising the HCDR1, the HCDR2, the HCDR3, the LCDR1, the LCDR2 and the LCDR3 sequences of SEQ ID NOs:

   a. 109, 113, 116, 77, 93 and 104, respectively;
   b. 109, 113, 116, 85, 93 and 96, respectively;
   c. 109, 113, 115, 79, 95 and 107, respectively;
   d. 109, 113, 116, 76, 93 and 103, respectively;
   e. 109, 113, 115, 85, 93 and 96, respectively;
   f. 109, 113, 115, 89, 95 and 100, respectively;
   g. 109, 113, 116, 86, 93 and 105, respectively;
   h. 109, 113, 115, 76, 93 and 103, respectively;
   i. 109, 113, 116, 80, 93 and 97, respectively;
   j. 109, 113, 116, 84, 93 and 97, respectively;
   k. 109, 113, 116, 90, 93 and 97, respectively;
   l. 109, 113, 116, 88, 93 and 102, respectively;
   m. 109, 113, 116, 87, 93 and 105, respectively;
   n. 109, 113, 116, 91, 93 and 106, respectively;
   o. 109, 113, 115, 80, 93 and 97, respectively;
   p. 109, 113, 116, 83, 93 and 101, respectively;
   q. 109, 113, 116, 82, 94 and 98, respectively;
   r. 109, 113, 115, 78, 95 and 100, respectively;
   s. 109, 111, 116, 81, 93 and 106, respectively;
   t. 109, 113, 116, 82, 94 and 99, respectively;
   u. 109, 113, 115, 81, 93 and 106, respectively;
   v. 109, 112, 116, 81, 93 and 106, respectively; or

w. 109, 113, 116, 81, 93 and 106, respectively;

H. an antibody which comprises a heavy chain variable region (VH) amino acid sequence of SEQ ID NOs: 28, 31, 157 or 158 and a light chain variable region (VL) amino acid sequence of SEQ ID NOs: 35, 39, 40, 42, 46, 52, 53, 54, 57, 61, 62, 68, 71, 73, 75, 135 or 150; or

I. an antibody which comprises a heavy chain variable region (VH) amino acid sequence and a light chain variable region (VL) amino acid sequence of SEQ ID NOs:

a. 28 and 40, respectively;
b. 28 and 39, respectively;
c. 31 and 62, respectively;
d. 28 and 54, respectively;
e. 31 and 39, respectively;
f. 31 and 68, respectively;
g. 28 and 42, respectively;
h. 31 and 54, respectively;
i. 28 and 53, respectively;
j. 28 and 73, respectively;
k. 28 and 75, respectively;
l. 28 and 52, respectively;
m. 28 and 35, respectively;
n. 28 and 135, respectively;
o. 31 and 53, respectively;
p. 28 and 46, respectively;
q. 28 and 61, respectively;
r. 31 and 57, respectively;
s. 157 and 71, respectively;
t. 28 and 150, respectively;
u. 31 and 71, respectively;
v. 158 and 71, respectively; or
w. 28 and 71, respectively.

2) The antibody of claim 1, wherein the biological activity of the human IFN-ω and the human IFN-α subtypes is the human IFN-ω or the human IFN-α subtype-induced expression of secreted embryonic alkaline phosphatase (SEAP) under interferon inducible ISG54 promoter in HEK293 cells stably expressing signal transducer and activator of transcription 2 (STAT2), interferon regulatory factor 9 (IRF9) and SEAP.

3) The antibody of claim 2, wherein the antibody neutralizes the biological activity of the human IFN-ο with an IC_{50} value of at least about $1x10^{-9}$M or less, about $1x10^{-10}$ M or less, about $5x10^{-11}$M or less, or about $1x10^{-11}$M or less.

4) The antibody of claim 3, wherein the antibody neutralizes the biological activity of the human IFN-ο with an IC_{50} value of at least about $1x10^{-10}$ M or less.

5) The antibody of claim 4, wherein the antibody neutralizes the activity of the human IFN-ο with an IC_{50} value of between about $1x10^{-10}$ M to about $6x10^{-12}$ M.

6) The antibody of claim 5, wherein the antibody neutralizes the activity of at least three, four, five, six, seven, eight, nine, ten or eleven human IFN-α subtypes with an IC_{50} value of at least about $2x10^{-10}$ M or less, about 1.5×10^{-10} M or less, or about $1x10^{-10}$ M or less.

7) The antibody of claim 6, wherein the IFN-α subtypes are selected from the group consisting of IFN-αA, IFN-αB2, IFN-αC, IFN-αF, IFN-αG, IFN-αH2, IFN-αI, IFN-αJ1, IFN-αK, IFN-αWA and IFN-α4a.

8) The antibody of claim 6, comprising

a. the HCDR1 amino acid sequence of SEQ ID NO: 109;
b. the HCDR2 amino acid sequences of SEQ ID NOs: 111, 112 or 113;
c. the HCDR3 amino acid sequences of SEQ ID NOs: 115 or 116;
d. the LCDR1 amino acid sequences of SEQ ID NOs: 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90 or 91;
e. the LCDR2 amino acid sequences of SEQ ID NOs: 93, 94 or 95; and
f. the LCDR3 amino acid sequences of SEQ ID NOs: 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106 or 107.

9) The antibody of claim 8, wherein the antibody comprises heavy chain complementarity determining region (HCDR) 1 (HCDR1), 2 (HCDR2) and 3 (HCDR3) amino acid sequences of SEQ ID NOs: 109, 113 and 116, respectively, and light chain complementarity determining region (LCDR) 1 (LCDR1), 2 (LCDR2) and 3 (LCDR3) amino acid sequences of SEQ ID NOs: 82, 94 and 99, respectively.

10) The antibody of claim 6, wherein the antibody comprises heavy chain complementarity determining region (HCDR) 1 (HCDR1), 2 (HCDR2) and 3 (HCDR3) amino acid sequences of SEQ ID NOs: 109, 114 and 121, respectively, and light chain complementarity determining region (LCDR) 1 (LCDR1), 2 (LCDR2) and 3 (LCDR3) amino acid sequences of SEQ ID NOs: 118, 119 and 120, respectively.

11) The antibody of claim 6, wherein the antibody neutralizes at least six human IFN-α subtypes selected from the group consisting of IFN-αA, IFN-αB2, IFN-αC, IFN-αF, IFN-αG, IFN-αH2, IFN-αI, IFN-αJ1, IFN-αK, IFN-αWA and IFN-α4a.

12) The antibody of claim 11, wherein the antibody comprises the HCDR1, the HCDR2, the HCDR3, the LCDR1, the LCDR2 and the LCDR3 amino acid sequences of SEQ ID NOs: 109, 114, 121, 159, 119 and 160, respectively.

13) The antibody of claim 6, wherein the antibody neutralizes at least ten human IFN-α subtypes selected from the group consisting of IFN-αA, IFN-αB2, IFN-αC, IFN-αF, IFN-αG, IFN-αH2, IFN-αI, IFN-αJ1, IFN-αK, IFN-αWA and IFN-α4a.

14) The antibody of claim 13, wherein the antibody binds human IFN- ω of SEQ ID NO: 1 at least at amino acid residues F27, L30 and R33.

15) The antibody of claim 14, wherein the antibody comprises the HCDR1, the HCDR2, the HCDR3, the LCDR1, the LCDR2 and the LCDR3 amino acid sequences of SEQ ID NOs: 109, 114, 121, 161, 119 and 162, respectively.

16) The antibody of claim 15, wherein the antibody neutralizes at least the human IFN-α subtypes IFN-αA, IFN-αB2, IFN-αC, IFN-αF, IFN-αG, IFN-αH2, IFN-αJ1 and IFN-α4a.

17) The antibody of claim 16, wherein the antibody further neutralizes IFN-αI, IFN-αK or IFN-αWA.

18) The antibody of claim 14, wherein the antibody

a. inhibits leukocyte interferon-induced IP-10 release in whole blood induced by 250U/ml of interferon by about 50% or more in the presence of 10 μg/ml antibody than in the absence of the antibody; or

b. inhibits systemic lupus erythematosus (SLE) immune complex-induced IP-10 release in whole blood by about 50% or more in the presence of 10 μg/ml antibody than in the absence of the antibody.

19) The antibody of claim 5, wherein the antibody comprises a heavy chain variable region (VH) amino acid sequence of SEQ ID NO: 28 and a light chain variable region (VL) amino acid sequence of SEQ ID NO: 150.

20) The antibody of claim 5, comprising the HCDR1, the HCDR2, the HCDR3, the LCDR1, the LCDR2 and the LCDR3 sequences of SEQ ID NOs:

a. 109, 113, 116, 77, 93 and 104, respectively;

b. 109, 113, 116, 85, 93 and 96, respectively;

c. 109, 113, 115, 79, 95 and 107, respectively;

d. 109, 113, 116, 76, 93 and 103, respectively;

e. 109, 113, 115, 85, 93 and 96, respectively;
f. 109, 113, 115, 89, 95 and 100, respectively;
g. 109, 113, 116, 86, 93 and 105, respectively;
h. 109, 113, 115, 76, 93 and 103, respectively;
i. 109, 113, 116, 80, 93 and 97, respectively;
j. 109, 113, 116, 84, 93 and 97, respectively;
k. 109, 113, 116, 90, 93 and 97, respectively;
l. 109, 113, 116, 88, 93 and 102, respectively;
m. 109, 113, 116, 87, 93 and 105, respectively;
n. 109, 113, 116, 91, 93 and 106, respectively;
o. 109, 113, 115, 80, 93 and 97, respectively;
p. 109, 113, 116, 83, 93 and 101, respectively;
q. 109, 113, 116, 82, 94 and 98, respectively;
r. 109, 113, 115, 78, 95 and 100, respectively;
s. 109, 111, 116, 81, 93 and 106, respectively;
t. 109, 113, 116, 82, 94 and 99, respectively;
u. 109, 113, 115, 81, 93 and 106, respectively;
v. 109, 112, 116, 81, 93 and 106, respectively; or
w. 109, 113, 116, 81, 93 and 106, respectively.

21) The antibody of claim 20, wherein the antibody is humanized or human.

22) The antibody of claim 21, wherein the human antibody heavy chain variable region framework is derived from human germline gene IGHV5-51 (SEQ ID NO: 155).

23) The antibody of claim 22, wherein the human antibody light chain variable region framework is derived from human germline gene IGKV1D-39 (SEQ ID NO: 156).

24) The antibody of claim 21, wherein the antibody is of IgG1, IgG2, IgG3 or IgG4 subtype.

25) The antibody of claim 24, wherein the antibody has at least one substitution in an Fc region.

26) The antibody of claim 25, wherein the substitution comprises a substitution of one or more of M252Y/S254T/T256E, of one or more of V234A/G237A/P238S/H28A/V309L/A330S/P331S or of one or more of P238S/L234A/L235A, wherein residue numbering is according to the EU numbering.

27) The antibody of claim 5 comprising a heavy chain variable region (VH) and a light chain variable region (VL), wherein the a) VH comprises the amino acid sequence of SEQ ID NOs: 28, 31, 157 or 158 and

b) the VL comprises the amino acid sequence of SEQ ID NOs: 35, 39, 40, 42, 46, 52, 53, 54, 57, 61, 62, 68, 71, 73, 75, 135 or 150.

28). The antibody of claim 27 comprising the VH and the VL of SEQ ID NOs:

a. 28 and 40, respectively;
b. 28 and 39, respectively;
c. 31 and 62, respectively;
d. 28 and 54, respectively;
e. 31 and 39, respectively;
f. 31 and 68, respectively;
g. 28 and 42, respectively;
h. 31 and 54, respectively;
i. 28 and 53, respectively;
j. 28 and 73, respectively;
k. 28 and 75, respectively;
l. 28 and 52, respectively;
m. 28 and 35, respectively;
n. 28 and 135, respectively;
o. 31 and 53, respectively;
p. 28 and 46, respectively;
q. 28 and 61, respectively;
r. 31 and 57, respectively;
s. 157 and 71, respectively;
t. 28 and 150, respectively;
u. 31 and 71, respectively;
v. 158 and 71, respectively; or
w. 28 and 71, respectively.

29) The antibody of any one of claim 1 to 28, wherein the antibody is bispecific.

30) The antibody of claim 29, wherein the antibody binds BLyS, CD40L, IL-6, CD27, BDCA2, IL-12, IL-23, IFN-αD, IL-17, CD20, IL-10, CD22, IL-21, ICOS, ICOSL or IFN-γ.

31) A pharmaceutical composition comprising the antibody of any one of claims 1 to 30 and a pharmaceutically acceptable carrier.

32) A polynucleotide encoding the antibody VH and VL of any one of claims 1 to 30.

33) A vector comprising the polynucleotide of claim 32.

34) A host cell comprising the vector of claim 33.

35) A method of producing the antibody of any one of claims 1 to 30, comprising culturing the host cell of claim 34 in conditions that the antibody is expressed, and recovering the antibody produced by the host cell.

36) Use of a therapeutically effective amount of an isolated antibody of any one of claims 1 to 30 in the manufacture of a medicament for the treatment of an immune-mediated inflammatory disease, an autoimmune disease or chronic viral infection, the disease or infection associated with increased production of IFN-α and/or IFN- ω or type I IFN signature,

wherein the immune-mediated inflammatory disease or the autoimmune disease is lupus, psoriasis, immune thrombocytopenia (ITP), Aicardi-Goutieres syndrome (AGS), systemic sclerosis, Sjögren's syndrome, myositis, common variable immune deficiency (CVID), autoimmune thyroid disease, type I diabetes, rheumatoid arthritis, transplant rejection or graft versus host disease (GVHD).

37) The use of claim 36, wherein lupus is systemic lupus erythematosus (SLE) or cutaneous lupus erythematosus (CLE).

38) The use of claim 37, wherein the patient has lupus nephritis.

39) The use of claim 36, wherein the patient exhibits a Type I interferon signature.

40) The useof claim 36, wherein the chronic viral infection is HIV or hepatitis C infection.

41) The use of claim 36, wherein the antibody comprises the antibody of claim 20 or 29.

42) The use of claim 36, wherein the antibody is a bispecific antibody.

43) The method of claim 42, wherein the bispecific antibody neutralizes BLyS, CD40L, IL-6, CD27, BDCA2, IL-12, IL-23, IFN-αD, IL-17, CD20, IL-10, CD22, IL-21, ICOS, ICOSL or IFN-γ.

44) The use of claim 36, wherein the medicament is to be administered with a second therapeutic agent.

45) The use of claim 44, wherein the second therapeutic agent is an antibody that binds BLyS, CD40L, IL-6, CD27, BDCA2, IL-12, IL-23, IFN-αD, IL-17, CD20, IL-10, CD22, IL-21, ICOS, ICOSL or IFN-γ.

46) The use of claim 44, wherein the second therapeutic agent is a corticosteroid, an antimalarial drug, an immunosuppressant, a cytotoxic drug, or a B-cell modulator.

47) The use of claim 46, wherein the second therapeutic agent is prednisone, prednisolone, methylprednisolone, deflazcort, hydroxychloroquine, azathioprine, methotrexate, cyclophosphamide, mycophenolate mofetil (MMF), mycophenolate sodium, cyclosporine, leflunomide, tacrolimus, rituximabTM or belimumabTM.

48) The antibody of any one of claims 1 to 30, wherein the antibody does not neutralize IFN-αD, IFN-α1 and/or IFN-13.