(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
10 June 2021 (10.06.2021)

WIPO | PCT

(10) International Publication Number
WO 2021/110561 A1

(51) International Patent Classification:
A61K 39/395 (2006.01) *C07K 16/28* (2006.01)
A61P 31/20 (2006.01) *A61K 47/68* (2017.01)

(21) International Application Number:
PCT/EP2020/083737

(22) International Filing Date:
27 November 2020 (27.11.2020)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
19306551.3 03 December 2019 (03.12.2019) EP
19306572.9 04 December 2019 (04.12.2019) EP

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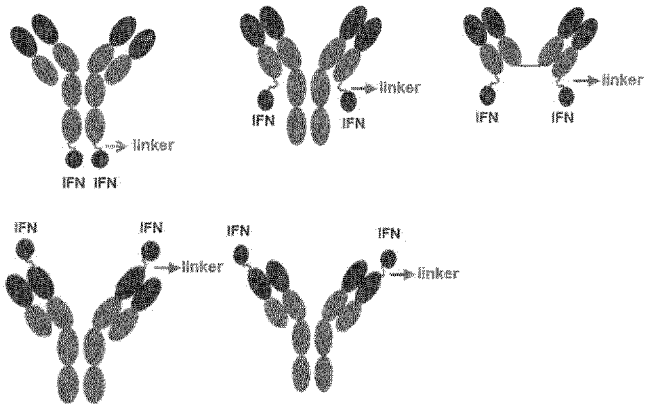
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, IT, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report (Art. 21(3))*
— *with sequence listing part of description (Rule 5.2(a))*

(54) Title: INTERFERON-ASSOCIATED ANTIGEN BINDING PROTEINS FOR USE IN TREATING HEPATITIS B INFECTION

Fig.1



(57) Abstract: The present invention relates to novel interferon-associated antigen binding proteins as well as nucleic acids and expression vectors encoding such interferon-associated antigen binding proteins for use in therapy, more particularly for use in treating hepatitis B virus (HBV) infection. The present invention also relates to pharmaceutical compositions comprising such interferon-associated antigen binding proteins or nucleic acids or expression vectors for use in therapy, more particularly for use in treating hepatitis B virus (HBV) infection. The present invention further provides methods of treatment using such interferon-associated antigen binding proteins or nucleic acids or expression vectors or pharmaceutical compositions. Said novel interferon-associated antigen binding proteins afford beneficial improvements over the current state of the art, for example in that they effectively disrupt viral replication and thereby reduce HBV viral load.

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Interferon-associated antigen binding proteins for use in treating hepatitis B infection.

FIELD OF THE INVENTION

[0001] The present invention relates to novel interferon-associated antigen binding proteins as well as nucleic acids and expression vectors encoding such interferon-associated antigen binding proteins for use in therapy, more particularly for use in treating hepatitis B virus (HBV) infection. The present invention also relates to pharmaceutical compositions comprising such interferon-associated antigen binding proteins or nucleic acids or expression vectors for use in therapy, more particularly for use in treating hepatitis B virus (HBV) infection. The present invention further provides methods of treatment using such interferon-associated antigen binding proteins or nucleic acids or expression vectors or pharmaceutical compositions. Said novel interferon-associated antigen binding proteins afford beneficial improvements over the current state of the art, for example in that they effectively disrupt viral replication and thereby reduce HBV viral load.

BACKGROUND

[0002] HBV infects more than 300 million people worldwide and is a common cause of liver disease and liver cancer (Liang (2009) Hepatology 49:S13). HBV is a small DNA virus with unusual features similar to retroviruses, which replicates through an RNA intermediate (pre-genomic RNA, pgRNA) and can integrate into the host genome. The unique features of the HBV replication cycle confer a distinct ability of the virus to persist in infected cells. HBV infection leads to a wide spectrum of liver disease ranging from acute (including fulminant hepatic failure) to chronic hepatitis, cirrhosis and hepatocellular carcinoma. Acute HBV infection can be either asymptomatic or present with symptomatic acute hepatitis. 90-95% of children and 5-10% of adults infected with HBV are unable to clear the virus and become chronically infected. Many chronically infected persons have mild liver disease with little or no long-term morbidity or mortality. Other individuals with chronic HBV

infection develop active disease, which can progress to cirrhosis and liver cancer. These patients require careful monitoring and warrant therapeutic intervention.

[0003] Novel methods for treating HBV infection by modulating HBV infection in a cell are needed. In particular, methods for effectively disrupting viral replication, reducing HBV viral load of HBV-infected cells, reducing transcription of covalently closed circular HBV DNA in HBV-infected cells, and/or reducing the amount of pre-genomic HBV RNA in HBV-infected cells are needed.

SUMMARY OF THE INVENTION

[0004] The invention relates to an interferon-associated antigen binding protein comprising (I) an agonistic anti-CD40 antibody or an agonistic antigen binding fragment thereof, and (II) an Interferon (IFN) or a functional fragment thereof for use in treating hepatitis B virus (HBV) infection.

[0005] According to this aspect of the invention, the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof may comprise (a) a heavy chain or a fragment thereof comprising a complementarity determining region (CDR) CDRH1 that is at least 90% identical to SEQ ID NO 56, a CDRH2 that is at least 90% identical to SEQ ID NO 57, and a CDRH3 that is at least 90% identical to SEQ ID NO 58; and (b) a light chain or a fragment thereof comprising a CDRL1 that is at least 90% identical to SEQ ID NO 52, a CDRL2 that is at least 90% identical to SEQ ID NO 53, and a CDRL3 that is at least 90% identical to SEQ ID NO 54. Alternatively, the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof may comprise (a) a heavy chain or a fragment thereof comprising a complementarity determining region (CDR) CDRH1 that is identical to SEQ ID NO 56, a CDRH2 that is identical to SEQ ID NO 57, and a CDRH3 that is identical to SEQ ID NO 58; and (b) a light chain or a fragment thereof comprising a CDRL1 that is identical to SEQ ID NO 52, a CDRL2 that is identical to SEQ ID NO 53, and a CDRL3 that is identical to SEQ ID NO 54.

[0006] According to one embodiment, the agonistic anti-CD40 antibody, or the agonistic antigen binding fragment thereof, comprises a light chain variable region V_L comprising the sequence as set forth in SEQ ID NO 51, or a sequence at least 90% identical thereto; and/or a heavy chain variable region V_H comprising the sequence as set forth in SEQ ID NO 55, or a sequence at least 90% identical thereto.

[0007] According to another embodiment, the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof comprises a light chain (LC) that comprises a sequence as set forth in SEQ ID NO 3, or a sequence at least 90% identical thereto; and/or a heavy chain (HC) that comprises a sequence selected from the group consisting of SEQ ID NO 6, SEQ ID NO 9, SEQ ID NO 49 and SEQ ID NO 48, or a sequence at least 90% identical thereto.

[0008] According to a further embodiment, the IFN or the functional fragment thereof may be selected from the group consisting of a Type I IFN, a Type II IFN and a Type III IFN, or a functional fragment thereof. Preferably, the type I IFN or the functional fragment thereof is IFNα or IFNβ, or a functional fragment thereof.

[0009] According to another embodiment, the IFN or the functional fragment thereof is IFNα2a, or a functional fragment thereof. According to a preferred embodiment, the IFNα2a comprises the sequence as set forth in SEQ ID NO 17, or a sequence at least 90% identical thereto.

[0010] According to another embodiment, the IFN or the functional fragment thereof is IFNβ, or a functional fragment thereof. In a preferred embodiment, the IFNβ comprises the sequence as set forth in SEQ ID NO 14, or a sequence at least 90% identical thereto.

[0011] According to another embodiment, the IFN or the functional fragment thereof is fused to a light chain of the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof, preferably to the C-terminus.

[0012] According to a further embodiment, the IFN or the functional fragment thereof is fused to a heavy chain of the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof, preferably to the C-terminus.

[0013] According to another embodiment, the agonistic anti-CD40 antibody or an agonistic antigen binding fragment thereof, and the IFN or the functional fragment thereof, are fused to each other via a linker. In a preferred embodiment, the linker comprises a sequence as set forth in SEQ ID NO 20, SEQ ID NO 21, SEQ ID NO 24, SEQ ID NO 25 or SEQ ID NO 26.

[0014] According to another embodiment, the interferon-associated antigen binding protein is an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic antigen binding fragment thereof comprising one of the sequence combinations disclosed in Table 9.

[0015] According to another embodiment, the use comprises administering the interferon-associated antigen binding protein to a subject in need thereof by means of genetic delivery with RNA or DNA sequences encoding the interferon-associated antigen binding protein, or a vector or vector system encoding the interferon-associated antigen binding protein.

[0016] According to yet another embodiment, the interferon-associated antigen binding protein is comprised in a pharmaceutical composition.

BRIEF DESCRIPTION OF THE DRAWINGS

[0017] **Fig. 1:** This schematic drawing depicts exemplary interferon-associated antigen binding protein formats. The interferon-associated antigen binding protein is an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic antigen binding fragment thereof. IFNs are associated via linkers to different positions on the antibody or the antigen binding fragment thereof: N-terminal or C-terminal part of the light chain (LC) or the heavy chain (HC). In particular, IFNs are chosen from Type I, Type II and Type III interferon families.

[0018] **Fig. 2A** depicts an exemplary map of a pcDNA3.1 plasmid encoding SEQ ID NO 32 under the control of the pCMV promoter. The nucleic acid sequence encoding for SEQ ID NO 32 (SEQ ID NO 78) is also shown on the right. Italic: signal peptide sequence; black color: CP870,893 heavy chain coding sequence; underlined: HL linker coding sequence; bold: IFNβ coding sequence.

[0019] **Fig. 2B** shows examples of SDS PAGE in reduced conditions of some IFAs, with IFNα or IFNβ fused either at the heavy chain or the light chain. Migration of the parental CP870,893 is also shown on the left.

[0020] **Fig. 3A-3B** graphically depict a dose dependent effect of a number of IFA molecules with IFNβ fusions on activating the CD40-mediated NFκB pathway reporter assay in HEK-Blue™ CD40L cells. **Fig. 3A** shows examples of anti-CD40 activities for IFAs with IFNβ fused to the C-terminal part of the heavy chain (HC). **Fig. 3B** shows examples of anti-CD40 activities for IFAs with IFNβ fused to the N-terminal part of the LC (IFA34) or the HC (IFA36) and the corresponding fusions on the C-terminal part (IFA35 and IFA37). Purification yield of the latter group of IFAs was very low, thus to test their activity, the supernatants from HEK transfected cells were used and serially diluted to evaluate the anti-CD40 activity on HEK-Blue™ CD40L cells.

[0021] **Fig. 3C-3D** graphically depict a dose dependent effect of a number of IFA molecules with IFNβ fusions on activating the Type I IFN- pathway in reporter HEK-Blue-IFN-α/β cells. **Fig. 3C** shows examples of IFN activity for IFAs with IFNβ fused to the C-terminal part of the HC. **Fig. 3D** shows examples of IFN activity for IFAs with IFNβ fused to the N-terminal part of the LC (IFA34) or the HC (IFA36) and the corresponding fusions on the C-terminal part (IFA35 and IFA37). The same supernatants from HEK transfected cells as in Fig. 3B were used and serially diluted to evaluate the IFN activity. Parental antibody CP870,893 was used as negative control and recombinant human IFNβ was used as positive control. NS: Non Stimulated.

[0022] **Fig. 4A** graphically depicts a dose effect of a number of IFA molecules with IFNα fusions on activating the CD40-mediated NFκB pathway reporter assay in HEK-Blue™ CD40L cells.

[0023] **Fig. 4B** graphically depicts a dose effect of a number of IFA molecules with IFNα fusions on activating the Type I IFN-mediated pathway in reporter HEK-Blue-IFN-α/β cells. The activity of Pegasys is indicated in the insert in the lower right corner.

[0024] **Fig. 4C** graphically depicts the effect of IFA molecules with IFNα fusions and HL linker on HC (IFA38) or LC (IFA39) on activating the CD40-mediated NFκB pathway reporter assay in HEK-Blue™ CD40L cells.

[0025] **Fig. 4D** graphically depicts the effect of IFA38 and IFA39 on activation of the Type I IFN-pathway in reporter HEK-Blue-IFNα/β cells.

[0026] **Fig. 5** depicts the effect of IFNβ based IFAs in a dose dependent manner on HBeAg release from primary hepatocytes infected with HBV. IFA1, IFA12: fusion of IFNβ to the C-terminus of LC via HL or RL linkers, respectively. IFA2 and IFA13: fusion of IFNβ_C17S to the C-terminus of the LC via HL or RL linkers, respectively.

[0027] **Fig. 6A** depicts the effect of IFA25, IFA26 and IFA27 in a dose dependent manner on HBeAg release from primary human hepatocytes infected by HBV.

[0028] **Fig. 6B** depicts the effect of IFA28, IFA29 and IFA30 in a dose dependent manner on HBeAg release from primary human hepatocytes infected by HBV.

[0029] **Fig. 6C** depicts a dose response anti-viral activity (HBeAg release) of IFAs with HL linker (IFA38 and IFA39) on HBV-infected PHHs.

[0030] **Figs. 6D-6H** depict a dose response anti-viral activity of 4 IFAmolecules with fusion to IFNα via a peptide linker on primary human hepatocytes infected with HBV. **Fig. 6D**: Cartoon illustrating the study design. **Fig. 6E**: Effect of IFAs on HBeAg release in comparison to Pegasys. **Fig. 6F**: Effect of IFAs on HBsAg release in comparison to Pegasys. **Fig. 6G**: Effect of IFAs on pgRNA levels in comparison to Pegasys. **Fig. 6H**: Effect of IFAs on CXCL10 release in comparison to Pegasys.

[0031] **Fig. 7** depicts results from an *in vitro* Cytokines Release Assay of Human Whole Blood Cells (WBCs): Example of data obtained after stimulation of WBCs from 4 healthy volunteer donors. WBC were left Non-Stimulated (NS), treated with LPS (10 ng/mL) or with IFA1 (1 µg/mL) for 24 h. Supernatants were collected and submitted to cytokines release quantification using the MSD u-Plex kit for human cytokines. Results represent the mean of two independent stimulations from each donor. The profile of CXCL10 (IP10), IL6, IL1β and TNFα are shown.

[0032] **Tables 11a-b:** These tables summarize data obtained after in vitro stimulation of whole blood cells (WBCs) obtained from healthy volunteers. Each IFA was tested

on WBCs from four different donors. WBCs were left Non-Treated (NT), treated with LPS (10 ng/mL) or with IFAs (1 µg/mL) for 24 h. Supernatants were collected and submitted to cytokines release quantification using the MSD u-Plex kit for human cytokines. Results represent the mean of two independent stimulations from each donor and are expressed in pg/mL (nd: not detected).

[0033] Fig. 8: Pharmacokinetic profile of IFA25, IFA26, IFA27, IFA28, IFA29, and IFA30 after 0.5 mg/kg (IFAs) or 0.3 mg/kg (Pegasys) intravenous bolus injection to mice. Data expressed as mean +/- SD on semi-logarithmic scale. Samples were collected up to 10 days after administration. ELISA assay using anti-IFNα as secondary antibody for quantification method was used for IFA27, IFA29 and IFA30 **(Fig. 8A)** and for IFA25, IFA26 and IFA28 **(Fig. 8B)**. ELISA assay using anti-IgG2 as secondary antibody for quantification method was used for IFA25 and IFA27 **(Fig. 8C)**. **Fig. 8D**: Pegasys quantification was done using human IFNα matched antibody pairs. The marked line (LLOQ) denotes the limit of detection for the Pegasys assay.

[0034] Table 12A: PK Report Summary: PK parameters for CP870,893, IFA27, IFA29 and IFA30 following single intravenous administration of 0.5 mg/kg to male CD1 Swiss mice. PK parameters for CP870,893 were explored in a 7-day experiment and those for IFA27, IFA29 and IFA30 in 10-day experiments (quantification for IFA27 was performed using 2 different ELISA approaches).

[0035] Table 12B: PK Report Summary: PK parameters for CP870,893, Pegasys and for three different IFAs (IFA25, IFA26 and IFA28) following single intravenous bolus administration of 0.5 mg/kg to male CD1 Swiss mice. PK parameters for CP870,893 and IFA25, IFA26, IFA28 and Pegasys were explored in 21-day experiments (quantification for IFA25 was performed using 2 different ELISA approaches).

[0036] Fig. 9A depicts CD40 agonistic activity in a dose dependent manner of IFA50 and IFA51 with no Fc region in comparison to the parental anti-CD40 antibody in reporter HEK-Blue™ CD40L cells. **Fig. 9B** depicts the IFNα activity in a dose dependent manner of IFA50 and IFA51 in reporter HEK-Blue™ hIFN-α/β cells. **Fig. 9C:** Effect of IFA50 and IFA51 on HBeAg release from HBV-infected PHHs.

[0037] **Fig. 10A** depicts CD40 agonistic activity in a dose dependent manner of IFNε based IFA49, in comparison to parental anti-CD40 antibody, in HEK-Blue™ CD40L reporter cells. IFA49 corresponds to fusion of IFNε to the HC via a peptide linker. **Fig. 10B** depicts the IFN activity in a dose dependent manner of IFA49 on reporter HEK-Blue™ hIFN-α/β reporter cells which are activated by Type I interferons. **Fig. 10C**: Effect of IFA49 on HbeAg release from HBV-infected PHHs.

[0038] **Fig. 11A** depicts CD40 agonistic activity in a dose dependent manner of IFNω based IFA46, in comparison to parental anti-CD40 antibody, in HEK-Blue™ CD40L reporter cells. IFA46 correspond to fusion of IFNω to the LC via a peptide linker. **Fig. 11B** depicts the IFN activity in a dose dependent manner of IFA46 on reporter HEK-Blue™ hIFN-α/β reporter cells which are activated by Type I interferons. **Fig. 11C**: Effect of IFA46 on HbeAg release from HBV-infected PHHs.

[0039] **Fig. 12A** depicts CD40 agonistic activity in a dose dependent manner of IFNγ based IFAs (IFA42 and IFA43), in comparison to parental anti-CD40 antibody, in HEK-Blue™ CD40L reporter cells. IFA42 corresponds to fusion of IFNγ to the LC via a peptide linker and IFA43 corresponds to fusion of IFNγ to the HC via a peptide linker. **Fig. 12B** depicts the IFN activity in a dose dependent manner of IFA42 and IFA43 in reporter HEK-Blue-hIFNγ cells; **Fig. 12C:** Effect of IFA42 and IFA43 on HbeAg release from HBV-infected PHHs.

[0040] **Fig. 13A** depicts CD40 agonistic activity in a dose dependent manner of IFNλ based IFAs (IFA44 and IFA45), in comparison to parental anti-CD40 antibody, in HEK-Blue™ CD40L reporter cells. IFA44 corresponds to fusion of IFNλ to the LC via a peptide linker and IFA45 correspond to fusion of IFNλ to the HC via a peptide linker. **Fig. 13B** depicts the IFN activity in a dose dependent manner of IFA44 and IFA45 in reporter HEK-Blue-hIFNλ cells. **Fig. 13C:** Effect of the IFNλ based IFAs (IFA44 and IFA45) on HbeAg release from HBV-infected PHHs.

[0041] **Fig. 14** shows examples of SDS PAGE in reduced conditions of some IFAs, with IFNα or IFNβ fused on the heavy chain of 3G5-antiCD40 antibody. Migration of the parental 3G5 antiCD40 antibody is also shown on the left.

[0042] **Figs. 15A-B** graphically show a dose dependent effect of a number of 3G5-based IFA molecules with IFNβ fusions on activating the CD40-mediated NFκB

pathway reporter assay in HEK-Blue™ CD40L cells. Comparison to the parental antibody 3G5 (designated in this figure as CDX-3G5) is likewise shown. **Fig. 15A** shows examples of anti-CD40 activities for IFAs with fusion of IFNβ to the C-terminal part of the heavy chain (HC). Purification yield of IFAs with fusions of IFNβ on the light chain was very low, thus to test their activity, supernatants from HEK transfected cells were used and serially diluted to evaluate the anti-CD40 activity on HEK-Blue™ CD40L cells; an example of activity is shown in **Fig. 15B** and 3G5 containing supernatant was used as control.

[0043] **Figs. 15C-D** graphically show a dose dependent effect of a number of IFA molecules with IFNβ fusions on activating the Type I IFN-pathway in reporter HEK-Blue-IFN-α/β cells. **Fig. 15C** shows examples of IFN activity for IFAs with fusion of IFNβ to the C-terminal part of the HC. **Fig. 15D** shows IFN activity of IFAs with IFNβ fused on the light chain; the production level of these proteins was very low and thus an example of activity for two IFAs is shown in **Fig. 15D** using the same supernatant as in Fig. 15B.

[0044] **Fig. 16A** graphically shows a dose effect of four IFAs molecules with IFNα fusions on activating the CD40-mediated NFκB pathway reporter assay in HEK-Blue™ CD40L cells. Comparison to the parental antibody 3G5 (designated in this figure as CDX-3G5) is likewise shown.

[0045] **Fig. 16B** graphically shows a dose effect of a number of IFAs molecules with IFNα fusions on activating the Type I IFN-mediated pathway in reporter HEK-Blue-IFN-α/β cells.

[0046] **Fig. 17** shows the effect of Type-I IFN based IFAs in a dose dependent manner on HBeAg release from PHHs infected by HBV. **Fig. 17A** shows results obtained with IFNβ based IFAs (IFA106, IFA107, IFA108 and IFA109) with fusion of IFNβ to the C-terminal part of the HC. **Fig. 17B** shows results obtained with four IFNα based IFAs (IFA121, IFA122, IFA123 and IFA124) with fusion of IFNα to the C-terminal part of the HC. NI-NT: non-infected, non-treated. MOI: multiplicity of infection.

[0047] **Fig. 18:** In vitro Cytokines Release Assay of Human Whole Blood Cells (WBCs): Example of data obtained after stimulation of WBCs from 4 healthy

volunteer donors. WBCs were left non-treated (NT), treated with LPS (10 ng/mL) or with IFA109 (1 μg/mL) for 24 h. Supernatants were collected and submitted to cytokines release quantification using the MSD u-Plex kit for human cytokines. Results represent the mean of two independent stimulations from each donor. The profile of CXCL10 (IP10), IL6, IL1β and TNFα are shown.

[0048] **Table 13** This table summarizes data obtained after in vitro stimulation of whole blood cells obtained from healthy volunteers. IFA109 was tested on WBCs from four different donors. WBCs were left Non-Treated (NT), treated with LPS (10 ng/mL) or with IFA109 (1 μg/mL) for 24 h. Supernatants were collected and submitted to cytokines release quantification using the MSD u-Plex kit for human cytokines. Results represent the mean of two independent stimulations from each donor and are expressed in pg/mL (nd: not detected).

[0049] The foregoing and other features and advantages of the present invention will be more fully understood from the following detailed description of illustrative embodiments taken in conjunction with the accompanying drawings.

DETAILED DESCRIPTION

[0050] The present invention is based in part on the discovery of a therapy that is based on the use of "interferon-associated antigen-binding proteins", variants or derivatives thereof comprising (I) an agonistic anti-CD40 antibody or an agonistic antigen binding fragment thereof, and (II) an interferon (IFN) or a functional fragment thereof in hepatitis B virus (HBV) therapy. Said interferon-associated antigen-binding proteins inhibit transcription of hepatitis B virus covalently closed circular DNA (cccDNA) into pre-genomic HBV RNA (pgRNA) in HBV-infected cells, inhibit release of hepatitis B e-antigen (HBeAg) from HBV-infected cells, and enhance the IFN pathway in uninfected and HBV infected hepatocytes, in particular in uninfected and HBV infected primary human hepatocytes and in a synergistic fashion. HBV therapy comprising administering an interferon-associated antigen-binding protein to an HBV-infected cell, or a subject infected with HBV, is provided.

[0051] The invention may be more readily understood in the light of the selected terms defined below.

[0052] As used herein, the term **"CD40"** refers to "Cluster of differentiation 40", a member of the tumor necrosis factor receptor (TNFR) superfamily. CD40 is a costimulatory protein found on antigen presenting cells (e.g., B cells, dendritic cells, monocytes), hematopoietic precursors, endothelial cells, smooth muscle cells, epithelial cells, as well as the majority of human tumors (Grewal & Flavell, Ann. Rev. lmmunol., 1996, 16: 111-35; Toes & Schoenberger, Seminars in Immunology, 1998, 10(6): 443-8). The binding of the natural ligand CD154 (CD40L) on T_H cells to CD40 activates antigen presenting cells and induces a variety of downstream effects. The TNF-receptor associated factor adaptor proteins TRAF1, TRAF2, TRAF6 and TRAF5 interact with CD40 and serve as mediators of the signal transduction. Ultimately, CD40 signaling activates both the canonical and the noncanonical NF-κB pathways.

Agonistic anti-CD40 antibodies and antigen binding fragments thereof

[0053] As used herein, the term **"antibody"** refers to immunoglobulin molecules comprising four polypeptide chains, two heavy (H) chains and two light (L) chains inter-connected by disulfide bonds, as well as multimers thereof (e.g., IgM). Each heavy chain comprises a heavy chain variable region (abbreviated VH or V_H) and a heavy chain constant region (CH or C_H). The heavy chain constant region comprises three domains, CH1, CH2 and CH3. Each light chain comprises a light chain variable region (abbreviated VL or V_L) and a light chain constant region (CL or C_L). The light chain constant region comprises one domain (CL1). The VH and VL regions can be further subdivided into regions of hypervariability, termed "**complementarity determining regions (CDRs)**", interspersed with regions that are more conserved, termed "**framework regions**" (FR). Each VH and VL is composed of three CDRs and four FRs, arranged from amino-terminus to carboxy-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4. Framework regions can aid in maintaining the proper conformation of the CDRs to promote binding between the antigen binding region and an antigen.

[0054] The most commonly used immunoglobulin for therapeutic applications is immunoglobulin G (or IgG), a tetrameric glycoprotein. In a naturally-occurring immunoglobulin, each tetramer is composed of two identical pairs of polypeptide

chains, each pair having one light (about 25 kDa) and one heavy chain (about 50-70 kDa). The amino-terminal portion of each chain includes a variable region of about 100 to 110 or more amino acids primarily responsible for antigen recognition. The carboxy-terminal portion of each chain defines a constant region primarily responsible for effector function. Immunoglobulins can be assigned to different classes depending on the amino acid sequence of the constant domain of their heavy chains.

[0055] Heavy chains are classified as mu (μ), delta (δ), gamma (γ), alpha (α), and epsilon (ε), and define the antibody's isotype as IgM, IgD, IgG, IgA, and IgE, respectively. Several of these may be further divided into subclasses or isotypes, e.g. IgG1, IgG2, IgG3, IgG4, IgA1 and IgA2. Different isotypes have different effector functions; for example, IgG1 and IgG3 isotypes have antibody-dependent cellular cytotoxicity (ADCC) activity. In preferred embodiments, the agonistic antiCD40 antibodies or agonistic antigen binding fragments thereof comprised in the interferon-associated antigen binding proteins according to the invention are of the IgG class. In more preferred embodiments, the agonistic antiCD40 antibodies or agonistic antigen binding fragments thereof comprised in the interferon-associated antigen binding proteins according to the invention are of the IgG1 or IgG3 subclasses. In specifically preferred embodiments, the agonistic antiCD40 antibodies or agonistic antigen binding fragments thereof comprised in the interferon-associated antigen binding proteins according to the invention are of the IgG1 subclass. In other more preferred embodiments, the agonistic antiCD40 antibodies or agonistic antigen binding fragments thereof comprised in the interferon-associated antigen binding proteins according to the invention are of the IgG2 or IgG4 subclasses. In specifically preferred embodiments, the agonistic antiCD40 antibodies or agonistic antigen binding fragments thereof comprised in the interferon-associated antigen binding proteins according to the invention are of the IgG2 subclass.

[0056] Human light chains are classified as kappa (κ) and lambda (λ) light chains. Accordingly, in some embodiments, the agonistic antiCD40 antibodies or agonistic antigen binding fragments thereof comprised in the interferon-associated antigen binding proteins according to the invention comprise a light chain of the κ class. In other embodiments, the agonistic antiCD40 antibodies or agonistic antigen binding

fragments thereof comprised in the interferon-associated antigen binding proteins according to the invention comprise a light chain of the λ class. Within light and heavy chains, the variable and constant regions are joined by a "J" region of about 12 or more amino acids, wherein the heavy chain additionally includes a "D" region of about 10 more amino acids. See generally, Fundamental Immunology, Ch. 7 (Paul, W., ed., 2nd ed. Raven Press, N.Y. (1989)).

[0057] The term "antibody" further includes, but is not limited to, monoclonal antibodies, bispecific antibodies, minibodies, domain antibodies, synthetic antibodies (sometimes referred to as "antibody mimetics"), chimeric antibodies, humanized antibodies, human antibodies, and fragments thereof, respectively. Unless otherwise indicated, the term "antibody" includes, in addition to antibodies comprising two full-length heavy chains and two full-length light chains, derivatives, variants, antigen binding fragments, and muteins thereof, examples of which are described below.

[0058] As used herein, the term **"agonistic CD40 antibody"** or **"agonistic anti-CD40 antibody"** refers to an antibody that binds to CD40 and mediates CD40 signaling. In a preferred embodiment, it binds to human CD40. As described below, binding to CD40 may be determined using surface plasmon resonance, preferably using the BIAcore® system. The agonistic anti-CD40 antibody may increase one or more CD40 activities by at least about 20% when added to a cell, tissue or organism expressing CD40. In some embodiments, the antibody activates CD40 activity by at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, or at least 85%. **CD40 activity** of the agonistic anti-CD40 antibody may be measured using a whole blood surface molecule upregulation assay or using an *in vitro* reporter cell assay, e.g., using HEK-Blue™ CD40L cells (InvivoGen Cat. #: hkb-cd40), as described in greater detail in Example I. These reporter cells were generated by stable transfection of HEK293 cells with the human CD40 gene and an NFκB-inducible secreted embryonic alkaline phosphatase (SEAP) construct to measure the activity of CD40 agonists. Stimulation of CD40 leads to NFκB activation and thus to production of SEAP, which can be detected in the supernatant using chromogenic substrates such as QUANTI-Blue™.

[0059] In the context of the present invention, the interferon-associated antigen binding proteins activate both the CD40 and an IFN pathway. In certain embodiments, the interferon-associated antigen binding protein activates the CD40 pathway with an EC_{50} of less than 400, 300, 200, 150, 100, 70, 60, 50, 40, 30, 25, 20, or 15 ng/mL. In more specific embodiments, the interferon-associated antigen binding protein activates the CD40 pathway with an EC_{50} ranging from 10 to 200 ng/mL. In even more specific embodiments, the interferon-associated antigen binding protein activates the CD40 pathway with an EC_{50} ranging from 10 to 50 ng/mL, preferably 10 to 30 ng/mL.

[0060] Examples of suitable agonistic anti-CD40 antibodies include, but are not limited to, CP870,893 (Pfizer / Roche), SGN-40 (Seattle Genetics), ADC-1013 (Janssen / Alligator BioSciences), Chi Lob 7/4 (University of Southampton), dacetumumab (Seattle Genetics), APX005M (Apexigen, Inc.), 3G5 (Celldex) and CDX-1140 (Celldex). Exemplary light and heavy chain sequences of the agonistic anti-CD40 antibody CP870,893 are shown in **Table 7**. Exemplary light and heavy chain sequences of the agonistic anti-CD40 antibody 3G5 are shown in **Table 8**.

[0061] As used herein, the term "**agonistic antigen binding fragment**" of an agonistic anti-CD40 antibody refers to a fragment of an agonistic anti-CD40 antibody that retains one or more functional activities of the original antibody, such as the ability to bind to and act as an agonist of CD40 signaling in a cell, e.g., it mediates CD40 pathway signaling. Such fragment may compete with the intact antibody for binding to CD40.

[0062] Agonistic antigen binding fragments of an agonistic anti-CD40 antibody can be produced by recombinant DNA techniques, or can be produced by enzymatic or chemical cleavage of an anti-CD40 antibody. Agonistic antigen binding fragments include, but are not limited to, a Fab fragment, a diabody (heavy chain variable domain on the same polypeptide as a light chain variable domain, connected via a short peptide linker that is too short to permit pairing between the two domains on the same chain), a Fab' fragment, a $F(ab')_2$ fragment, a Fv fragment, domain antibodies and single-chain antibodies, and can be derived from any mammalian source, including but not limited to human, mouse, rat, camelid or rabbit.

[0063] The term "**variable region**" or "**variable domain**" refers to a portion of the light and/or heavy chains of an antibody, typically including approximately the amino-terminal 120 to 130 amino acids in the heavy chain and about 100 to 110 amino terminal amino acids in the light chain. Variable regions of different antibodies differ extensively in amino acid sequence even among antibodies derived from the same species or of the same class. Exemplary V_L and V_H domain sequences of the agonistic anti-CD40 antibody CP870,893 are shown in **Table 1**. The variable region of an antibody typically determines specificity of a particular antibody for its target as it contains the CDRs. **Table 1** also shows exemplary CDR sequences of the agonistic anti-CD40 antibody CP870,893.

Table 1. Anti-CD40 antibody heavy/light chain variable regions and CDRs of the agonistic anti-CD40 antibody CP870,893. Bold italic sequences correspond to CDR regions according to the Kabat definition.

Anti-CD40 antibody regions	Sequence
antiCD40 Antibody V_L domain (SEQ ID NO 51)	DIQMTQSPSSVSASVGDRVTITC***RASQGIYSWLA***WY QQKPGKAPNLLIY***TASTLQS***GVPSRFSGSGSGTDFTL TISSLQPEDFATYYC***QQANIFPLT***FGGGTKVEIK
antiCD40 Antibody CDRL1 (SEQ ID NO 52)	RASQGIYSWLA
antiCD40 Antibody CDRL2 (SEQ ID NO 53)	TASTLQS
antiCD40 Antibody CDRL3 (SEQ ID NO 54)	QQANIFPLT

antiCD40 Antibody V_H domain (SEQ ID NO 55)	QVQLVQSGAEVKKPGASVKVSCKASGYTF***TGYYMH*** WVRQAPGQGLEWMG***WINPDSGGTNYAQKFQG***RVT MTRDTSISTAYMELNRLRSDDTAVYYCAR***DQPLGY CTNGVCSYFDY***WGQGTLVTVSS
antiCD40 Antibody CDRH1 (SEQ ID NO 56)	TGYYMH
antiCD40 Antibody CDRH2 (SEQ ID NO 57)	WINPDSGGTNYAQKFQG
antiCD40 Antibody CDRH3 (SEQ ID NO 58)	DQPLGYCTNGVCSYFDY

[0064] Delineation of a CDR and identification of residues comprising the binding site of an antibody may be accomplished by solving the structure of the antibody and/or solving the structure of the antibody-ligand complex. This can be accomplished by any of a variety of techniques known to those skilled in the art, such as X-ray crystallography. Various methods of analysis can be employed to identify or approximate the CDR regions. Examples of such methods include, but are not limited to, the Kabat definition, the Chothia definition, the AbM definition and the contact definition.

[0065] The Kabat definition is a standard for numbering the residues in an antibody and is typically used to identify CDR regions. *See, e.g.,* Johnson & Wu, Nucleic Acids Res., 28: 214-8 (2000). The Chothia definition is similar to the Kabat definition, but the Chothia definition takes into account positions of certain structural loop regions. *See, e.g.,* Chothia *et al.*, J. Mol. Biol., 196: 901-17 (1986); Chothia *et al.*, Nature, 342: 877-83 (1989). The AbM definition uses an integrated suite of computer programs produced by Oxford Molecular Group that model antibody structure. *See, e.g.,* Martin *et al.*, Proc Natl Acad Sci (USA), 86:9268-9272 (1989); "AbM™, A Computer Program for Modeling Variable Regions of Antibodies,"

Oxford, UK; Oxford Molecular, Ltd. The AbM definition models the tertiary structure of an antibody from primary sequence using a combination of knowledge databases and *ab initio* methods, such as those described by Samudrala *et al.*, "*Ab Initio* Protein Structure Prediction Using a Combined Hierarchical Approach," in PROTEINS, Structure, Function and Genetics Suppl., 3:194-198 (1999). The contact definition is based on an analysis of the available complex crystal structures. *See, e.g.,* MacCallum *et al.,* J. Mol. Biol., 5:732-45 (1996).

[0066] In certain embodiments, the complementarity determining regions (CDRs) of the light and heavy chain variable regions of an agonistic anti-CD40 antibody, or an agonistic antigen binding fragment thereof, can be grafted to framework regions (FRs) from the same, or another, species. In certain embodiments, the CDRs of the light and heavy chain variable regions of an agonistic anti-CD40 antibody, or an agonistic antigen binding fragment thereof, can be grafted to consensus human FRs. To create consensus human FRs, in certain embodiments, FRs from several human heavy chain or light chain amino acid sequences are aligned to identify a consensus amino acid sequence. In certain embodiments, the FRs of the heavy chain or light chain of an agonistic anti-CD40 antibody, or an agonistic antigen binding fragment thereof, are replaced with the FRs from a different heavy chain or light chain. In certain embodiments, rare amino acids in the FRs of the heavy and light chains of an agonistic anti-CD40 antibody, or an agonistic antigen binding fragment thereof, are not replaced, while the rest of the FR amino acids are replaced. Rare amino acids are specific amino acids that are in positions in which they are not usually found in FRs. In certain embodiments, the grafted variable regions from an agonistic anti-CD40 antibody, or an agonistic antigen binding fragment thereof, can be used with a constant region that is different from the constant region of an agonistic anti-CD40 antibody, or an agonistic antigen binding fragment thereof. In certain embodiments, the grafted variable regions are part of a single chain Fv antibody. CDR grafting is described, e.g., in U.S. Patent Nos. 6,180,370, 6,054,297, 5,693,762, 5,859,205, 5,693,761, 5,565,332, 5,585,089, and 5,530,101, and in Jones *et al.*, Nature, 321: 522-525 (1986); Riechmann *et al.*, Nature, 332: 323-327 (1988); Verhoeyen *et al.*, Science, 239:1534-1536 (1988), Winter, FEBS Letts., 430:92-94 (1998), which are hereby incorporated by reference for any purpose.

[0067] An "**Fc**" region typically comprises two heavy chain fragments comprising the C_H2 and C_H3 domains of an antibody. The two heavy chain fragments are held together by two or more disulfide bonds and by hydrophobic interactions of the C_H3 domains.

[0068] A "**Fab fragment**" comprises one full-length light chain as well as the C_H1 and variable regions of one heavy chain (the combination of the V_H and C_H1 regions is referred to herein as "**fab region heavy chain**").

[0069] A "**Fab' fragment**" comprises one light chain and a portion of one heavy chain that contains the VH domain and the C_H1 domain and also the region between the C_H1 and C_H2 domains, such that an interchain disulfide bond can be formed between the two heavy chains of two Fab' fragments to form an $F(ab')_2$ molecule.

[0070] A "**$F(ab')_2$ fragment**" contains two light chains and two heavy chains containing a portion of the constant region between the C_H1 and C_H2 domains, such that an interchain disulfide bond is formed between the two heavy chains. A $F(ab')_2$ fragment thus is composed of two Fab' fragments that are held together by a disulfide bond between the two heavy chains.

[0071] The "**Fv region**" comprises the variable regions from both the heavy and light chains, but lacks the constant regions.

[0072] "**Single-chain antibodies**" are Fv molecules in which the heavy and light chain variable regions have been connected by a flexible linker to form a single polypeptide chain, which forms an antigen binding region. Single chain antibodies are discussed in detail in International Patent Application Publication No. WO 88/01649 and United States Patent Nos. 4,946,778 and No. 5,260,203, the disclosures of which are incorporated by reference.

[0073] A "**domain antibody**" is an immunologically functional immunoglobulin fragment containing only the variable region of a heavy chain or the variable region of a light chain. In some instances, two or more V_H regions are covalently joined with a peptide linker to create a bivalent domain antibody. The two V_H regions of a bivalent domain antibody can target the same or different antigens.

[0074] An antibody or antigen binding protein, such as an interferon-associated antigen binding protein according to the invention, preferably binds to its target antigen with a dissociation constant (K_d) of $\leq 10^{-7}$ M. The antibody or antigen binding protein binds its antigen with "high affinity" when the K_d is $\leq 5 \times 10^{-9}$ M, and with "very high affinity" when the K_d is $\leq 5 \times 10^{-10}$ M. More preferably, the antibody or antigen binding protein has a K_d of $\leq 10^{-9}$ M. In some embodiment, the off-rate is $< 1 \times 10^{-5}$. In other embodiments, the antibody or antigen binding protein will bind to human CD40 with a K_d of between about 10^{-9} M and 10^{-13} M, and in yet another embodiment the antibody or antigen binding protein will bind with a $K_d \leq 5 \times 10^{-10}$. As will be appreciated by one of skill in the art, in some embodiments, any or all of the antigen binding fragments can bind to CD40. Preferably, said constants are determined using surface plasmon resonance, more preferably using the BIAcore® system.

[0075] The term "**surface plasmon resonance**" means an optical phenomenon that allows for the analysis of real-time biospecific interactions by detection of alterations in protein concentrations within a biosensor matrix, for example using the BIAcore® system (BIAcore International AB, a GE Healthcare company, Uppsala, Sweden and Piscataway, N.J.). For further descriptions, see Jönsson et al. (1993) Ann. Biol. Clin. 51:19-26. The term "**K_{on}**" means the on rate constant for association of a binding protein (e.g., an antibody or antigen binding protein) to the antigen to form the, e.g., antigen binding protein/antigen complex. The term "**K_{on}**", or "**on-rate**" also means "**association rate constant**", or "**ka**", as is used interchangeably herein. This value indicating the binding rate of a binding protein to its target antigen or the rate of complex formation between a binding protein, e.g., an antibody or an antigen binding protein, and antigen also is shown by the equation below:

Antibody("**Ab**")+Antigen("**Ag**")→Ab-Ag

[0076] The term "**K_{off}**", or "**off-rate**", means the off rate constant for dissociation, or "**dissociation rate constant**", of a binding protein (e.g., an antibody or antigen binding protein) from the, e.g., antigen binding protein/antigen complex as is known in the art. This value indicates the dissociation rate of a binding protein, e.g., an antibody or an antigen binding protein, from its target antigen or separation of Ab-

Ag complex over time into free antibody and antigen as shown by the equation below:

$$Ab+Ag \leftarrow Ab-Ag$$

[0077] The terms "**K_d**" and "**equilibrium dissociation constant**" means the value obtained in a titration measurement at equilibrium, or by dividing the dissociation rate constant (K_{off}) by the association rate constant (K_{on}). The association rate constant, the dissociation rate constant and the equilibrium dissociation constant, are used to represent the binding affinity of a binding protein (e.g., an antibody or an antigen binding protein) to an antigen. Methods for determining association and dissociation rate constants are well known in the art. Using fluorescence-based techniques offers high sensitivity and the ability to examine samples in physiological buffers at equilibrium. Other experimental approaches and instruments such as a BIAcore® (biomolecular interaction analysis) assay, can be used (e.g., instrument available from BIAcore International AB, a GE Healthcare company, Uppsala, Sweden). Additionally, a KinExA® (Kinetic Exclusion Assay) assay, available from Sapidyne Instruments (Boise, Id.), can also be used.

[0078] An antigen binding protein according to the invention may bind to one target with an affinity at least one order of magnitude, preferably at least two orders of magnitude higher than for a second target.

[0079] The term "**target**" refers to a molecule or a portion of a molecule capable of being bound by an antigen binding protein. In certain embodiments, a target can have one or more epitopes. It will therefore be understood that the target may serve as "antigen" for the "antigen binding protein" of the present invention.

[0080] The term "**epitope**" includes any determinant capable of being bound by an antigen binding protein, such as an antibody. An epitope is a region of an antigen that is bound by an antigen binding protein that targets that antigen, and when the antigen is a protein, includes specific amino acids that directly contact the antigen binding protein. Most often, epitopes reside on proteins, but in some instances can reside on other kinds of molecules, such as nucleic acids. Epitope determinants can include chemically active surface groupings of molecules such as amino acids, sugar side

chains, phosphoryl or sulfonyl groups, and can have specific three-dimensional structural characteristics, and/or specific charge characteristics. Generally, antibodies specific for a particular target antigen will preferentially/specifically recognize an epitope on the target antigen in a complex mixture of proteins and/or macromolecules.

[0081] In exemplary embodiments, the agonistic anti-CD40 antibody, or the agonistic antigen binding fragment thereof forming part (I) of the interferon-associated antigen binding proteins of the invention comprises three light chain complementarity determining regions (CDRs) that are at least 90% identical to the CDRL1, CDRL2 and CDRL3 sequences within SEQ ID NO 3; and three heavy chain CDRs that are at least 90% identical to the CDRH1, CDRH2 and CDRH3 sequences within SEQ ID NO 6. The agonistic anti-CD40 antibody, or the agonistic antigen binding fragment thereof, may also comprise three light chain complementarity determining regions (CDRs) that are identical to the CDRL1, CDRL2 and CDRL3 sequences within SEQ ID NO 3; and three heavy chain CDRs that are identical to the CDRH1, CDRH2 and CDRH3 sequences within SEQ ID NO 6. In such embodiments, each CDR is defined in accordance with the Kabat definition, the Chothia definition, the AbM definition, or the contact definition of CDR; preferably wherein each CDR is defined in accordance with the CDR definition of Kabat or the CDR definition of Chothia. In particular embodiments, each CDR is defined in accordance with the Kabat definition. In other particular embodiments, each CDR is defined in accordance with the Chothia definition.

[0082] Alternatively, the agonistic anti-CD40 antibody, or the agonistic antigen binding fragment thereof forming part (I) of the interferon-associated antigen binding proteins of the invention may comprise (a) a heavy chain or a fragment thereof comprising a complementarity determining region (CDR) CDRH1 that is at least 90%, at least 95%, at least 98% or at least 99% identical to SEQ ID NO 56, a CDRH2 that is at least 90%, at least 95%, at least 98% or at least 99% identical to SEQ ID NO 57, and a CDRH3 that is at least 90%, at least 95%, at least 98% or at least 99% identical to SEQ ID NO 58; and (b) a light chain or a fragment thereof comprising a CDRL1 that is at least 90%, at least 95%, at least 98% or at least 99% identical to SEQ ID NO 52, a CDRL2 that is at least 90%, at least 95%, at least 98% or at least

99% identical to SEQ ID NO 53, and a CDRL3 that is at least 90%, at least 95%, at least 98% or at least 99% identical to SEQ ID NO 54.

[0083] In some embodiments, the agonistic anti-CD40 antibody, or the agonistic antigen binding fragment thereof, comprises (a) a heavy chain or a fragment thereof comprising a complementarity determining region (CDR) CDRH1 that is identical to SEQ ID NO 56, a CDRH2 that is identical to SEQ ID NO 57, and a CDRH3 that is identical to SEQ ID NO 58; and (b) a light chain or a fragment thereof comprising a CDRL1 that is identical to SEQ ID NO 52, a CDRL2 that is identical to SEQ ID NO 53, and a CDRL3 that is identical to SEQ ID NO 54.

[0084] More specifically the agonistic anti-CD40 antibody, or the agonistic antigen binding fragment thereof, comprises a light chain variable region V_L comprising the sequence as set forth in SEQ ID NO 51, or a sequence at least 90%, at least 95%, at least 98% or at least 99% identical thereto; and/or a heavy chain variable region V_H comprising the sequence as set forth in SEQ ID NO 55, or a sequence at least 90%, at least 95%, at least 98% or at least 99% identical thereto.

[0085] The interferon-associated antigen binding proteins of the invention may also comprise an agonistic anti-CD40 antibody or an agonistic antigen binding fragment thereof, comprising a Fab region heavy chain comprising an amino acid sequence as set forth in SEQ ID NO 12, or a sequence at least 90%, at least 95%, at least 98% or at least 99% identical thereto.

[0086] In some embodiments, the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof comprises a light chain (LC) that comprises a sequence as set forth in SEQ ID NO 3, or a sequence at least 90%, at least 95%, at least 98% or at least 99% identical thereto; and/or a heavy chain (HC) that comprises a sequence selected from the group consisting of SEQ ID NO 6, SEQ ID NO 9, SEQ ID NO 49, SEQ ID NO 12 and SEQ ID NO 50, or a sequence at least 90%, at least 95%, at least 98% or at least 99% identical thereto.

[0087] In more specific embodiments, the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof comprises a light chain (LC) that comprises a sequence as set forth in SEQ ID NO 3, or a sequence at least 90%, at least 95%, at least 98% or at least 99% identical thereto; and/or a heavy chain (HC)

that comprises a sequence as set forth in SEQ ID NO 6, or a sequence at least 90%, at least 95%, at least 98% or at least 99% identical thereto.

[0088] In more specific embodiments, the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof comprises a light chain (LC) that comprises a sequence as set forth in SEQ ID NO 3, or a sequence at least 90%, at least 95%, at least 98% or at least 99% identical thereto; and/or a heavy chain (HC) that comprises a sequence as set forth in SEQ ID NO 9, or a sequence at least 90%, at least 95%, at least 98% or at least 99% identical thereto.

[0089] In other more specific embodiments, the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof comprises a light chain (LC) that comprises a sequence as set forth in SEQ ID NO 3, or a sequence at least 90%, at least 95%, at least 98% or at least 99% identical thereto; and/or a heavy chain (HC) that comprises a sequence as set forth in SEQ ID NO 49, or a sequence at least 90%, at least 95%, at least 98% or at least 99% identical thereto.

[0090] In other more specific embodiments, the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof comprises a light chain (LC) that comprises a sequence as set forth in SEQ ID NO 3, or a sequence at least 90%, at least 95%, at least 98% or at least 99% identical thereto; and/or a heavy chain (HC) that comprises a sequence as set forth in SEQ ID NO 12, or a sequence at least 90%, at least 95%, at least 98% or at least 99% identical thereto.

[0091] In other more specific embodiments, the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof comprises a light chain (LC) that comprises a sequence as set forth in SEQ ID NO 3, or a sequence at least 90%, at least 95%, at least 98% or at least 99% identical thereto; and/or a heavy chain (HC) that comprises a sequence as set forth in SEQ ID NO 50, or a sequence at least 90%, at least 95%, at least 98% or at least 99% identical thereto.

[0092] In some embodiments, the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof comprises a light chain (LC) that comprises a sequence as set forth in SEQ ID NO 59, or a sequence at least 90%, at least 95%, at least 98% or at least 99% identical thereto; and/or a heavy chain (HC) that comprises a sequence selected from the group consisting of SEQ ID NO 61, SEQ ID NO 63 and

SEQ ID NO 65, or a sequence at least 90%, at least 95%, at least 98% or at least 99% identical thereto.

[0093] In more specific embodiments, the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof comprises a light chain (LC) that comprises a sequence as set forth in SEQ ID NO 59, or a sequence at least 90%, at least 95%, at least 98% or at least 99% identical thereto; and/or a heavy chain (HC) that comprises a sequence as set forth in SEQ ID NO 61, or a sequence at least 90%, at least 95%, at least 98% or at least 99% identical thereto.

[0094] In other more specific embodiments, the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof comprises a light chain (LC) that comprises a sequence as set forth in SEQ ID NO 59, or a sequence at least 90%, at least 95%, at least 98% or at least 99% identical thereto; and/or a heavy chain (HC) that comprises a sequence as set forth in SEQ ID NO 63, or a sequence at least 90%, at least 95%, at least 98% or at least 99% identical thereto.

[0095] In other more specific embodiments, the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof comprises a light chain (LC) that comprises a sequence as set forth in SEQ ID NO 59, or a sequence at least 90%, at least 95%, at least 98% or at least 99% identical thereto; and/or a heavy chain (HC) that comprises a sequence as set forth in SEQ ID NO 65, or a sequence at least 90%, at least 95%, at least 98% or at least 99% identical thereto.

Variants and derivatives of interferon-associated antigen binding protein or components thereof

[0096] A **"variant"** of a polypeptide (*e.g.*, an interferon-associated antigen binding protein, an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic antigen binding fragment thereof, an antibody, an antigen binding protein, or an IFN, or components thereof) comprises an amino acid sequence wherein one, two, three, four, five or more amino acid residues are inserted into, deleted from and/or substituted into the amino acid sequence relative to another polypeptide sequence. Preferably, the variant comprises up to ten insertions, deletions and/or substitutions, more preferably up to eight insertions, deletions and/or substitutions.

More specifically, the variant may comprise up to ten, more preferably up to eight insertions. The variant may also comprise up to ten, more preferably up to eight deletions. In even more preferred embodiments, the variant comprises up to ten substitutions, most preferably up to eight substitutions. In some embodiments, these substitutions are conservative amino acid substitution as described below.

[0097] A "**variant**" of a polynucleotide sequence (e.g., RNA or DNA) comprises one or more mutations within the polynucleotide sequence relative to another polynucleotide sequence, wherein one, two, three, four, five or more nucleic acid residues are inserted into, deleted from and/or substituted into the nucleic acid sequence. Preferably, the variant comprises up to ten insertions, deletions and/or substitutions, more preferably up to eight insertions, deletions and/or substitutions. More specifically, the variant may comprise up to ten, more preferably up to eight insertions. The variant may also comprise up to ten, more preferably up to eight deletions. In even more preferred embodiments, the variant comprises up to ten substitutions, most preferably up to eight substitutions. Said one, two, three, four, five or more mutations can cause one, two, three, four, five or more amino acid exchanges within the amino acid sequence the variant encodes for as compared to another amino acid sequence (i.e. a "*non-silent mutation*"). Variants also include nucleic acid sequences wherein one, two, three, four, five or more codons have been replaced by their synonyms which does not cause an amino acid exchange and is thus called a "*silent mutation*".

[0098] The term "**identity**" or "**homology**", in the context of variants of polypeptide or nucleotide sequences, refers to a relationship between the sequences of two or more polypeptide molecules or two or more nucleic acid molecules, as determined by aligning and comparing the sequences. "**Percent identity**" means the percent of identical residues between the amino acids or nucleotides in the compared molecules and is calculated based on the size of the smallest of the molecules being compared. Preferably, identity is determined over the full length of a sequence. It is understood that the expression "at least 80% identical", includes embodiments wherein the claimed sequence is at least 85%, at least 90%, at least 95%, at least 98% or at least 99% identical to the reference sequence. The expression "at least 90 % identical" includes embodiments wherein the claimed sequence is at least 90%, at least 91 %,

at least 92 %, at least 93%, at least 94%, at least 95 %, at least 96 %, at least 97 %, at least 98% or at least 99% identical to the reference sequence.

[0099] For the calculation of percent identity, gaps in alignments (if any) are preferably addressed by a particular mathematical model or computer program (*i.e.*, an "algorithm"). Methods that can be used to calculate the identity of the aligned nucleic acids or polypeptides include those described in *Computational Molecular Biology*, (Lesk, A. M., ed.), 1988, New York: Oxford University Press; Biocomputing Informatics and Genome Projects, (Smith, D. W., ed.), 1993, New York: Academic Press; Computer Analysis of Sequence Data, Part I, (Griffin, A. M., and Griffin, H. G., eds.), 1994, New Jersey: Humana Press; von Heinje, G., 1987, Sequence Analysis in Molecular Biology, New York: Academic Press; Sequence Analysis Primer, (Gribskov, M. and Devereux, J., eds.), 1991, New York: M. Stockton Press; and Carillo *et al.*, 1988, *SIAM J. Applied Math.* 48:1073.

[00100] In calculating percent identity, the sequences being compared are typically aligned in a way that gives the largest match between the sequences. One example of a computer program that can be used to determine percent identity is the GCG program package, which includes GAP (Devereux *et al.*, 1984, *Nucl. Acid Res.* 12:387; Genetics Computer Group, University of Wisconsin, Madison, WI). The computer algorithm GAP is used to align the two polypeptides or polynucleotides for which the percent sequence identity is to be determined. The sequences are aligned for optimal matching of their respective amino acid or nucleotide (the "matched span", as determined by the algorithm). A gap opening penalty (which is calculated as 3x the average diagonal, wherein the "average diagonal" is the average of the diagonal of the comparison matrix being used; the "diagonal" is the score or number assigned to each perfect amino acid match by the particular comparison matrix) and a gap extension penalty (which is usually 1/10 times the gap opening penalty), as well as a comparison matrix such as PAM 250 or BLOSum 62 are used in conjunction with the algorithm. In certain embodiments, a standard comparison matrix (*see*, Dayhoff *et al.*, 1978, *Atlas of Protein Sequence and Structure* 5:345-352 for the PAM 250 comparison matrix; Henikoff *et al.*, 1992, *Proc. Natl. Acad. Sci. U.S.A.* 89:10915-10919 for the BLOSum 62 comparison matrix) is also used by the algorithm.

[00101] Examples of parameters that can be employed in determining percent identity for polypeptides or nucleotide sequences using the GAP program are the following:

- Algorithm: Needleman *et al.*, 1970, *J. Mol. Biol.* 48:443-453
- Comparison matrix: BLOSum 62 from Henikoff *et al.*, 1992, *supra*
- Gap Penalty: 12 (but with no penalty for end gaps)
- Gap Length Penalty: 4
- Threshold of Similarity: 0

[00102] Certain alignment schemes for aligning two amino acid sequences may result in matching of only a short region of the two sequences, and this small aligned region may have very high sequence identity even though there is no significant relationship between the two full-length sequences. Accordingly, the selected alignment method (GAP program) can be adjusted if so desired to result in an alignment that spans at least 50 or at least 100, preferably the entire length, of contiguous amino acids of the target polypeptide.

[00103] Conservative amino acid substitutions can encompass non-naturally occurring amino acid residues, which are typically incorporated by chemical peptide synthesis rather than by synthesis in biological systems. These include peptidomimetics and other reversed or inverted forms of amino acid moieties.

[00104] Naturally occurring residues can be divided into classes based on common side chain properties:

1) hydrophobic: Norleucine, Met, Ala, Val, Leu, Ile;
2) neutral hydrophilic: Cys, Ser, Thr, Asn, Gln;
3) acidic: Asp, Glu;
4) basic: His, Lys, Arg;
5) residues that influence chain orientation: Gly, Pro; and
6) aromatic: Trp, Tyr, Phe.

[00105] For example, non-conservative substitutions can involve the exchange of a member of one of these classes for a member from another class. Such substituted residues can be introduced, for example, into regions of a human antibody that are homologous with non-human antibodies, or into the non-homologous regions of the molecule.

[00106] In making changes to the interferon-associated antigen binding protein, according to certain embodiments, the hydropathic index of amino acids can be considered. Each amino acid has been assigned a hydropathic index on the basis of its hydrophobicity and charge characteristics. They are: isoleucine (+4.5); valine (+4.2); leucine (+3.8); phenylalanine (+2.8); cysteine/cystine (+2.5); methionine (+1.9); alanine (+1.8); glycine (-0.4); threonine (-0.7); serine (-0.8); tryptophan (-0.9); tyrosine (-1.3); proline (-1.6); histidine (-3.2); glutamate (-3.5); glutamine (-3.5); aspartate (-3.5); asparagine (-3.5); lysine (-3.9); and arginine (-4.5).

[00107] The importance of the hydropathic amino acid index in conferring interactive biological function on a protein is understood in the art. Kyte *et al.*, J. Mol. Biol., 157:105-131 (1982). It is known that certain amino acids can be substituted for other amino acids having a similar hydropathic index or score and still retain a similar biological activity. In making changes based upon the hydropathic index, in certain embodiments, the substitution of amino acids whose hydropathic indices are within ±2 is included. In certain embodiments, those which are within ±1 are included, and in certain embodiments, those within ±0.5 are included.

[00108] It is also understood in the art that the substitution of like amino acids can be made effectively on the basis of hydrophilicity. In certain embodiments, the greatest local average hydrophilicity of a protein, as governed by the hydrophilicity of its adjacent amino acids, correlates with its immunogenicity and antigenicity, i.e., with a biological property of the protein.

[00109] The following hydrophilicity values have been assigned to these amino acid residues: arginine (+3.0); lysine (+3.0); aspartate (+3.0 ± 1); glutamate (+3.0 ± 1); serine (+0.3); asparagine (+0.2); glutamine (+0.2); glycine (0); threonine (-0.4); proline (-0.5 ± 1); alanine (-0.5); histidine (-0.5); cysteine (-1.0); methionine (-1.3); valine (-1.5); leucine (-1.8); isoleucine (-1.8); tyrosine (-2.3); phenylalanine (-2.5) and tryptophan (-3.4). In making changes based upon similar hydrophilicity values, in certain embodiments, the substitution of amino acids whose hydrophilicity values are within ±2 is included, in certain embodiments, those which are within ±1 are included, and in certain embodiments, those within ±0.5 are included.

[00110] Exemplary amino acid substitutions are set forth in **Table 2**.

Table 2. Amino Acid Substitutions.

Original Residues	Exemplary Substitutions	Preferred Substitutions
Ala	Val, Leu, Ile	Val
Arg	Lys, Gln, Asn	Lys
Asn	Gln	Gln
Asp	Glu	Glu
Cys	Ser, Ala	Ser
Gln	Asn	Asn
Glu	Asp	Asp
Gly	Pro, Ala	Ala
His	Asn, Gln, Lys, Arg	Arg
Ile	Leu, Val, Met, Ala, Phe, Norleucine	Leu
Leu	Norleucine, Ile, Val, Met, Ala, Phe	Ile
Lys	Arg, 1,4 Diamino-butyric Acid, Gln, Asn	Arg
Met	Leu, Phe, Ile	Leu
Phe	Leu, Val, Ile, Ala, Tyr	Leu
Pro	Ala, Gly	Ala
Ser	Thr, Ala, Cys	Thr
Thr	Ser	Ser
Trp	Tyr, Phe	Tyr
Tyr	Trp, Phe, Thr, Ser	Phe
Val	Ile, Met, Leu, Phe, Ala, Norleucine	Leu

[00111] In light of the present invention, a skilled artisan will be able to determine suitable variants of the interferon-associated antigen binding proteins as set forth herein using well-known techniques. In certain embodiments, one skilled in the art

can identify suitable areas of the molecule that may be changed without destroying activity by targeting regions not believed to be important for activity. In certain embodiments, one can identify residues and portions of the molecules that are conserved among similar polypeptides. In certain embodiments, even areas that can be important for biological activity or for structure can be subject to conservative amino acid substitutions without destroying the biological activity or without adversely affecting the polypeptide structure.

[00112] Additionally, one skilled in the art can review structure-function studies identifying residues in similar polypeptides that are important for activity or structure. In view of such a comparison, one can predict the importance of amino acid residues in a protein that correspond to amino acid residues which are important for activity or structure in similar proteins. One skilled in the art can opt for chemically similar amino acid substitutions for such predicted important amino acid residues.

[00113] One skilled in the art can also analyze the three-dimensional structure and amino acid sequence in relation to that structure in similar proteins or protein domains. In view of such information, one skilled in the art can predict the alignment of amino acid residues of interferon-associated antigen binding protein, an antibody or an antigen binding fragment thereof or an interferon or a functional fragment thereof as described herein with respect to its three dimensional structure. In certain embodiments, one skilled in the art can choose not to make radical changes to amino acid residues predicted to be on the surface of the protein, since such residues can be involved in important interactions with other molecules. Moreover, one skilled in the art can generate test variants containing a single amino acid substitution at each desired amino acid residue. The variants can then be screened using activity assays known to those skilled in the art. Such variants can be used to gather information about suitable variants. For example, if one discovered that a change to a particular amino acid residue resulted in destroyed, undesirably reduced, or unsuitable activity, variants with such a change can be avoided. In other words, based on information gathered from such experiments, one skilled in the art can readily determine the amino acids where further substitutions should be avoided either alone or in combination with other mutations.

[00114] According to certain embodiments, amino acid substitutions are those which: (1) reduce susceptibility to proteolysis, (2) reduce susceptibility to oxidation, (3) alter binding affinity for forming protein complexes, (4) alter binding affinities, and/or (5) confer or modify other physicochemical or functional properties on such polypeptides. According to certain embodiments, single or multiple amino acid substitutions (in certain embodiments, conservative amino acid substitutions) can be made in the naturally-occurring sequence (in certain embodiments, in the portion of the polypeptide outside the domain(s) forming intermolecular contacts). In certain embodiments, a conservative amino acid substitution typically may not substantially change the structural characteristics of the parent sequence (e.g., a replacement amino acid should not tend to break a helix that occurs in the parent sequence, or disrupt other types of secondary structure that characterizes the parent sequence). Examples of art-recognized polypeptide secondary and tertiary structures are described in *Proteins, Structures and Molecular Principles* (Creighton, Ed., W. H. Freeman and Company, New York (1984)); *Introduction to Protein Structure* (C. Branden & J. Tooze, eds., Garland Publishing, New York, N.Y. (1991)); and Thornton *et al.*, Nature, 354:105 (1991), which are each incorporated herein by reference.

[00115] The term "**derivative**" refers to a molecule that includes a chemical modification other than an insertion, deletion, or substitution of amino acids (or nucleic acids). In certain embodiments, derivatives comprise covalent modifications, including, but not limited to, chemical bonding with polymers, lipids, or other organic or inorganic moieties. In certain embodiments, a chemically modified interferon-associated antigen binding protein can have a greater circulating half-life than an interferon-associated antigen binding protein that is not chemically modified. In certain embodiments, a chemically modified interferon-associated antigen binding protein can have improved targeting capacity for desired cells, tissues, and/or organs. In some embodiments, a derivative interferon-associated antigen binding protein is covalently modified to include one or more water-soluble polymer attachments, including, but not limited to, polyethylene glycol, polyoxyethylene glycol, or polypropylene glycol. *See, e.g.,* U.S. Patent Nos: 4,640,835, 4,496,689, 4,301,144, 4,670,417, 4,791,192 and 4,179,337. In certain embodiments, a derivative interferon-

associated antigen binding protein comprises one or more polymer, including, but not limited to, monomethoxy-polyethylene glycol, dextran, cellulose, or other carbohydrate based polymers, poly-(N-vinyl pyrrolidone)-polyethylene glycol, propylene glycol homopolymers, a polypropylene oxide/ethylene oxide co-polymer, polyoxyethylated polyols (e.g., glycerol) and polyvinyl alcohol, as well as mixtures of such polymers.

[00116] In certain embodiments, a derivative of an interferon-associated antigen binding protein as described herein is covalently modified with polyethylene glycol (PEG) subunits. In certain embodiments, one or more water-soluble polymer is bonded at one or more specific position, for example at the amino terminus, of a derivative. In certain embodiments, one or more water-soluble polymer is randomly attached to one or more side chains of a derivative. In certain embodiments, PEG is used to improve the therapeutic capacity of the interferon-associated antigen binding protein. Certain such methods are discussed, for example, in U.S. Patent No. 6,133,426, which is hereby incorporated by reference for any purpose.

[00117] In certain embodiments, interferon-associated antigen binding protein variants include glycosylation variants wherein the number and/or type of glycosylation site has been altered compared to the amino acid sequences of a parent polypeptide. In certain embodiments, protein variants comprise a greater number of N-linked glycosylation sites than the native protein. In other embodiments, protein variants comprise a lesser number of N-linked glycosylation sites than the native protein. An N-linked glycosylation site is characterized by the sequence: Asn-X-Ser or Asn-X-Thr, wherein the amino acid residue designated as X can be any amino acid residue except proline. The substitution of amino acid residues to create this sequence provides a potential new site for the addition of an N-linked carbohydrate chain. Alternatively, substitutions which eliminate this sequence will remove an existing N-linked carbohydrate chain. Also provided is a rearrangement of N-linked carbohydrate chains wherein one, two, three, four, five or more N-linked glycosylation sites (typically those that are naturally occurring) are eliminated and one or more new N-linked sites are created. Additional preferred variants include cysteine variants wherein one or more cysteine residues are deleted from or substituted for another amino acid (e.g., serine) as compared to the parent amino acid

sequence. Cysteine variants can be useful when antibodies must be refolded into a biologically active conformation such as after the isolation of insoluble inclusion bodies. Cysteine variants generally have fewer cysteine residues than the native protein, and typically have an even number to minimize interactions resulting from unpaired cysteines.

HBV and HBV marker

[00118] As used herein, **"hepatitis B virus" or "HBV**" refers to the double stranded DNA virus that causes hepatitis B, which belongs to a family of closely related DNA viruses called the Hepadnaviruses. Hepadnaviruses have a strong preference for infecting liver cells, but small amounts of hepadnaviral DNA can be found in kidney, pancreas, and mononuclear cells. However, infection at these sites is not linked to extra hepatic disease.

[00119] The **HBV virion**, i.e., the *Dane particle*, consists of an outer lipid envelope and an icosahedral nucleocapsid core composed of protein. The nucleocapsid encloses the viral DNA and a DNA polymerase that has reverse transcriptase activity similar to retroviruses. The outer envelope contains embedded proteins, which are involved in viral binding of, and entry into, susceptible cells. The virus is one of the smallest enveloped animal viruses with a virion diameter of 42 nm, but pleomorphic forms exist, including filamentous and spherical bodies lacking a core. These particles are not infectious and are composed of the lipid and protein that forms part of the surface of the virion, which is called the surface antigen (HBsAg), and is produced in excess during the life cycle of the virus. HBV comprises HBsAg, HBcAg (and its splice variant HBeAg), DNA polymerase and Hbx. HBV is one of a few known non-retroviral viruses which employ reverse transcription as a part of its replication process.

[00120] The HBV nucleocapsid contains a relatively small and partially duplex 3.2 kb circular DNA, viral polymerase and core protein. The genome has only four long open reading frames. The pre-S-S (pre-surface-surface) region of the genome encodes the three viral surface antigens by differential initiation of translation at each of three in-frame initiation codons.

[00121] The most abundant protein of HBV is the 24 kD S protein (which is known as HBsAg). The pre-C-C (pre-core-core) region encodes HBcAg (HBV core Antigen) and HBeAg (HBV e Antigen). HBeAg is not required for viral replication and plays no role in viral assembly but is nevertheless a useful indicator of active viral replication. Since HBeAg is secreted by HBV-infected hepatocytes, it can be detected in the blood via standard diagnostic tests (such as ELISA) and is thus used as a laboratory marker for a viremic HBV infection (Testoni et al., Serum hepatitis B core-related antigen (HBcrAg) correlates with covalently closed circular DNA. J. Hepatol. 2019, 70, 615–625. http://dx.doi.org/10.1016/j.jhep.2018.11.030).

[00122] The P-coding region is specific for the viral polymerase, a multifunctional enzyme involved in DNA synthesis and RNA encapsidation. The X open reading frame encodes the viral X protein (HBx), which modulates host-cell signal transduction and can directly and indirectly affect host and viral gene expression.

[00123] The life cycle of HBV is believed to begin when the virus attaches to the host cell membrane via its envelope proteins. It has been suggested that HBV binds to a receptor on the plasma membrane that is predominantly expressed on human hepatocytes via the pre-S1 domain of the large envelope protein as an initial step in HBV infection. However, the nature of the receptor remains controversial. Then, the viral membrane fuses with the cell membrane and the viral genome is released into the cells.

[00124] Replication of HBV can be regulated by a variety of factors, including hormones, growth factors, and cytokines. After the viral genome reaches the nucleus, the cellular DNA repair machinery convert the partial double-stranded DNA (dsDNA; also called relaxed circular HBV DNA (rcDNA)), genome into covalently closed circular DNA (cccDNA). The resulting cccDNA is the template for host RNA Pol-II for further transcription of pre-genomic RNA and sub-genomic RNA (Allweiss L and Dandri M, The Role of cccDNA in HBV Maintenance. Viruses 2017, 9(6):156; doi:10.3390/v9060156; Nur K. Mohd-Ismail , Zijie Lim, Jayantha Gunaratne and Yee-Joo Tan, Mapping the Interactions of HBV cccDNA with Host Factors. Int. J. Mol. Sci. 2019, 20(17):4276; doi:10.3390/ijms20174276).

[00125] The pre-genomic RNA is bifunctional, serving as both the template for viral DNA synthesis and as the messenger for pre-C, C, and P translation. The sub-genomic RNAs function exclusively for translation of the envelope and X protein. All viral RNA is transported to the cytoplasm, where its translation yields the viral envelope, core, and polymerase proteins, as well as HBx and HBcAg.

[00126] HBV core particles are assembled in the cytosol and during this process, a single molecule of pre-genomic RNA is incorporated into the assembling viral core. Once the viral RNA is encapsidated, reverse transcription begins. The synthesis of the two viral DNA strands is sequential. The first DNA strand is made from the encapsidated RNA template; during or after the synthesis of this strand, the RNA template is degraded and the synthesis of the second DNA strand proceeds, with the use of the newly made first DNA strand as a template. Some cores bearing the mature genome are transported back to the nucleus, where their newly minted DNA genomes can be converted to cccDNA to maintain a stable intranuclear pool of transcriptional templates.

[00127] HBV surface antigen (HBsAg) proteins are initially synthesized and polymerized in the rough endoplasmic reticulum. These proteins are transported to the post-ER and pre-Golgi compartments, where budding of the nucleocapsid follows. The assembled HBV virion and sub-viral particles are transported to the Golgi for further modification of glycans of the surface proteins, and then are secreted out of the host cell to finish the life cycle.

[00128] The interferon-associated antigen binding proteins, the nucleic acids, vectors, vector systems, methods and compositions described herein can be used to treat HBV infection. As used herein, "**treat HBV infection**" and "**treatment of HBV infection**" refers to one or more of: (i) reducing HBV viral load / viral titer; (ii) reducing the transcription of cccDNA; (iii) reducing the level of pre-genomic RNA in cells; (iv) decreasing one or more HBV-related disorders; and (v) decreasing one or more HBV-related symptoms in a subject.

[00129] The terms "**viral load**" and "**viral titer**" refer to the number of viral particles in a cell, an organ or a bodily fluid such as blood or serum. Viral load or viral titer is often expressed as viral particles, or infectious particles per mL depending on the

type of assay. Today, viral load is usually measured using international units per milliliter (IU/mL). Viral load or viral titer may alternatively be determined as so-called viral genome equivalent. A higher viral burden, titer, or viral load often correlates with the severity of an active viral infection. Accordingly, reducing the viral load or viral titer correlates with a reduced number of infectious viral particles, e.g., in the serum. Viral load is usually determined using nucleic acid amplification based tests (NATs or NAATss). NAT/NAAT tests utilize, for example, PCR, (quantitative) reverse transcription polymerase chain reaction (RT-PCR or qRT-PCR), nucleic acid sequence based amplification (NASBA) or probe-based assays. Real-time PCR assays for hepatitis B virus DNA quantification are described, e.g., in Liu et al., *Virol J* **14,** 94 (2017) doi:10.1186/s12985-017-0759-8. Due to the ease of detection of viral DNA using PCR, the viral load is useful in clinical settings to monitor success during treatment. A viral load of >10.000 copies/mL (2.000 IU/mL) is a strong risk predictor of hepatocellular carcinoma, independent of HBeAg status.

[00130] The terms "**patient**" and "**subject**" are used interchangeably and include human and non-human animal subjects, preferably human subjects, as well as those with formally diagnosed disorders, those without formally recognized disorders, those receiving medical attention, those at risk of developing the disorders, etc.

[00131] In particular embodiments, the interferon-associated antigen binding protein, the nucleic acids, vectors, vector systems, methods and compositions described herein can be used to reduce the HBV viral load / viral titer in an HBV-infected cell (such as in a cell culture, in an HBV-infected organ or in an HBV-infected patient). HBV viral load / viral titer may be reduced by about 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100% compared to an untreated HBV-infected cell culture or to the same patient before treatment. In some embodiments, HBV viral load / viral titer is reduced by at least 20%, at least 25%, at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90% or at least 95%. Preferably, HBV viral load / viral titer is reduced by at least 35%, more preferably by at least 50%. In some embodiments, viral load / viral titer is determined by PCR or qRT-PCR.

[00132] In particular embodiments, the interferon-associated antigen binding protein, the nucleic acids, vectors, vector systems, methods and compositions described herein can be used to reduce transcription of HBV cccDNA in an HBV-infected cell (such as in a cell culture, in an HBV-infected organ or in an HBV-infected patient). cccDNA transcription may be reduced by about 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100% compared to an untreated HBV-infected cell culture or to the same patient before treatment. In some embodiments, transcription of HBV cccDNA is reduced by at least 20%, at least 25%, at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90% or at least 95%. Preferably, transcription of HBV cccDNA is reduced by at least 35%, more preferably by at least 50%. In some embodiments, transcription of HBV cccDNA is determined by PCR or qPCR.

[00133] In particular embodiments, the interferon-associated antigen binding protein, the nucleic acids, vectors, vector systems, methods and compositions described herein can be used to reduce the level of pre-genomic HBV RNA in an HBV-infected cell (such as in a cell culture, in an HBV-infected organ or in an HBV-infected patient). Pre-genomic HBV RNA levels may be reduced by about 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 100% compared to an untreated HBV-infected cell culture or to the same patient before treatment. In some embodiments, the level of pre-genomic HBV RNA is reduced by at least 20%, at least 25%, at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90% or at least 95%. Preferably, the level of pre-genomic HBV RNA is reduced by at least 35%, more preferably by at least 50%. In some embodiments, the level of pre-genomic HBV RNA is determined by qRT-PCR.

[00134] As used herein, an "**HBV-related disorder**" refers to a disorder that results from infection of a subject by HBV. HBV-related disorders include, but are not limited to acute hepatitis, chronic hepatitis, icteric hepatitis, fulminant hepatitis, sub-fulminant hepatitis, and symptoms and/or complications arising from any of these disorders.

[00135] As used herein, an **"HBV-related symptom**," a "**symptom of HBV infection**" or an "**HBV-related complication**" includes one or more physical dysfunctions related to HBV infection. HBV symptoms and complications include, but are not limited to, cirrhosis, hepatocellular carcinoma (HCC), membranous glomerulonephritis (MGN), death, acute necrotizing vasculitis (polyarteritis nodosa), membranous glomerulonephritis, papular acrodermatitis of childhood (Gianotti–Crosti syndrome), HBV-associated nephropathy (e.g., membranous glomerulonephritis), immune-mediated hematological disorders (e.g., essential mixed cryoglobulinemia, aplastic anemia), portal hypertension, ascites, encephalopathy, jaundice, pruritus, pale stools, steatorrhea, polyarteritis nodosa, glomerular disease, abnormal ALT levels, abnormal AST levels, abnormal alkaline phosphatase levels, increased bilirubin levels, anorexia, malaise, fever, nausea, vomiting and the like.

Interferons

[00136] As used herein, an **"interferon"** or **"IFN"** refers to a cytokine, or derivative thereof, that is typically produced and released by cells in response to the presence of a pathogen or a tumor cell. IFNs include type I IFNs (e.g., IFNα, IFNβ, IFNε, IFNκ, IFNτ, IFNζ and IFNω), type II IFNs (e.g., IFNγ) and type III IFNs (e.g., IFNλ1, IFNλ2 and IFNλ3). The term "interferon" or "IFN" includes without limitation full-length IFN, a variant or a derivative thereof (e.g., a chemically (e.g., PEGylated) modified derivative or mutein), or a functionally active fragment thereof, that retains one or more signaling activities of a full-length IFN.

[00137] As used herein, the term "**functional fragment**" refers to a fragment of a substance that retains one or more functional activities of the original substance. For example, a functional fragment of an interferon refers to a fragment of an interferon that retains an IFN function as described herein, e.g., it mediates IFN pathway signaling.

[00138] The IFN may increase one or more IFN receptor activities by at least about 20% when added to a cell, tissue or organism expressing a cognate IFN receptor (IFNAR for IFNα, IFNBR for IFNβ, etc). In some embodiments, the interferon

activates IFN receptor activity by at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, or at least 85%. The activity of the IFN (i.e., the "**IFN activity**") may be measured, e.g., using an *in vitro* reporter cell assay, e.g., using HEK-Blue™ IFN-α/β cells (InvivoGen, Cat. #: hkb-ifnαβ), HEK-Blue™ IFN-λ (InvivoGen, Cat. #: hkb-ifnl) or HEK-Blue™ Dual IFN-γ cells (InvivoGen, Cat. #: hkb-ifng), as described in greater detail in Example I. These reporter cells were generated by stable transfection of HEK293 cells with human IFN receptor genes and an *IFN-stimulated response element*-controlled secreted embryonic alkaline phosphatase (SEAP) construct to measure the activity of IFNs. HEK-Blue™ IFN-cells are designed to monitor the activation of the JAK/STAT/ISGF3 pathways induced by type I, type II or type III interferons. Activation of these pathways induces the production and release of SEAP.

[00139] In the context of the present invention, the interferon-associated antigen binding proteins activate both the CD40 and an IFN pathway. In certain embodiments, the interferon-associated antigen binding protein activates the IFN pathway with an EC_{50} of less than 100, 60, 50, 40, 30, 20, 10, or 1 ng/mL, preferably with an EC_{50} of less than 11 ng/mL, more preferably with an EC_{50} of less than 6 ng/mL. In some of these embodiments, the IFN pathway is the IFNα (interferon alpha), IFNβ (interferon beta), IFNε (interferon epsilon), IFNω (interferon omega), IFNγ (interferon gamma), or IFNλ (interferon lambda) pathway.

[00140] According to certain exemplary embodiments, an interferon-associated antigen binding protein as described herein comprises full-length IFN, a variant or a derivative thereof (e.g., a chemically (e.g., PEGylated) modified derivative or mutein), or a functionally active fragment thereof, that retains one or more signaling activities of a full-length IFN. In certain embodiments, the IFN is a human IFN.

[00141] In certain embodiments, an interferon-associated antigen binding protein as described herein comprises an IFN or a functional fragment thereof selected from the group consisting of a Type I IFN, a Type II IFN and a Type III IFN, or a functional fragment thereof.

[00142] In particular embodiments, the IFN or the functional fragment thereof is a Type I IFN, or a functional fragment thereof. In specific embodiments, the type I IFN

or the functional fragment thereof is IFNα, IFNβ, IFNω or IFNε, or a functional fragment thereof. In more specific embodiments, the type I IFN or the functional fragment thereof is IFNα or IFNβ, or a functional fragment thereof. In other more specific embodiments, the type I IFN or the functional fragment thereof is IFN α, or a functional fragment thereof. In other more specific embodiments, the type I IFN or the functional fragment thereof is IFN β, or a functional fragment thereof. In other more specific embodiments, the type I IFN or the functional fragment thereof is IFNω, or a functional fragment thereof. In other more specific embodiments, the type I IFN or the functional fragment thereof is IFNε, or a functional fragment thereof.

[00143] In particular embodiments, the IFN or the functional fragment thereof is IFNα, IFNβ, IFNγ, IFNλ, IFNε or IFNω, or a functional fragment thereof. In specific embodiments, the IFN or a functional fragment thereof is IFNα or IFNβ, or a functional fragment thereof.

[00144] In some embodiments, the IFN or the functional fragment thereof is IFNα, or a functional fragment thereof. In more specific embodiments, the IFN or functional fragment thereof is IFNα2a, or a functional fragment thereof. The IFNα2a may comprise the sequence as set forth in SEQ ID NO 17, or a sequence at least 90% identical thereto.

[00145] In some embodiments, the IFN or the functional fragment thereof is IFNβ, or a functional fragment thereof. The IFNβ may comprise the sequence as set forth in SEQ ID NO 14, or a sequence at least 90% identical thereto. The IFNβ or the functional fragment thereof may comprise one or two amino acid substitution(s) relative to SEQ ID NO 14, selected from C17S and N80Q. In some embodiments, the IFNβ or the functional fragment thereof comprises the amino acid substitution C17S relative to SEQ ID NO 14. In some embodiments, the IFNβ comprises the amino acid sequence as set forth in SEQ ID NO 15. In other embodiments, the IFNβ comprises the amino acid substitutions C17S and N80Q relative to SEQ ID NO 14. In yet other embodiments, the IFNβ comprises the amino acid sequence as set forth in SEQ ID NO 16.

[00146] In some embodiments, the IFN or the functional fragment thereof is IFNγ or IFNλ, or a functional fragment thereof. In specific embodiments, the IFN or

functional fragment thereof is IFNγ, or a functional fragment thereof. In more specific embodiments, the IFNγ comprises the sequence as set forth in SEQ ID NO 19, or a sequence at least 90% identical thereto. In other specific embodiments, the IFN or functional fragment thereof is IFNλ, or a functional fragment thereof. In more specific embodiments, the IFNλ or the functional fragment thereof is IFNλ2, or a functional fragment thereof. The IFNλ2 may comprise the sequence as set forth in SEQ ID NO 18, or a sequence at least 90% identical thereto.

[00147] In some embodiments, the IFN or the functional fragment thereof is IFNε, or a functional fragment thereof. The IFNε may comprise the sequence as set forth in SEQ ID NO 80, or a sequence at least 90% identical thereto.

[00148] In some embodiments, the IFN or the functional fragment thereof is IFNω, or a functional fragment thereof. The IFNω may comprise the sequence as set forth in SEQ ID NO 79, or a sequence at least 90% identical thereto.

[00149] In certain embodiments, the expression level of one or more IFN signaling pathway biomarkers is altered, i.e., upregulated or downregulated, in an HBV-infected cell **treated** with an interferon-associated antigen binding protein described herein. According to certain exemplary embodiments, the expression level of one or more IFN pathway biomarkers is upregulated in an HBV-infected cell treated with an interferon-associated antigen binding protein described herein. In this context, a "**biomarker**" is to be understood as a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention.

[00150] According to certain embodiments, a suitable IFN pathway biomarker featured herein is a chemokine, e.g., a C-X-C chemokine, selected from the group consisting of CXCL9, CXCL10 and CXCL11. In certain exemplary embodiments, a suitable biomarker induced by the IFN pathway is CXCL9, CXCL10 and/or CXCL11, and also the interferon stimulated gene ISG20. Cytokine induction or release may be quantified using techniques known in the art, such as ELISA. Alternatively, induction may also be determined using RNA-based assays such as RNAseq or qRT-PCR. In certain embodiments, upregulation may refer to an at least

at 1.5-fold, at least 2-fold, at least 2.5-fold, at least 3-fold, at least 4-fold, at least 5-fold or at least 10-fold increased expression or secretion of these cytokines.

[00151] In these or in other exemplary embodiments, the expression level of pro-inflammatory cytokines, e.g., IL10, IL1β and/or IL2 is not significantly upregulated in human Whole Blood cells upon treatment with an interferon-associated antigen binding protein of the invention. In some embodiments, the expression level of IL10 is not significantly upregulated in human Whole Blood cells upon treatment with an interferon-associated antigen binding protein of the invention. In some embodiments, the expression level of IL1β is not significantly upregulated in human Whole Blood cells upon treatment with an interferon-associated antigen binding protein of the invention. In some embodiments, the expression level of IL2 is not significantly upregulated in an HBV-infected cell upon treatment with an interferon-associated antigen binding protein of the invention. In some embodiments, the expression levels of IL10 and IL1β are not significantly upregulated in an HBV-infected cell upon treatment with an interferon-associated antigen binding protein of the invention. In some embodiments, the expression levels of IL10 and IL2 are not significantly upregulated in an HBV-infected cell upon treatment with an interferon-associated antigen binding protein of the invention. In some embodiments, the expression levels of IL1β and IL2 are not significantly upregulated in an HBV-infected cell upon treatment with an interferon-associated antigen binding protein of the invention. In some embodiments, the expression levels of IL10, IL1β and IL2 are not significantly upregulated in an HBV-infected cell upon treatment with an interferon-associated antigen binding protein of the invention.

Interferon-associated antigen binding proteins

[00152] The term "**associated**", as used herein, generally refers to a covalent or non-covalent linkage of two (or more) molecules. Associated proteins are created by joining two or more distinct peptides or proteins, resulting in a protein with one or more functional properties derived from each of the original proteins. In the context of the present invention, the interferon-associated antigen binding proteins activate both the CD40 and an IFN pathway. An associated protein encompasses monomeric and multimeric, e.g., dimeric, trimeric, tetrameric or the like, complexes of distinct

associated or fused proteins. In this context, non-covalent linkage results from strong interactions between two protein surface regions, usually via ionic, Van-der-Waals, and/or hydrogen bond interactions. Covalent linkage, on the other hand, requires the presence of actual chemical bonds, such as peptide bonds, disulphide bridges, etc. The term "**fused**" as used herein, generally refers to the joining of two or more distinct peptides or proteins in a covalent fashion via a peptide bond. Thus, a "**fused protein**" refers to single protein created by joining two or more distinct peptides or proteins via a peptide bond with one or more functional properties derived from each of the original proteins. In certain embodiments, two or more distinct peptides or proteins may be fused to one another via one or more peptide linkers ("L").

[00153] In all aspects of the invention, an interferon-associated antigen binding protein is a protein comprising an agonistic anti-CD40 antibody or an agonistic antigen binding fragment thereof and an IFN or a functional fragment thereof.

[00154] In some embodiments, the IFN or the functional fragment thereof is non-covalently associated with the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof. In more specific embodiments, the IFN or the functional fragment thereof is non-covalently associated with the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof via ionic, Van-der-Waals, and/or hydrogen bond interactions.

[00155] In other embodiments, the IFN or the functional fragment thereof is covalently associated with the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof. In preferred embodiments, the IFN or the functional fragment thereof is fused to the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof. The IFN or the functional fragment thereof may be fused to a light chain of the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof. In some embodiments, the IFN or the functional fragment thereof is fused to the N-terminus of a light chain of the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof. In other embodiments, the IFN or the functional fragment thereof is fused to the C-terminus of a light chain of the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof. The IFN or the functional fragment thereof may be also be fused to a heavy chain of the agonistic

anti-CD40 antibody or the agonistic antigen binding fragment thereof. In some embodiments, the IFN or the functional fragment thereof is fused to the N-terminus of a heavy chain of the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof. In other embodiments, the IFN or the functional fragment thereof is fused to the C-terminus of a heavy chain of the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof. In any of these embodiments, the agonistic anti-CD40 antibody or an agonistic antigen binding fragment thereof, and the IFN or the functional fragment thereof may be fused to each other via a linker.

[00156] The term **"linker" or "L**," as used herein, refers to any moiety that covalently joins one or more agonistic anti-CD40 antibody or an agonistic antigen binding fragment thereof to one or more interferon, or a functional fragment thereof. In exemplary embodiments, a linker is a peptide linker. The term "**peptide linker**", as used herein, refers to a peptide adapted to link two or more moieties. A peptide linker referred to herein may have one or more of the properties outlined in the following. The sequences of peptide linker according to certain exemplary embodiments are set forth in **Table 7**.

[00157] A peptide linker may have any length, i.e., comprise any number of amino acid residues. In exemplary embodiments, the linker comprises at least 1, at least 2, at least 3, at least 4, at least 5 amino acids. The linker may comprise at least 4 amino acids. The linker may comprise at least 11 amino acids. The linker may comprise at least 12 amino acids. The linker may comprise at least 13 amino acids. The linker may comprise at least 15 amino acids. The linker may comprise at least 20 amino acids. The linker may comprise at least 21 amino acids. The linker may comprise at least 24 amino acids.

[00158] A linker is typically long enough to provide an adequate degree of flexibility to prevent the linked moieties from interfering with each other's activity, e.g., the ability of a moiety to bind to a receptor. In exemplary embodiments, the linker comprises up to 10, up to 20, up to 30, up to 40, up to 50, up to 60, up to 70, up to 80, up to 90, or up to 100 amino acids. The linker may comprise up to 80 amino acids. The linker may comprise up to 40 amino acids. The linker may comprise up to 24 amino acids. The linker may comprise up to 21 amino acids. The linker may

comprise up to 20 amino acids. The linker may comprise up to 15 amino acids. The linker may comprise up to 13 amino acids. The linker may comprise up to 12 amino acids. The linker may comprise up to 11 amino acids. The linker may comprise up to 4 amino acids.

[00159] In some embodiments, the linker is selected from the group comprising rigid, flexible and/or helix-forming linkers. It is understood that helix-forming linkers can also be rigid linkers, since an α-helix has less degrees of freedom than a peptide assuming a more random-coil conformation. In some embodiments, the linker is a rigid linker. An exemplary rigid linker comprises a sequence as set forth in SEQ ID NO 20. Further exemplary rigid linkers comprise a sequence as set forth in SEQ ID NO 22 or SEQ ID NO 23. In related embodiments, the linker is a helix-forming linker. Exemplary helix-forming linkers comprise a sequence as set forth in SEQ ID NO 22 or SEQ ID NO 23. In other embodiments, the linker is a flexible linker. Exemplary flexible linkers comprise a sequence as set forth in SEQ ID NO 21, SEQ ID NO 24, SEQ ID NO 25 or SEQ ID NO 26.

[00160] The linker can also have different chemical properties. A linker can be selected from acidic, basic or neutral linkers. Typically, acidic linkers contain one or more acidic amino acid, such as Asp or Glu. Basic linkers typically contain one or more basic amino acids, such as Arg, His and Lys. Both types of amino acids are very hydrophilic. In some embodiments, the linker is an acidic linker. Exemplary acidic linkers comprise a sequence as set forth in SEQ ID NO 22 or SEQ ID NO 23. In other embodiments, the linker is a basic linker. In yet other embodiments, the linker is a neutral linker. Exemplary neutral linkers comprise a sequence as set forth in SEQ ID NO 20, SEQ ID NO 21, SEQ ID NO 24, SEQ ID NO 25 or SEQ ID NO 26.

[00161] In preferred embodiments, the linker is Gly-Ser or a Gly-Ser-Thr linker composed of multiple glycine, serine and, where applicable, threonine residues. In some of these embodiments, the linker comprises the amino acids glycine and serine. In more specific embodiments, the linker comprises the sequence as set forth in SEQ ID NO 21, SEQ ID NO 24, SEQ ID NO 25, SEQ ID NO 26. In some embodiments,

the linker further comprises the amino acid threonine. In a more specific embodiment, the linker comprises the sequence as set forth in SEQ ID NO 21.

[00162] In exemplary embodiments of the present invention, the interferon-associated antigen binding protein comprises a linker comprising a sequence selected from the sequences as set forth in SEQ ID NOs 20 to 26, preferably from the sequences as set forth in SEQ ID NO 24, SEQ ID NO 25 or SEQ ID NO 26. In a preferred embodiment, the linker comprises a sequence as set forth in SEQ ID NO 24. In another preferred embodiment, the linker comprises a sequence as set forth in SEQ ID NO 25. In another preferred embodiment, the linker comprises a sequence as set forth in SEQ ID NO 26.

[00163] In various embodiments of any one of the aspects of the invention, the interferon-associated antigen binding protein comprises no amino acids other than those forming (I) said agonistic anti-CD40 antibody, or agonistic antigen binding fragment thereof and (II) said IFN or functional fragment thereof. In related embodiments, the interferon-associated antigen binding protein comprises no amino acids other than those forming (I) said agonistic anti-CD40 antibody, or agonistic antigen binding fragment thereof, (II) said IFN or functional fragment thereof and (III) said linker.

[00164] Exemplary embodiments representing the various different configurations of (I) the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof, (II) the interferon (IFN) or the functional fragment thereof and (III) the linker are outlined in the following.

[00165] In certain preferred embodiments, the IFN or a functional fragment thereof is fused to the C-terminus of a heavy chain of the agonistic anti-CD40 antibody, or the agonistic antigen binding fragment thereof, via the linker, as set forth in **Table 3A or Table 3B**. In these embodiments, the heavy chain of the agonistic anti-CD40 antibody, or the agonistic antigen binding fragment thereof, may comprise a sequence as set forth in SEQ ID NO 6, SEQ ID NO 9, SEQ ID NO 12, SEQ ID NO 48 or SEQ ID NO 49, SEQ ID NO 61, or SEQ ID NO 63. The IFNα2a may comprise the sequence as set forth in SEQ ID NO 17. The IFNβ may comprise the sequence as set forth in SEQ ID NO 14, SEQ ID NO 15 or SEQ ID NO 16. The IFNβ may

comprise the sequence as set forth in SEQ ID NO 14. The IFNβ_C17S may comprise the sequence as set forth in SEQ ID NO 15. The IFNβ_C17S,N80Q may comprise the sequence as set forth in SEQ ID NO 16. The IFNγ may comprise the sequence as set forth in SEQ ID NO 19. The IFNλ2 may comprise the sequence as set forth in SEQ ID NO 18. The IFNε may comprise the sequence as set forth in SEQ ID NO 80. The IFNω may comprise the sequence as set forth in SEQ ID NO 79. The linkers referred to are those listed in **Table 7**.

[00166] In the embodiments where the IFN is fused to the C-terminus of the heavy chain of the agonistic anti-CD40 antibody, or the agonistic antigen binding fragment thereof, the interferon-associated antigen binding protein further comprises a light chain of an agonistic anti-CD40 antibody, or an agonistic antigen binding fragment thereof. In more specific embodiments, a heavy chain comprises a sequence as set forth in SEQ ID NO 6, SEQ ID NO 9, SEQ ID NO 12, SEQ ID NO 48, or SEQ ID NO 49 and a light chain comprises a sequence as set forth in SEQ ID NO 3. In other more specific embodiments, a heavy chain comprises a sequence as set forth in SEQ ID 61 or SEQ ID 63 and a light chain comprises a sequence as set forth in SEQ ID NO 59.

Table 3. *Interferon or a functional fragment thereof fused to the C-terminus of a heavy chain of the anti-CD40 antibody or an agonistic antigen binding fragment thereof.*

A	IFNα2a	IFNβ	IFNβ_C17S	IFNβ_C17S,N80Q	IFNγ	IFNλ2
RL linker	antiCD40_HC--RL--IFNα2a	antiCD40_HC--RL--IFNβ	antiCD40_HC--RL--IFNβ_C17S	antiCD40_HC--RL--IFNβ_C17S,N80Q	antiCD40_HC--RL--IFNγ	antiCD40_HC--RL--IFNλ2
GST linker	antiCD40_HC--GST--IFNα2a	antiCD40_HC--GST--IFNβ	antiCD40_HC--GST--IFNβ_C17S	antiCD40_HC--GST--IFNβ_C17S,N80Q	antiCD40_HC--GST--IFNγ	antiCD40_HC--GST--IFNλ2
HL linker	antiCD40_HC--HL--IFNα2a	antiCD40_HC--HL--IFNβ	antiCD40_HC--HL--IFNβ_C17S	antiCD40_HC--HL--IFNβ_C17S,N80Q	antiCD40_HC--HL--IFNγ	antiCD40_HC--HL--IFNλ2
HL2 linker	antiCD40_HC--HL2--IFNα2a	antiCD40_HC--HL2--IFNβ	antiCD40_HC--HL2--IFNβ_C17S	antiCD40_HC--HL2--IFNβ_C17S,N80Q	antiCD40_HC--HL2--IFNγ	antiCD40_HC--HL2--IFNλ2
(G4S)2 linker	antiCD40_HC--(G4S)2--IFNα2a	antiCD40_HC--(G4S)2--IFNβ	antiCD40_HC--(G4S)2--IFNβ_C17S	antiCD40_HC--(G4S)2--IFNβ_C17S,N80Q	antiCD40_HC--(G4S)2--IFNγ	antiCD40_HC--(G4S)2--IFNλ2
(G4S)3 linker	antiCD40_HC--(G4S)3--IFNα2a	antiCD40_HC--(G4S)3--IFNβ	antiCD40_HC--(G4S)3--IFNβ_C17S	antiCD40_HC--(G4S)3--IFNβ_C17S,N80Q	antiCD40_HC--(G4S)3--IFNγ	antiCD40_HC--(G4S)3--IFNλ2
(G4S)4 linker	antiCD40_HC--(G4S)4--IFNα2a	antiCD40_HC--(G4S)4--IFNβ	antiCD40_HC--(G4S)4--IFNβ_C17S	antiCD40_HC--(G4S)4--IFNβ_C17S,N80Q	antiCD40_HC--(G4S)4--IFNγ	antiCD40_HC--(G4S)4--IFNλ2

B	IFNε	IFNω
RL linker	antiCD40_HC--RL--IFNε	antiCD40_HC--RL--IFNω
GST linker	antiCD40_HC--GST--IFNε	antiCD40_HC--GST--IFNω
HL linker	antiCD40_HC--HL--IFNε	antiCD40_HC--HL--IFNω
HL2 linker	antiCD40_HC--HL2--IFNε	antiCD40_HC--HL2--IFNω
(G4S)2 linker	antiCD40_HC--(G4S)2--IFNε	antiCD40_HC--(G4S)2--IFNω
(G4S)3 linker	antiCD40_HC--(G4S)3--IFNε	antiCD40_HC--(G4S)3--IFNω
(G4S)4 linker	antiCD40_HC--(G4S)4--IFNε	antiCD40_HC--(G4S)4--IFNω

[00167] In certain preferred embodiments, the IFN or a functional fragment thereof is fused to the N-terminus of a heavy chain of the agonistic anti-CD40 antibody, or the agonistic antigen binding fragment thereof, via the linker, as set forth in **Table 4A or Table 4B**. In these embodiments, the heavy chain of the agonistic anti-CD40 antibody, or the agonistic antigen binding fragment thereof, may comprise a sequence as set forth in SEQ ID NO 6, SEQ ID NO 9, SEQ ID NO 12, SEQ ID NO 48, SEQ ID NO 49, SEQ ID NO 50, SEQ ID NO 61, SEQ ID NO 63 or SEQ ID NO 65. The IFNα2a may comprise the sequence as set forth in SEQ ID NO 17. The IFNβ may comprise the sequence as set forth in SEQ ID NO 14, SEQ ID NO 15 or SEQ ID NO 16. The IFNβ may comprise the sequence as set forth in SEQ ID NO 14. The IFNβ_C17S may comprise the sequence as set forth in SEQ ID NO 15. The IFNβ_C17S,N80Q may comprise the sequence as set forth in SEQ ID NO 16. The IFNγ may comprise the sequence as set forth in SEQ ID NO 19. The IFNλ2 may comprise the sequence as set forth in SEQ ID NO 18. The IFNε may comprise the sequence as set forth in SEQ ID NO 80. The IFNω may comprise the sequence as set forth in SEQ ID NO 79. The linkers referred to are those listed in **Table 7**.

[00168] In the embodiments where the IFN is fused to the N-terminus of a heavy chain of the agonistic anti-CD40 antibody, or the agonistic antigen binding fragment thereof, the interferon-associated antigen binding protein further comprises a light chain of an agonistic anti-CD40 antibody, or an agonistic antigen binding fragment thereof. In more specific embodiments, a heavy chain comprises a sequence as set forth in SEQ ID NO 6, SEQ ID NO 9, SEQ ID NO 12, SEQ ID NO 48, SEQ ID NO

49 or SEQ ID NO 50 and a light chain comprises a sequence as set forth in SEQ ID NO 3. In other more specific embodiments, a heavy chain comprises a sequence as set forth in SEQ ID 61, SEQ ID 63 or SEQ ID 65 and a light chain comprises a sequence as set forth in SEQ ID NO 59.

Table 4. *Interferon or a functional fragment thereof fused to the N-terminus of a heavy chain of the anti-CD40 antibody or an agonistic antigen binding fragment thereof.*

A	IFNα2a	IFNβ	IFNβ_C17S	IFNβ_C17S,N80Q	IFNγ	IFNλ2
RL linker	IFNα2a--RL--antiCD40_HC	IFNβ--RL--antiCD40_HC	IFNβ_C17S--RL--antiCD40_HC	IFNβ_C17S,N80Q--RL--antiCD40_HC	IFNγ--RL--antiCD40_HC	IFNλ2--RL--antiCD40_HC
GST linker	IFNα2a--GST--antiCD40_HC	IFNβ--GST--antiCD40_HC	IFNβ_C17S--GST--antiCD40_HC	IFNβ_C17S,N80Q--GST--antiCD40_HC	IFNγ--GST--antiCD40_HC	IFNλ2--GST--antiCD40_HC
HL linker	IFNα2a--HL--antiCD40_HC	IFNβ--HL--antiCD40_HC	IFNβ_C17S--HL--antiCD40_HC	IFNβ_C17S,N80Q--HL--antiCD40_HC	IFNγ--HL--antiCD40_HC	IFNλ2--HL--antiCD40_HC
HL2 linker	IFNα2a--HL2--antiCD40_HC	IFNβ--HL2--antiCD40_HC	IFNβ_C17S--HL2--antiCD40_HC	IFNβ_C17S,N80Q--HL2--antiCD40_HC	IFNγ--HL2--antiCD40_HC	IFNλ2--HL2--antiCD40_HC
(G4S)2 linker	IFNα2a--(G4S)2--antiCD40_HC	IFNβ--(G4S)2--antiCD40_HC	IFNβ_C17S--(G4S)2--antiCD40_HC	IFNβ_C17S,N80Q--(G4S)2--antiCD40_HC	IFNγ--(G4S)2--antiCD40_HC	IFNλ2--(G4S)2--antiCD40_HC
(G4S)3 linker	IFNα2a--(G4S)3--antiCD40_HC	IFNβ--(G4S)3--antiCD40_HC	IFNβ_C17S--(G4S)3--antiCD40_HC	IFNβ_C17S,N80Q--(G4S)3--antiCD40_HC	IFNγ--(G4S)3--antiCD40_HC	IFNλ2--(G4S)3--antiCD40_HC
(G4S)4 linker	IFNα2a--(G4S)4--antiCD40_HC	IFNβ--(G4S)4--antiCD40_HC	IFNβ_C17S--(G4S)4--antiCD40_HC	IFNβ_C17S,N80Q--(G4S)4--antiCD40_HC	IFNγ--(G4S)4--antiCD40_HC	IFNλ2--(G4S)4--antiCD40_HC

B	IFNε	IFNω
RL linker	IFNε--RL--antiCD40_HC	IFNω--RL--antiCD40_HC
GST linker	IFNε--GST--antiCD40_HC	IFNω--GST--antiCD40_HC
HL linker	IFNε--HL--antiCD40_HC	IFNω--HL--antiCD40_HC
HL2 linker	IFNε--HL2--antiCD40_HC	IFNω--HL2--antiCD40_HC
(G4S)2 linker	IFNε--(G4S)2--antiCD40_HC	IFNω--(G4S)2--antiCD40_HC
(G4S)3 linker	IFNε--(G4S)3--antiCD40_HC	IFNω--(G4S)3--antiCD40_HC
(G4S)4 linker	IFNε--(G4S)4--antiCD40_HC	IFNω--(G4S)4--antiCD40_HC

[00169] In certain preferred embodiments, the IFN is fused to the C-terminus of a light chain of the agonistic anti-CD40 antibody, or the agonistic antigen binding

fragment thereof, via the linker, as set forth in **Table 5A or Table 5B**. In these embodiments, the light chain of the agonistic anti-CD40 antibody, or the agonistic antigen binding fragment thereof, may comprise a sequence as set forth in SEQ ID NO 3. In other embodiments, the light chain may comprise a sequence as set forth in SEQ ID NO 59. The IFNα2a may comprise the sequence as set forth in SEQ ID NO 17. The IFNβ may comprise the sequence as set forth in SEQ ID NO 14, SEQ ID NO 15 or SEQ ID NO 16. The IFNβ may comprise the sequence as set forth in SEQ ID NO 14. The IFNβ_C17S may comprise the sequence as set forth in SEQ ID NO 15. The IFNβ_C17S,N80Q may comprise the sequence as set forth in SEQ ID NO 16. The IFNγ may comprise the sequence as set forth in SEQ ID NO 19. The IFNλ2 may comprise the sequence as set forth in SEQ ID NO 18. The IFNε may comprise the sequence as set forth in SEQ ID NO 80. The IFNω may comprise the sequence as set forth in SEQ ID NO 79. The linkers referred to are those listed in **Table 7**.

[00170] In the embodiments where the IFN is fused to the C-terminus of a light chain of the agonistic anti-CD40 antibody, or the agonistic antigen binding fragment thereof, the interferon-associated antigen binding protein further comprises a heavy chain of an agonistic anti-CD40 antibody, or an agonistic antigen binding fragment thereof. In more specific embodiments, a light chain comprises a sequence as set forth in SEQ ID NO 3 and a heavy chain comprises a sequence as set forth in SEQ ID NO 6, SEQ ID NO 9, SEQ ID NO 49, SEQ ID NO 48, SEQ ID NO 50 or SEQ ID NO 12. In other more specific embodiments, a light chain comprises a sequence as set forth in SEQ ID NO 59 and a heavy chain comprises a sequence as set forth in SEQ ID NO 61, SEQ ID NO 63 or SEQ ID NO 65.

Table 5. *Interferon or a functional fragment thereof fused to the C-terminus of a light chain of the anti-CD40 antibody or an agonistic antigen binding fragment thereof.*

A	IFNα2a	IFNβ	IFNβ_C17S	IFNβ_C17S,N80Q	IFNγ	IFNλ2
RL linker	antiCD40_LC—RL--IFNα2a	antiCD40_LC--RL--IFNβ	antiCD40_LC--RL--IFNβ_C17S	antiCD40_LC--RL--IFNβ_C17S,N80Q	antiCD40_LC--RL--IFNγ	antiCD40_LC--RL--IFNλ2
GST linker	antiCD40_LC--GST--IFNα2a	antiCD40_LC--GST--IFNβ	antiCD40_LC--GST--IFNβ_C17S	antiCD40_LC--GST--IFNβ_C17S,N80Q	antiCD40_LC--GST--IFNγ	antiCD40_LC--GST--IFNλ2
HL linker	antiCD40_LC--HL--IFNα2a	antiCD40_LC--HL--IFNβ	antiCD40_LC--HL--IFNβ_C17S	antiCD40_LC--HL--IFNβ_C17S,N80Q	antiCD40_LC--HL--IFNγ	antiCD40_LC--HL--IFNλ2

HL2 linker	antiCD40_LC--HL2--IFNα2a	antiCD40_LC--HL2--IFNβ	antiCD40_LC--HL2--IFNβ_C17S	antiCD40_LC--HL2--IFNβ_C17S,N80Q	antiCD40_LC--HL2--IFNγ	antiCD40_LC--HL2--IFNλ2
(G4S)2 linker	antiCD40_LC--(G4S)2--IFNα2a	antiCD40_LC--(G4S)2--IFNβ	antiCD40_LC--(G4S)2--IFNβ_C17S	antiCD40_LC--(G4S)2--IFNβ_C17S,N80Q	antiCD40_LC--(G4S)2--IFNγ	antiCD40_LC--(G4S)2--IFNλ2
(G4S)3 linker	antiCD40_LC--(G4S)3--IFNα2a	antiCD40_LC--(G4S)3--IFNβ	antiCD40_LC--(G4S)3--IFNβ_C17S	antiCD40_LC--(G4S)3--IFNβ_C17S,N80Q	antiCD40_LC--(G4S)3--IFNγ	antiCD40_LC--(G4S)3--IFNλ2
(G4S)4 linker	antiCD40_LC--(G4S)4--IFNα2a	antiCD40_LC--(G4S)4--IFNβ	antiCD40_LC--(G4S)4--IFNβ_C17S	antiCD40_LC--(G4S)4--IFNβ_C17S,N80Q	antiCD40_LC--(G4S)4--IFNγ	antiCD40_LC--(G4S)4--IFNλ2

B	**IFNε**	**IFNω**
RL linker	antiCD40_LC--RL--IFNε	antiCD40_LC--RL--IFNω
GST linker	antiCD40_LC--GST--IFNε	antiCD40_LC--GST--IFNω
HL linker	antiCD40_LC--HL--IFNε	antiCD40_LC--HL--IFNω
HL2 linker	antiCD40_LC--HL2--IFNε	antiCD40_LC--HL2--IFNω
(G4S)2 linker	antiCD40_LC--(G4S)2--IFNε	antiCD40_LC--(G4S)2--IFNω
(G4S)3 linker	antiCD40_LC--(G4S)3--IFNε	antiCD40_LC--(G4S)3--IFNω
(G4S)4 linker	antiCD40_LC--(G4S)4--IFNε	antiCD40_LC--(G4S)4--IFNω

[00171] In certain preferred embodiments, the IFN is fused to the N-terminus of a light chain of the agonistic anti-CD40 antibody, or the agonistic antigen binding fragment thereof, via the linker, as set forth in **Table 6A or Table 6B**. In these embodiments, the light chain of the agonistic anti-CD40 antibody, or the agonistic antigen binding fragment thereof, may comprise a sequence as set forth in SEQ ID NO 3 or SEQ ID NO 59. The IFNα2a may comprise the sequence as set forth in SEQ ID NO 17. The IFNβ may comprise the sequence as set forth in SEQ ID NO 14, SEQ ID NO 15 or SEQ ID NO 16. The IFNβ may comprise the sequence as set forth in SEQ ID NO 14. The IFNβ_C17S may comprise the sequence as set forth in SEQ ID NO 15. The IFNβ_C17S,N80Q may comprise the sequence as set forth in SEQ ID NO 16. The IFNγ may comprise the sequence as set forth in SEQ ID NO 19. The IFNλ2 may comprise the sequence as set forth in SEQ ID NO 18. The IFNε may comprise the sequence as set forth in SEQ ID NO 80. The IFNω may comprise the

sequence as set forth in SEQ ID NO 79. The linkers referred to are those listed in **Table 7**.

[00172] In the embodiments where the IFN is fused to the N-terminus of a light chain of the agonistic anti-CD40 antibody, or the agonistic antigen binding fragment thereof, the interferon-associated antigen binding protein further comprises a heavy chain of an agonistic anti-CD40 antibody, or an agonistic antigen binding fragment thereof. In more specific embodiments, a light chain comprises a sequence as set forth in SEQ ID NO 3 and a heavy chain comprises a sequence as set forth in SEQ ID NO 6, SEQ ID NO 9, SEQ ID NO 49, SEQ ID NO 48, SEQ ID NO 12 or SEQ ID NO 50. In other more specific embodiments, a light chain comprises a sequence as set forth in SEQ ID NO 59 and a heavy chain comprises a sequence as set forth in SEQ ID NO 61, SEQ ID NO 63 or SEQ ID NO 65.

Table 6. *Interferon or a functional fragment thereof fused to the N-terminus of a light chain of the anti-CD40 antibody or an agonistic antigen binding fragment thereof.*

A	IFNα2a	IFNβ	IFNβ_C17S	IFNβ_C17S,N80Q	IFNγ	IFNλ2
RL linker	IFNα2a--RL--antiCD40_LC	IFNβ--RL--antiCD40_LC	IFNβ_C17S--RL--antiCD40_LC	IFNβ_C17S,N80Q--RL--antiCD40_LC	IFNγ--RL--antiCD40_LC	IFNλ2--RL--antiCD40_LC
GST linker	IFNα2a--GST--antiCD40_LC	IFNβ--GST--antiCD40_LC	IFNβ_C17S--GST--antiCD40_LC	IFNβ_C17S,N80Q--GST--antiCD40_LC	IFNγ--GST--antiCD40_LC	IFNλ2--GST--antiCD40_LC
HL linker	IFNα2a--HL--antiCD40_LC	IFNβ--HL--antiCD40_LC	IFNβ_C17S--HL--antiCD40_LC	IFNβ_C17S,N80Q--HL--antiCD40_LC	IFNγ--HL--antiCD40_LC	IFNλ2--HL--antiCD40_LC
HL2 linker	IFNα2a--HL2--antiCD40_LC	IFNβ--HL2--antiCD40_LC	IFNβ_C17S--HL2--antiCD40_LC	IFNβ_C17S,N80Q--HL2--antiCD40_LC	IFNγ--HL2--antiCD40_LC	IFNλ2--HL2--antiCD40_LC
(G4S)2 linker	IFNα2a--(G4S)2--antiCD40_LC	IFNβ--(G4S)2--antiCD40_LC	IFNβ_C17S--(G4S)2--antiCD40_LC	IFNβ_C17S,N80Q--(G4S)2--antiCD40_LC	IFNγ--(G4S)2--antiCD40_LC	IFNλ2--(G4S)2--antiCD40_LC
(G4S)3 linker	IFNα2a--(G4S)3--antiCD40_LC	IFNβ--(G4S)3--antiCD40_LC	IFNβ_C17S--(G4S)3--antiCD40_LC	IFNβ_C17S,N80Q--(G4S)3--antiCD40_LC	IFNγ--(G4S)3--antiCD40_LC	IFNλ2--(G4S)3--antiCD40_LC
(G4S)4 linker	IFNα2a--(G4S)4--antiCD40_LC	IFNβ--(G4S)4--antiCD40_LC	IFNβ_C17S--(G4S)4--antiCD40_LC	IFNβ_C17S,N80Q--(G4S)4--antiCD40_LC	IFNγ--(G4S)4--antiCD40_LC	IFNλ2--(G4S)4--antiCD40_LC

B	IFNε	IFNω
RL linker	IFNε--RL--antiCD40_LC	IFNω--RL--antiCD40_LC
GST linker	IFNε--GST--antiCD40_LC	IFNω--GST--antiCD40_LC

HL linker	IFNε--HL--antiCD40_LC	IFNω--HL--antiCD40_LC
HL2 linker	IFNε--HL2--antiCD40_LC	IFNω--HL2--antiCD40_LC
(G4S)2 linker	IFNε--(G4S)2--antiCD40_LC	IFNω--(G4S)2--antiCD40_LC
(G4S)3 linker	IFNε--(G4S)3--antiCD40_LC	IFNω--(G4S)3--antiCD40_LC
(G4S)4 linker	IFNε--(G4S)4--antiCD40_LC	IFNω--(G4S)4--antiCD40_LC

[00173] Exemplary sequences comprised in interferon-associated antigen binding proteins of the invention or precursors thereof are listed in **Table 7**.

[00174] In exemplary preferred embodiments, the interferon-associated antigen binding protein comprises an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic antigen binding fragment thereof comprising a sequence selected from SEQ ID NOs 28-47 or SEQ ID NOs 66-75. In other exemplary embodiments, the interferon-associated antigen binding protein comprises an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic antigen binding fragment thereof comprising a sequence selected from SEQ ID NOs 81-88. In exemplary preferred embodiments, the interferon-associated antigen binding protein is an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic antigen binding fragment thereof comprising a sequence selected from SEQ ID NOs 28-47 or SEQ ID NOs 66-75. In other exemplary embodiments, the interferon-associated antigen binding protein is an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic antigen binding fragment thereof comprising a sequence selected from SEQ ID NOs 81-88.

[00175] In certain exemplary embodiments, the interferon-associated antigen binding protein comprises an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 81. In another exemplary embodiment, the interferon-associated antigen binding protein is an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 81.

[00176] In certain exemplary embodiments, the interferon-associated antigen binding protein comprises an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 82. In another exemplary embodiment, the interferon-associated antigen binding protein is an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 82.

[00177] In certain exemplary embodiments, the interferon-associated antigen binding protein comprises an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 83. In another exemplary embodiment, the interferon-associated antigen binding protein is an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 83.

[00178] In certain exemplary embodiments, the interferon-associated antigen binding protein comprises an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 84. In another exemplary embodiment, the interferon-associated antigen binding protein is an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 84.

[00179] In certain exemplary embodiments, the interferon-associated antigen binding protein comprises an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 85. In another exemplary embodiment, the interferon-associated antigen binding protein is an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 85.

[00180] In certain exemplary embodiments, the interferon-associated antigen binding protein comprises an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ

ID NO 86. In another exemplary embodiment, the interferon-associated antigen binding protein is an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 86.

[00181] In certain exemplary embodiments, the interferon-associated antigen binding protein comprises an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 87. In another exemplary embodiment, the interferon-associated antigen binding protein is an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 87.

[00182] In certain exemplary embodiments, the interferon-associated antigen binding protein comprises an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 88. In another exemplary embodiment, the interferon-associated antigen binding protein is an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 88.

[00183] In more preferred embodiments, the interferon-associated antigen binding protein comprises an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic antigen binding fragment thereof comprising a sequence selected from SEQ ID NO 38, SEQ ID NO 39, SEQ ID NO 40, SEQ ID NO 41, SEQ ID NO 42 or SEQ ID NO 43. In more preferred embodiments, the interferon-associated antigen binding protein is an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic antigen binding fragment thereof comprising a sequence selected from SEQ ID NO 38, SEQ ID NO 39, SEQ ID NO 40, SEQ ID NO 41, SEQ ID NO 42 or SEQ ID NO 43. In other more preferred embodiments, the interferon-associated antigen binding protein comprises an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic antigen binding fragment thereof comprising a sequence selected from SEQ ID NO 72, SEQ ID NO 73, SEQ ID NO 74 and SEQ ID NO 75. In still other more preferred embodiments, the interferon-

associated antigen binding protein is an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic antigen binding fragment thereof comprising a sequence selected from SEQ ID NO 72, SEQ ID NO 73, SEQ ID NO 74 and SEQ ID NO 75.

[00184] In an even more preferred embodiment, the interferon-associated antigen binding protein comprises an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 38. In still another even more preferred embodiment, the interferon-associated antigen binding protein is an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 38.

[00185] In another even more preferred embodiment, the interferon-associated antigen binding protein comprises an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 39. In another even more preferred embodiment, the interferon-associated antigen binding protein is an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 39.

[00186] In another even more preferred embodiment, the interferon-associated antigen binding protein comprises an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 40. In another even more preferred embodiment, the interferon-associated antigen binding protein is an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 40.

[00187] In another even more preferred embodiment, the interferon-associated antigen binding protein comprises an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 41. In another even more preferred embodiment, the interferon-associated antigen binding protein is an interferon-fused agonistic anti-

CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 41.

[00188] In another even more preferred embodiment, the interferon-associated antigen binding protein comprises an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 42. In another even more preferred embodiment, the interferon-associated antigen binding protein is an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 42.

[00189] In another even more preferred embodiment, the interferon-associated antigen binding protein comprises an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 43. In another even more preferred embodiment, the interferon-associated antigen binding protein is an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 43.

[00190] In another even more preferred embodiment, the interferon-associated antigen binding protein comprises an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 72. In another even more preferred embodiment, the interferon-associated antigen binding protein is an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 72.

[00191] In another even more preferred embodiment, the interferon-associated antigen binding protein comprises an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 73. In another even more preferred embodiment, the interferon-associated antigen binding protein is an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 73.

[00192] In another even more preferred embodiment, the interferon-associated antigen binding protein comprises an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 74. In another even more preferred embodiment, the interferon-associated antigen binding protein is an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 74.

[00193] In another even more preferred embodiment, the interferon-associated antigen binding protein comprises an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 75. In another even more preferred embodiment, the interferon-associated antigen binding protein is an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic binding fragment thereof comprising a sequence as set forth in SEQ ID NO 75.

Table 7. *Sequences of exemplary interferon-associated antigen binding protein and components thereof based on the antiCD40 antibody CP870,893. Italic sequences correspond to signal peptides. Bold italic sequences in SEQ ID NOs 3 and 6 correspond to CDR regions. Bold non-italic sequences correspond to linkers. Mutated amino acids are underlined.*

Name / SEQ ID Number	Sequence
Signal peptide 1 (SEQ ID NO 1)	*MGWSCIILFLVATATGVHS*
Signal peptide 2 (SEQ ID NO 2)	*MDMRVPAQLLGLLLLWLRGARC*

antiCD40 antibody light chain (SEQ ID NO 3)	DIQMTQSPSSVSASVGDRVTITC***RASQGIYSWLA***WYQQKPGKAP NLLIY***TASTLQS***GVPSRFSGSGSGTDFTLTISSLQPEDFATYYC***QQ ANIFPLT***FGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
antiCD40 antibody light chain with signal peptide 1 (SEQ ID NO 4)	*MGWSCIILFLVATATGVHS*DIQMTQSPSSVSASVGDRVTITCRASQ GIYSWLAWYQQKPGKAPNLLIYTASTLQSGVPSRFSGSGSGTDF TLTISSLQPEDFATYYCQQANIFPLTFGGGTKVEIKRTVAAPSVFI FPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQ ESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSP VTKSFNRGEC
antiCD40 antibody light chain with signal peptide 2 (SEQ ID NO 5)	*MDMRVPAQLLGLLLLWLRGARC*DIQMTQSPSSVSASVGDRVTITC RASQGIYSWLAWYQQKPGKAPNLLIYTASTLQSGVPSRFSGSGS GTDFTLTISSLQPEDFATYYCQQANIFPLTFGGGTKVEIKRTVAAP SVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSG NSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGL SSPVTKSFNRGEC
antiCD40 antibody heavy chain hIgG2 dK (SEQ ID NO 6)	QVQLVQSGAEVKKPGASVKVSCKASGYTF***TGYYMH***WVRQAPG QGLEWMG***WINPDSGGTNYAQKFQG***RVTMTRDTSISTAYMELNR LRSDDTAVYYCAR***DQPLGYCTNGVCSYFDY***WGQGTLVTVSSAS TKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALT SGVHTFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSNT KVDKTVERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPE VTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTFR VVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPRE PQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPEN NYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEAL HNHYTQKSLSLSPG

antiCD40 antibody heavy chain hIgG2 dK with signal peptide 1 (SEQ ID NO 7)	*MGWSCIILFLVATATGVHS*QVQLVQSGAEVKKPGASVKVSCKASG YTFTGYYMHWVRQAPGQGLEWMGWINPDSGGTNYAQKFQGR VTMTRDTSISTAYMELNRLRSDDTAVYYCARDQPLGYCTNGVC SYFDYWGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLV KDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSS NFGTQTYTCNVDHKPSNTKVDKTVERKCCVECPPCPAPPVAGPS VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVE VHNAKTKPREEQFNSTFRVVSVLTVVHQDWLNGKEYKCKVSN KGLPAPIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVK GFYPSDIAVEWESNGQPENNYKTTPPMLDSDGSFFLYSKLTVDK SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG
antiCD40 antibody heavy chain hIgG2 dK with signal peptide 2 (SEQ ID NO 8)	*MDMRVPAQLLGLLLLWLRGARC*QVQLVQSGAEVKKPGASVKVSC KASGYTFTGYYMHWVRQAPGQGLEWMGWINPDSGGTNYAQK FQGRVTMTRDTSISTAYMELNRLRSDDTAVYYCARDQPLGYCT NGVCSYFDYWGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAA LGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV VTVPSSNFGTQTYTCNVDHKPSNTKVDKTVERKCCVECPPCPAP PVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNW YVDGVEVHNAKTKPREEQFNSTFRVVSVLTVVHQDWLNGKEY KCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREEMTKNQVS LTCLVKGFYPSDIAVEWESNGQPENNYKTTPPMLDSDGSFFLYS KLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG
antiCD40 antibody heavy chain hIgG2 (SEQ ID NO 9)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPG QGLEWMGWINPDSGGTNYAQKFQGRVTMTRDTSISTAYMELN RLRSDDTAVYYCARDQPLGYCTNGVCSYFDYWGQGTLVTVSSA STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSN TKVDKTVERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTP EVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTF RVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPR

	EPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEA LHNHYTQKSLSLSPGK
antiCD40 antibody heavy chain hIgG2 with signal peptide 1 (SEQ ID NO 10)	*MGWSCIILFLVATATGVHS*QVQLVQSGAEVKKPGASVKVSCKASG YTFTGYYMHWVRQAPGQGLEWMGWINPDSGGTNYAQKFQGR VTMTRDTSISTAYMELNRLRSDDTAVYYCARDQPLGYCTNGVC SYFDYWGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLV KDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSS NFGTQTYTCNVDHKPSNTKVDKTVERKCCVECPPCPAPPVAGPS VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVE VHNAKTKPREEQFNSTFRVVSVLTVVHQDWLNGKEYKCKVSN KGLPAPIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVK GFYPSDIAVEWESNGQPENNYKTTPPMLDSDGSFFLYSKLTVDK SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
antiCD40 antibody heavy chain hIgG2 with signal peptide 2 (SEQ ID NO 11)	*MDMRVPAQLLGLLLLWLRGARC*QVQLVQSGAEVKKPGASVKVSC KASGYTFTGYYMHWVRQAPGQGLEWMGWINPDSGGTNYAQK FQGRVTMTRDTSISTAYMELNRLRSDDTAVYYCARDQPLGYCT NGVCSYFDYWGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAA LGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV VTVPSSNFGTQTYTCNVDHKPSNTKVDKTVERKCCVECPPCPAP PVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNW YVDGVEVHNAKTKPREEQFNSTFRVVSVLTVVHQDWLNGKEY KCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREEMTKNQVS LTCLVKGFYPSDIAVEWESNGQPENNYKTTPPMLDSDGSFFLYS KLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
antiCD40 antibody hIgG1 heavy chain - NNAS (SEQ ID NO 48)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPG QGLEWMGWINPDSGGTNYAQKFQGRVTMTRDTSISTAYMELN RLRSDDTAVYYCARDQPLGYCTNGVCSYFDYWGQGTLVTVSSA STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSN

	TKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY NNASRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKA KGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPGK
antiCD40 antibody hIgG1 heavy chain - NNAS-dK (SEQ ID NO 49)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPG QGLEWMGWINPDSGGTNYAQKFQGRVTMTRDTSISTAYMELN RLRSDDTAVYYCARDQPLGYCTNGVCSYFDYWGQGTLVTVSSA STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSN TKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY NNASRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKA KGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPG
antiCD40 antibody hIgG2 Fab region heavy chain (SEQ ID NO 12)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPG QGLEWMGWINPDSGGTNYAQKFQGRVTMTRDTSISTAYMELN RLRSDDTAVYYCARDQPLGYCTNGVCSYFDYWGQGTLVTVSSA STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSN TKVDKTVERKCCVE
antiCD40 antibody hIgG2 Fab region heavy chain with signal peptide 1 (SEQ ID NO 13)	*MGWSCIILFLVATATGVHS*QVQLVQSGAEVKKPGASVKVSCKASG YTFTGYYMHWVRQAPGQGLEWMGWINPDSGGTNYAQKFQGR VTMTRDTSISTAYMELNRLRSDDTAVYYCARDQPLGYCTNGVC SYFDYWGQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLV KDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSS NFGTQTYTCNVDHKPSNTKVDKTVERKCCVE

antiCD40 antibody hIgG2 Fab region heavy chain --TEV--6His tag (SEQ ID NO 50)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPG QGLEWMGWINPDSGGTNYAQKFQGRVTMTRDTSISTAYMELN RLRSDDTAVYYCARDQPLGYCTNGVCSYFDYWGQGTLVTVSSA STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSN TKVDKTVERKCCVEENLYFQSHHHHHH
IFNβ dM (SEQ ID NO 76)	SYNLLGFLQRSSNFQCQKLLWQLNGRLEYCLKDRMNFDIPEEIK QLQQFQKEDAALTIYEMLQNIFAIFRQDSSSTGWNETIVENLLAN VYHQINHLKTVLEEKLEKEDFTRGKLMSSLHLKRYYGRILHYLK AKEYSHCAWTIVRVEILRNFYFINRLTGYLRN
IFNβ dM C17S (SEQ ID NO 77)	SYNLLGFLQRSSNFQSQKLLWQLNGRLEYCLKDRMNFDIPEEIK QLQQFQKEDAALTIYEMLQNIFAIFRQDSSSTGWNETIVENLLAN VYHQINHLKTVLEEKLEKEDFTRGKLMSSLHLKRYYGRILHYLK AKEYSHCAWTIVRVEILRNFYFINRLTGYLRN
IFNβ (SEQ ID NO 14)	MSYNLLGFLQRSSNFQCQKLLWQLNGRLEYCLKDRMNFDIPEEI KQLQQFQKEDAALTIYEMLQNIFAIFRQDSSSTGWNETIVENLLA NVYHQINHLKTVLEEKLEKEDFTRGKLMSSLHLKRYYGRILHYL KAKEYSHCAWTIVRVEILRNFYFINRLTGYLRN
IFNβ C17S (SEQ ID NO 15)	MSYNLLGFLQRSSNFQSQKLLWQLNGRLEYCLKDRMNFDIPEEI KQLQQFQKEDAALTIYEMLQNIFAIFRQDSSSTGWNETIVENLLA NVYHQINHLKTVLEEKLEKEDFTRGKLMSSLHLKRYYGRILHYL KAKEYSHCAWTIVRVEILRNFYFINRLTGYLRN
IFNβ C17S,N80Q (SEQ ID NO 16)	MSYNLLGFLQRSSNFQSQKLLWQLNGRLEYCLKDRMNFDIPEEI KQLQQFQKEDAALTIYEMLQNIFAIFRQDSSSTGWQETIVENLLA NVYHQINHLKTVLEEKLEKEDFTRGKLMSSLHLKRYYGRILHYL KAKEYSHCAWTIVRVEILRNFYFINRLTGYLRN

IFNα2a (SEQ ID NO 17)	CDLPQTHSLGSRRTLMLLAQMRKISLFSCLKDRHDFGFPQEEFG NQFQKAETIPVLHEMIQQIFNLFSTKDSSAAWDETLLDKFYTELY QQLNDLEACVIQGVGVTETPLMKEDSILAVRKYFQRITLYLKEK KYSPCAWEVVRAEIMRSFSLSTNLQESLRSKE
IFNλ2 (SEQ ID NO 18)	VPVARLHGALPDARGCHIAQFKSLSPQELQAFKRAKDALEESLL LKDCRCHSRLFPRTWDLRQLQVRERPMALEAELALTLKVLEAT ADTDPALVDVLDQPLHTLHHILSQFRACIQPQPTAGPRTRGRLHH WLYRLQEAPKKESPGCLEASVTFNLFRLLTRDLNCVASGDLCV
IFNγ (SEQ ID NO 19)	QDPYVKEAENLKKYFNAGHSDVADNGTLFLGILKNWKEESDRK IMQSQIVSFYFKLFKNFKDDQSIQKSVETIKEDMNVKFFNSNKKK RDDFEKLTNYSVTDLNVQRKAIHELIQVMAELSPAAKTGKRKRS QMLFRGRRASQ
IFNω (SEQ ID NO 79)	LGCDLPQNHGLLSRNTLVLLHQMRRISPFLCLKDRRDFRFPQEM VKGSQLQKAHVMSVLHEMLQQIFSLFHTERSSAAWNMTLLDQL HTGLHQQLQHLETCLLQVVGEGESAGAISSPALTLRRYFQGIRV YLKEKKYSDCAWEVVRMEIMKSLFLSTNMQERLRSKDRDLGSS
IFNε (SEQ ID NO 80)	LDLKLIIFQQRQVNQESLKLLNKLQTLSIQQCLPHRKNFLLPQKSL SPQQYQKGHTLAILHEMLQQIFSLFRANISLDGWEENHTEKFLIQ LHQQLEYLEALMGLEAEKLSGTLGSDNLRLQVKMYFRRIHDYL ENQDYSTCAWAIVQVEISRCLFFVFSLTEKLSKQGRPLNDMKQE LTTEFRSPR
RL linker (SEQ ID NO 20)	**PAPA**
GST linker (SEQ ID NO 21)	**SGGTSGSTSGTGS**
HL linker	**AEAAAKEAAAKA**

(SEQ ID NO 22)	
HL2 linker (SEQ ID NO 23)	**AEAAAKEAAAKAAEAAAKEAAAKA**
(G4S)2 linker (SEQ ID NO 24)	**GGGGSGGGGS**
(G4S)3 linker (SEQ ID NO 25)	**GGGGSGGGGSGGGGS**
(G4S)4 linker (SEQ ID NO 26)	**GGGGSGGGGSGGGGSGGGGS**
TEV-6His tag (SEQ ID NO 27)	ENLYFQSHHHHHH
antiCD40_LC--HL--IFNβ (SEQ ID NO 28)	DIQMTQSPSSVSASVGDRVTITCRASQGIYSWLAWYQQKPGKAP NLLIYTASTLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQ ANIFPLTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC**AEAAAKEAA** **AKA**MSYNLLGFLQRSSNFQCQKLLWQLNGRLEYCLKDRMNFDI PEEIKQLQQFQKEDAALTIYEMLQNIFAIFRQDSSSTGWNETIVEN LLANVYHQINHLKTVLEEKLEKEDFTRGKLMSSLHLKRYYGRIL HYLKAKEYSHCAWTIVRVEILRNFYFINRLTGYLRN
antiCD40_LC--HL--IFNβ_C17S (SEQ ID NO 29)	DIQMTQSPSSVSASVGDRVTITCRASQGIYSWLAWYQQKPGKAP NLLIYTASTLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQ ANIFPLTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC**AEAAAKEAA** **AKA**MSYNLLGFLQRSSNFQSQKLLWQLNGRLEYCLKDRMNFDI

	PEEIKQLQQFQKEDAALTIYEMLQNIFAIFRQDSSSTGWNETIVEN LLANVYHQINHLKTVLEEKLEKEDFTRGKLMSSLHLKRYYGRIL HYLKAKEYSHCAWTIVRVEILRNFYFINRLTGYLRN
antiCD40_hIgG2_ dK_HC--RL-- IFNβ (SEQ ID NO 30)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPG QGLEWMGWINPDSGGTNYAQKFQGRVTMTRDTSISTAYMELN RLRSDDTAVYYCARDQPLGYCTNGVCSYFDYWGQGTLVTVSSA STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSN TKVDKTVERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTP EVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTF RVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPR EPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEA LHNHYTQKSLSLSPG**PAPA**MSYNLLGFLQRSSNFQCQKLLWQL NGRLEYCLKDRMNFDIPEEIKQLQQFQKEDAALTIYEMLQNIFAI FRQDSSSTGWNETIVENLLANVYHQINHLKTVLEEKLEKEDFTR GKLMSSLHLKRYYGRILHYLKAKEYSHCAWTIVRVEILRNFYFI NRLTGYLRN
antiCD40_hIgG2_ dK_HC--RL-- IFNβ_C17S (SEQ ID NO 31)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPG QGLEWMGWINPDSGGTNYAQKFQGRVTMTRDTSISTAYMELN RLRSDDTAVYYCARDQPLGYCTNGVCSYFDYWGQGTLVTVSSA STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSN TKVDKTVERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTP EVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTF RVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPR EPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEA LHNHYTQKSLSLSPG**PAPA**MSYNLLGFLQRSSNFQSQKLLWQLN GRLEYCLKDRMNFDIPEEIKQLQQFQKEDAALTIYEMLQNIFAIF RQDSSSTGWNETIVENLLANVYHQINHLKTVLEEKLEKEDFTRG

	KLMSSLHLKRYYGRILHYLKAKEYSHCAWTIVRVEILRNFYFINR LTGYLRN
antiCD40_hIgG2_ dK_HC--HL-- IFNβ (SEQ ID NO 32)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPG QGLEWMGWINPDSGGTNYAQKFQGRVTMTRDTSISTAYMELN RLRSDDTAVYYCARDQPLGYCTNGVCSYFDYWGQGTLVTVSSA STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSN TKVDKTVERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTP EVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTF RVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPR EPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEA LHNHYTQKSLSLSPG**AEAAAKEAAAKA**MSYNLLGFLQRSSNFQ CQKLLWQLNGRLEYCLKDRMNFDIPEEIKQLQQFQKEDAALTIY EMLQNIFAIFRQDSSSTGWNETIVENLLANVYHQINHLKTVLEEK LEKEDFTRGKLMSSLHLKRYYGRILHYLKAKEYSHCAWTIVRVE ILRNFYFINRLTGYLRN
antiCD40_hIgG2_ dK_HC--HL-- IFNβ_C17S (SEQ ID NO 33)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPG QGLEWMGWINPDSGGTNYAQKFQGRVTMTRDTSISTAYMELN RLRSDDTAVYYCARDQPLGYCTNGVCSYFDYWGQGTLVTVSSA STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSN TKVDKTVERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTP EVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTF RVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPR EPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEA LHNHYTQKSLSLSPG**AEAAAKEAAAKA**MSYNLLGFLQRSSNFQ SQKLLWQLNGRLEYCLKDRMNFDIPEEIKQLQQFQKEDAALTIY EMLQNIFAIFRQDSSSTGWNETIVENLLANVYHQINHLKTVLEEK

	LEKEDFTRGKLMSSLHLKRYYGRILHYLKAKEYSHCAWTIVRVE ILRNFYFINRLTGYLRN
antiCD40_LC--RL--IFNβ (SEQ ID NO 34)	DIQMTQSPSSVSASVGDRVTITCRASQGIYSWLAWYQQKPGKAP NLLIYTASTLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQ ANIFPLTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC**PAPA**MSYNL LGFLQRSSNFQCQKLLWQLNGRLEYCLKDRMNFDIPEEIKQLQQ FQKEDAALTIYEMLQNIFAIFRQDSSSTGWNETIVENLLANVYHQ INHLKTVLEEKLEKEDFTRGKLMSSLHLKRYYGRILHYLKAKEY SHCAWTIVRVEILRNFYFINRLTGYLRN
antiCD40_LC--RL--IFNβ_C17S (SEQ ID NO 35)	DIQMTQSPSSVSASVGDRVTITCRASQGIYSWLAWYQQKPGKAP NLLIYTASTLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQ ANIFPLTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC**PAPA**MSYNL LGFLQRSSNFQSQKLLWQLNGRLEYCLKDRMNFDIPEEIKQLQQ FQKEDAALTIYEMLQNIFAIFRQDSSSTGWNETIVENLLANVYHQ INHLKTVLEEKLEKEDFTRGKLMSSLHLKRYYGRILHYLKAKEY SHCAWTIVRVEILRNFYFINRLTGYLRN
antiCD40_LC--GST--IFNβ_C17S (SEQ ID NO 36)	DIQMTQSPSSVSASVGDRVTITCRASQGIYSWLAWYQQKPGKAP NLLIYTASTLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQ ANIFPLTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC**SGGTSGSTS GTGS**MSYNLLGFLQRSSNFQSQKLLWQLNGRLEYCLKDRMNFD IPEEIKQLQQFQKEDAALTIYEMLQNIFAIFRQDSSSTGWNETIVE NLLANVYHQINHLKTVLEEKLEKEDFTRGKLMSSLHLKRYYGRI LHYLKAKEYSHCAWTIVRVEILRNFYFINRLTGYLRN

antiCD40_LC--HL2--IFNβ_C17S (SEQ ID NO 37)	DIQMTQSPSSVSASVGDRVTITCRASQGIYSWLAWYQQKPGKAP NLLIYTASTLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQ ANIFPLTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC**AEAAAKEAA** **AKAAEAAAKEAAAKA**MSYNLLGFLQRSSNFQSQKLLWQLNGR LEYCLKDRMNFDIPEEIKQLQQFQKEDAALTIYEMLQNIFAIFRQ DSSSTGWNETIVENLLANVYHQINHLKTVLEEKLEKEDFTRGKL MSSLHLKRYYGRILHYLKAKEYSHCAWTIVRVEILRNFYFINRLT GYLRN
antiCD40_hIgG2_dK_HC--(G4S)2--IFNα2a (SEQ ID NO 38)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPG QGLEWMGWINPDSGGTNYAQKFQGRVTMTRDTSISTAYMELN RLRSDDTAVYYCARDQPLGYCTNGVCSYFDYWGQGTLVTVSSA STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSN TKVDKTVERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTP EVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTF RVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPR EPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEA LHNHYTQKSLSLSPG**GGGGSGGGGS**CDLPQTHSLGSRRTLMLL AQMRKISLFSCLKDRHDFGFPQEEFGNQFQKAETIPVLHEMIQQI FNLFSTKDSSAAWDETLLDKFYTELYQQLNDLEACVIQGVGVTE TPLMKEDSILAVRKYFQRITLYLKEKKYSPCAWEVVRAEIMRSFS LSTNLQESLRSKE
antiCD40_hIgG2_dK_HC--(G4S)3--IFNα2a (SEQ ID NO 39)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPG QGLEWMGWINPDSGGTNYAQKFQGRVTMTRDTSISTAYMELN RLRSDDTAVYYCARDQPLGYCTNGVCSYFDYWGQGTLVTVSSA STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSN

	TKVDKTVERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTP EVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTF RVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPR EPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEA LHNHYTQKSLSLSPG**GGGGSGGGGSGGGGS**CDLPQTHSLGSRR TLMLLAQMRKISLFSCLKDRHDFGFPQEEFGNQFQKAETIPVLHE MIQQIFNLFSTKDSSAAWDETLLDKFYTELYQQLNDLEACVIQG VGVTETPLMKEDSILAVRKYFQRITLYLKEKKYSPCAWEVVRAE IMRSFSLSTNLQESLRSKE
antiCD40_hIgG2_dK_HC--(G4S)4--IFNα2a (SEQ ID NO 40)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPG QGLEWMGWINPDSGGTNYAQKFQGRVTMTRDTSISTAYMELN RLRSDDTAVYYCARDQPLGYCTNGVCSYFDYWGQGTLVTVSSA STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSN TKVDKTVERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTP EVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTF RVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPR EPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEA LHNHYTQKSLSLSPG**GGGGSGGGGSGGGGSGGGGS**CDLPQTH SLGSRRTLMLLAQMRKISLFSCLKDRHDFGFPQEEFGNQFQKAE TIPVLHEMIQQIFNLFSTKDSSAAWDETLLDKFYTELYQQLNDLE ACVIQGVGVTETPLMKEDSILAVRKYFQRITLYLKEKKYSPCAW EVVRAEIMRSFSLSTNLQESLRSKE
antiCD40_LC--(G4S)2--IFNα2a (SEQ ID NO 41)	DIQMTQSPSSVSASVGDRVTITCRASQGIYSWLAWYQQKPGKAP NLLIYTASTLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQ ANIFPLTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC**GGGGSGGG** **GS**CDLPQTHSLGSRRTLMLLAQMRKISLFSCLKDRHDFGFPQEEF

	GNQFQKAETIPVLHEMIQQIFNLFSTKDSSAAWDETLLDKFYTEL YQQLNDLEACVIQGVGVTETPLMKEDSILAVRKYFQRITLYLKE KKYSPCAWEVVRAEIMRSFSLSTNLQESLRSKE
antiCD40_LC--(G4S)3--IFNα2a (SEQ ID NO 42)	DIQMTQSPSSVSASVGDRVTITCRASQGIYSWLAWYQQKPGKAP NLLIYTASTLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQ ANIFPLTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC**GGGGSGGG GSGGGGS**CDLPQTHSLGSRRTLMLLAQMRKISLFSCLKDRHDFG FPQEEFGNQFQKAETIPVLHEMIQQIFNLFSTKDSSAAWDETLLD KFYTELYQQLNDLEACVIQGVGVTETPLMKEDSILAVRKYFQRI TLYLKEKKYSPCAWEVVRAEIMRSFSLSTNLQESLRSKE
antiCD40_LC--(G4S)4--IFNα2a (SEQ ID NO 43)	DIQMTQSPSSVSASVGDRVTITCRASQGIYSWLAWYQQKPGKAP NLLIYTASTLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQ ANIFPLTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC**GGGGSGGG GSGGGGSGGGGS**CDLPQTHSLGSRRTLMLLAQMRKISLFSCLK DRHDFGFPQEEFGNQFQKAETIPVLHEMIQQIFNLFSTKDSSAAW DETLLDKFYTELYQQLNDLEACVIQGVGVTETPLMKEDSILAVR KYFQRITLYLKEKKYSPCAWEVVRAEIMRSFSLSTNLQESLRSKE
IFNβ--(G4S)3--antiCD40_LC) (SEQ ID NO 44)	MSYNLLGFLQRSSNFQCQKLLWQLNGRLEYCLKDRMNFDIPEEI KQLQQFQKEDAALTIYEMLQNIFAIFRQDSSSTGWNETIVENLLA NVYHQINHLKTVLEEKLEKEDFTRGKLMSSLHLKRYYGRILHYL KAKEYSHCAWTIVRVEILRNFYFINRLTGYLRN**GGGGSGGGGS GGGGS**DIQMTQSPSSVSASVGDRVTITCRASQGIYSWLAWYQQ KPGKAPNLLIYTASTLQSGVPSRFSGSGSGTDFTLTISSLQPEDFA TYYCQQANIFPLTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTA SVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTY SLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

antiCD40_LC--(G4S)4--IFNβ (SEQ ID NO 45)	DIQMTQSPSSVSASVGDRVTITCRASQGIYSWLAWYQQKPGKAPNLLIYTASTLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQANIFPLTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC**GGGGSGGGGSGGGGSGGGGS**MSYNLLGFLQRSSNFQCQKLLWQLNGRLEYCLKDRMNFDIPEEIKQLQQFQKEDAALTIYEMLQNIFAIFRQDSSSTGWNETIVENLLANVYHQINHLKTVLEEKLEKEDFTRGKLMSSLHLKRYYGRILHYLKAKEYSHCAWTIVRVEILRNFYFINRLTGYLRN
IFNβ--(G4S)3--antiCD40_HC_IgG1_NNAS_dK (SEQ ID NO 46)	MSYNLLGFLQRSSNFQCQKLLWQLNGRLEYCLKDRMNFDIPEEIKQLQQFQKEDAALTIYEMLQNIFAIFRQDSSSTGWNETIVENLLANVYHQINHLKTVLEEKLEKEDFTRGKLMSSLHLKRYYGRILHYLKAKEYSHCAWTIVRVEILRNFYFINRLTGYLRN**GGGGSGGGGSGGGGS**QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPGQGLEWMGWINPDSGGTNYAQKFQGRVTMTRDTSISTAYMELNRLRSDDTAVYYCARDQPLGYCTNGVCSYFDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNNASRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG
antiCD40_HC_IgG1_NNAS_dK--(G4S)4--IFNβ (SEQ ID NO 47)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPGQGLEWMGWINPDSGGTNYAQKFQGRVTMTRDTSISTAYMELNRLRSDDTAVYYCARDQPLGYCTNGVCSYFDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSN

	TKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY NNASRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKA KGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSV MHEALHNHYTQKSLSLSPG**GGGGSGGGGSGGGGSGGGGS**MS YNLLGFLQRSSNFQCQKLLWQLNGRLEYCLKDRMNFDIPEEIKQ LQQFQKEDAALTIYEMLQNIFAIFRQDSSSTGWNETIVENLLANV YHQINHLKTVLEEKLEKEDFTRGKLMSSLHLKRYYGRILHYLKA KEYSHCAWTIVRVEILRNFYFINRLTGYLRN
antiCD40_hIgG2dK_HC--HL--IFNα2A (SEQ ID NO 81)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPG QGLEWMGWINPDSGGTNYAQKFQGRVTMTRDTSISTAYMELN RLRSDDTAVYYCARDQPLGYCTNGVCSYFDYWGQGTLVTVSSA STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSN TKVDKTVERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTP EVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTF RVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPR EPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEA LHNHYTQKSLSLSPG**AEAAAKEAAAKA**CDLPQTHSLGSRRTLM LLAQMRKISLFSCLKDRHDFGFPQEEFGNQFQKAETIPVLHEMIQ QIFNLFSTKDSSAAWDETLLDKFYTELYQQLNDLEACVIQGVGV TETPLMKEDSILAVRKYFQRITLYLKEKKYSPCAWEVVRAEIMR SFSLSTNLQESLRSKE
antiCD40_LC-derivative--HL--IFNα2A (SEQ ID NO 82)	DIQMTQSPSSVSASVGDRVTITCRASQGIYSWLAWYQQKPGKAP NLLIYTASTLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQ ANIFPLTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEKSLSLSPG**AEA** **AAKEAAAKA**CDLPQTHSLGSRRTLMLLAQMRKISLFSCLKDRH

	DFGFPQEEFGNQFQKAETIPVLHEMIQQIFNLFSTKDSSAAWDET LLDKFYTELYQQLNDLEACVIQGVGVTETPLMKEDSILAVRKYF QRITLYLKEKKYSPCAWEVVRAEIMRSFSLSTNLQESLRSKE
antiCD40_LC--(G4S)4--IFNγ (SEQ ID NO 83)	DIQMTQSPSSVSASVGDRVTITCRASQGIYSWLAWYQQKPGKAP NLLIYTASTLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQ ANIFPLTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC**GGGGSGGG GSGGGGSGGGGS**QDPYVKEAENLKKYFNAGHSDVADNGTLFL GILKNWKEESDRKIMQSQIVSFYFKLFKNFKDDQSIQKSVETIKE DMNVKFFNSNKKKRDDFEKLTNYSVTDLNVQRKAIHELIQVMA ELSPAAKTGKRKRSQMLFRGRRASQ
antiCD40_hIgG2dK_HC--(G4S)4--IFNγ (SEQ ID NO 84)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPG QGLEWMGWINPDSGGTNYAQKFQGRVTMTRDTSISTAYMELN RLRSDDTAVYYCARDQPLGYCTNGVCSYFDYWGQGTLVTVSSA STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSN TKVDKTVERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTP EVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTF RVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPR EPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEA LHNHYTQKSLSLSPG**GGGGSGGGGSGGGGSGGGGS**QDPYVKE AENLKKYFNAGHSDVADNGTLFLGILKNWKEESDRKIMQSQIVS FYFKLFKNFKDDQSIQKSVETIKEDMNVKFFNSNKKKRDDFEKL TNYSVTDLNVQRKAIHELIQVMAELSPAAKTGKRKRSQMLFRG RRASQ

antiCD40_LC--(G4S)4--IFNλ2 (SEQ ID NO 85)	DIQMTQSPSSVSASVGDRVTITCRASQGIYSWLAWYQQKPGKAP NLLIYTASTLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQ ANIFPLTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC**GGGGSGGG** **GSGGGGSGGGGS**VPVARLHGALPDARGCHIAQFKSLSPQELQA FKRAKDALEESLLLKDCRCHSRLFPRTWDLRQLQVRERPMALE AELALTLKVLEATADTDPALVDVLDQPLHTLHHILSQFRACIQPQ PTAGPRTRGRLHHWLYRLQEAPKKESPGCLEASVTFNLFRLLTR DLNCVASGDLCV
antiCD40_hIgG2dK_HC--(G4S)4--IFNλ2 (SEQ ID NO 86)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPG QGLEWMGWINPDSGGTNYAQKFQGRVTMTRDTSISTAYMELN RLRSDDTAVYYCARDQPLGYCTNGVCSYFDYWGQGTLVTVSSA STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSN TKVDKTVERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTP EVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTF RVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPR EPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEA LHNHYTQKSLSLSPG**GGGGSGGGGSGGGGSGGGGS**VPVARLH GALPDARGCHIAQFKSLSPQELQAFKRAKDALEESLLLKDCRCH SRLFPRTWDLRQLQVRERPMALEAELALTLKVLEATADTDPALV DVLDQPLHTLHHILSQFRACIQPQPTAGPRTRGRLHHWLYRLQE APKKESPGCLEASVTFNLFRLLTRDLNCVASGDLCV
antiCD40_LC--(G4S)4--IFNω (SEQ ID NO 87)	DIQMTQSPSSVSASVGDRVTITCRASQGIYSWLAWYQQKPGKAP NLLIYTASTLQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQ ANIFPLTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC**GGGGSGGG**

	GSGGGGSGGGGSLGCDLPQNHGLLSRNTLVLLHQMRRISPFLC LKDRRDFRFPQEMVKGSQLQKAHVMSVLHEMLQQIFSLFHTERS SAAWNMTLLDQLHTGLHQQLQHLETCLLQVVGEGESAGAISSP ALTLRRYFQGIRVYLKEKKYSDCAWEVVRMEIMKSLFLSTNMQ ERLRSKDRDLGSS
antiCD40_hIgG2 dK_HC--(G4S)4--IFNε (SEQ ID NO 88)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPG QGLEWMGWINPDSGGTNYAQKFQGRVTMTRDTSISTAYMELN RLRSDDTAVYYCARDQPLGYCTNGVCSYFDYWGQGTLVTVSSA STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGAL TSGVHTFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSN TKVDKTVERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTP EVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTF RVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPR EPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEA LHNHYTQKSLSLSPG**GGGGSGGGGSGGGGSGGGGS**LDLKLIIF QQRQVNQESLKLLNKLQTLSIQQCLPHRKNFLLPQKSLSPQQYQ KGHTLAILHEMLQQIFSLFRANISLDGWEENHTEKFLIQLHQQLE YLEALMGLEAEKLSGTLGSDNLRLQVKMYFRRIHDYLENQDYS TCAWAIVQVEISRCLFFVFSLTEKLSKQGRPLNDMKQELTTEFRS PR

Table 8. *Sequences of exemplary interferon-associated antigen binding protein and components thereof based on the antiCD40 antibody 3G5. Italic sequences correspond to signal peptides. Bold non-italic sequences correspond to linkers. Mutated amino acids are underlined.*

Name / SEQ ID Number	Sequence
antiCD40_light chain (SEQ ID NO 59)	EIVMTQSPATLSVSPGERATLSCRASQSVRSNLAWYQQKPGQAP RLLIYGASTRATGIPARFSGSGSGTEFTLTINSLQSEDFAVYYCQQ HNKWITFGQGTRLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTL TLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
antiCD40_light chain with signal peptide 1 (SEQ ID NO 60)	*MGWSCIILFLVATATGVHS*EIVMTQSPATLSVSPGERATLSCRASQ SVRSNLAWYQQKPGQAPRLLIYGASTRATGIPARFSGSGSGTEFT LTINSLQSEDFAVYYCQQHNKWITFGQGTRLEIKRTVAAPSVFIF PPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPV TKSFNRGEC
antiCD40_heavy chain hIgG2 dK (SEQ ID NO 61)	QVQLVESGGGVVQPGKSLRLSCAASGFTFSSNGIHWVRQAPGK GLEWVAVIWSDGSNKFYADSVKGRFTISRDNSKNTLYLQMNSL RAEDTAVYYCARASGSGSYYNFFDYWGQGTLVTVSSASTKGPS VFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVH TFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSNTKVD KTVERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTC VVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTFRVVS VLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQ VYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHN HYTQKSLSLSPG

antiCD40_heavy chain hIgG2 dK with Signal peptide 1 (SEQ ID NO 62)	*MGWSCIILFLVATATGVHS*QVQLVESGGGVVQPGKSLRLSCAASG FTFSSNGIHWVRQAPGKGLEWVAVIWSDGSNKFYADSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCARASGSGSYYNFFDYW GQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPE PVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSNFGTQ TYTCNVDHKPSNTKVDKTVERKCCVECPPCPAPPVAGPSVFLFP PKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNA KTKPREEQFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKGLPA PIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS DIAVEWESNGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWQ QGNVFSCSVMHEALHNHYTQKSLSLSPG
antiCD40 antibody Fab region heavy chain hIgG2 (SEQ ID NO 63)	QVQLVESGGGVVQPGKSLRLSCAASGFTFSSNGIHWVRQAPGK GLEWVAVIWSDGSNKFYADSVKGRFTISRDNSKNTLYLQMNSL RAEDTAVYYCARASGSGSYYNFFDYWGQGTLVTVSSASTKGPS VFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVH TFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSNTKVD KTVERKCCVE
antiCD40 antibody Fab region heavy chain hIgG2 with signal peptide 1 (SEQ ID NO 64)	*MGWSCIILFLVATATGVHS*QVQLVESGGGVVQPGKSLRLSCAASG FTFSSNGIHWVRQAPGKGLEWVAVIWSDGSNKFYADSVKGRFTI SRDNSKNTLYLQMNSLRAEDTAVYYCARASGSGSYYNFFDYW GQGTLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPE PVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSNFGTQ TYTCNVDHKPSNTKVDKTVERKCCVE
antiCD40 antibody Fab region heavy chain hIgG2 --TEV--6His tag (SEQ ID NO 65)	QVQLVESGGGVVQPGKSLRLSCAASGFTFSSNGIHWVRQAPGK GLEWVAVIWSDGSNKFYADSVKGRFTISRDNSKNTLYLQMNSL RAEDTAVYYCARASGSGSYYNFFDYWGQGTLVTVSSASTKGPS VFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVH TFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSNTKVD KTVERKCCVEENLYFQSHHHHHH

antiCD40_hIgG2dK_HC--RL--IFNβdM (SEQ ID NO 66)	QVQLVESGGGVVQPGKSLRLSCAASGFTFSSNGIHWVRQAPGK GLEWVAVIWSDGSNKFYADSVKGRFTISRDNSKNTLYLQMNSL RAEDTAVYYCARASGSGSYYNFFDYWGQGTLVTVSSASTKGPS VFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVH TFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSNTKVD KTVERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTC VVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTFRVVS VLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQ VYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHN HYTQKSLSLSPG**PAPA**SYNLLGFLQRSSNFQCQKLLWQLNGRLE YCLKDRMNFDIPEEIKQLQQFQKEDAALTIYEMLQNIFAIFRQDS SSTGWNETIVENLLANVYHQINHLKTVLEEKLEKEDFTRGKLMS SLHLKRYYGRILHYLKAKEYSHCAWTIVRVEILRNFYFINRLTGY LRN
antiCD40_hIgG2dK_HC--RL--IFNβdM_C17S (SEQ ID NO 67)	QVQLVESGGGVVQPGKSLRLSCAASGFTFSSNGIHWVRQAPGK GLEWVAVIWSDGSNKFYADSVKGRFTISRDNSKNTLYLQMNSL RAEDTAVYYCARASGSGSYYNFFDYWGQGTLVTVSSASTKGPS VFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVH TFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSNTKVD KTVERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTC VVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTFRVVS VLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQ VYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHN HYTQKSLSLSPG**PAPA**SYNLLGFLQRSSNFQ<u>S</u>QKLLWQLNGRLE YCLKDRMNFDIPEEIKQLQQFQKEDAALTIYEMLQNIFAIFRQDS SSTGWNETIVENLLANVYHQINHLKTVLEEKLEKEDFTRGKLMS SLHLKRYYGRILHYLKAKEYSHCAWTIVRVEILRNFYFINRLTGY LRN

antiCD40_hIgG2dK_HC--HL--IFNβdM (SEQ ID NO 68)	QVQLVESGGGVVQPGKSLRLSCAASGFTFSSNGIHWVRQAPGK GLEWVAVIWSDGSNKFYADSVKGRFTISRDNSKNTLYLQMNSL RAEDTAVYYCARASGSGSYYNFFDYWGQGTLVTVSSASTKGPS VFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVH TFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSNTKVD KTVERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTC VVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTFRVVS VLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQ VYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHN HYTQKSLSLSPG**AEAAAKEAAAKA**SYNLLGFLQRSSNFQCQKL LWQLNGRLEYCLKDRMNFDIPEEIKQLQQFQKEDAALTIYEMLQ NIFAIFRQDSSSTGWNETIVENLLANVYHQINHLKTVLEEKLEKE DFTRGKLMSSLHLKRYYGRILHYLKAKEYSHCAWTIVRVEILRN FYFINRLTGYLRN
antiCD40_hIgG2dK_HC--HL--IFNβdM_C17S (SEQ ID NO 69)	QVQLVESGGGVVQPGKSLRLSCAASGFTFSSNGIHWVRQAPGK GLEWVAVIWSDGSNKFYADSVKGRFTISRDNSKNTLYLQMNSL RAEDTAVYYCARASGSGSYYNFFDYWGQGTLVTVSSASTKGPS VFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVH TFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSNTKVD KTVERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTC VVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTFRVVS VLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQ VYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHN HYTQKSLSLSPG**AEAAAKEAAAKA**SYNLLGFLQRSSNFQ<u>S</u>QKL LWQLNGRLEYCLKDRMNFDIPEEIKQLQQFQKEDAALTIYEMLQ NIFAIFRQDSSSTGWNETIVENLLANVYHQINHLKTVLEEKLEKE DFTRGKLMSSLHLKRYYGRILHYLKAKEYSHCAWTIVRVEILRN FYFINRLTGYLRN

antiCD40_LC--HL2--IFNβ_C17S (SEQ ID NO 70)	EIVMTQSPATLSVSPGERATLSCRASQSVRSNLAWYQQKPGQAP RLLIYGASTRATGIPARFSGSGSGTEFTLTINSLQSEDFAVYYCQQ HNKWITFGQGTRLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTL TLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC**AEAAAKEA** **AAKAAEAAAKEAAAKA**MSYNLLGFLQRSSNFQSQKLLWQLNG RLEYCLKDRMNFDIPEEIKQLQQFQKEDAALTIYEMLQNIFAIFR QDSSSTGWNETIVENLLANVYHQINHLKTVLEEKLEKEDFTRGK LMSSLHLKRYYGRILHYLKAKEYSHCAWTIVRVEILRNFYFINRL TGYLRN
antiCD40_LC--(G4S)3--IFNβ_C17S (SEQ ID NO 71)	EIVMTQSPATLSVSPGERATLSCRASQSVRSNLAWYQQKPGQAP RLLIYGASTRATGIPARFSGSGSGTEFTLTINSLQSEDFAVYYCQQ HNKWITFGQGTRLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTL TLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC**GGGGSGG** **GGSGGGGS**MSYNLLGFLQRSSNFQSQKLLWQLNGRLEYCLKD RMNFDIPEEIKQLQQFQKEDAALTIYEMLQNIFAIFRQDSSSTGW NETIVENLLANVYHQINHLKTVLEEKLEKEDFTRGKLMSSLHLK RYYGRILHYLKAKEYSHCAWTIVRVEILRNFYFINRLTGYLRN
antiCD40_hIgG2dK_HC--(G4S)2--IFNα2a (SEQ ID NO 72)	QVQLVESGGGVVQPGKSLRLSCAASGFTFSSNGIHWVRQAPGK GLEWVAVIWSDGSNKFYADSVKGRFTISRDNSKNTLYLQMNSL RAEDTAVYYCARASGSGSYYNFFDYWGQGTLVTVSSASTKGPS VFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVH TFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSNTKVD KTVERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTC VVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTFRVVS VLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQ VYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHN HYTQKSLSLSPG**GGGGSGGGGS**CDLPQTHSLGSRRTLMLLAQM

	RKISLFSCLKDRHDFGFPQEEFGNQFQKAETIPVLHEMIQQIFNLF STKDSSAAWDETLLDKFYTELYQQLNDLEACVIQGVGVTETPL MKEDSILAVRKYFQRITLYLKEKKYSPCAWEVVRAEIMRSFSLS TNLQESLRSKE
antiCD40_hIgG2 dK_HC--(G4S)3--IFNα2a (SEQ ID NO 73)	QVQLVESGGGVVQPGKSLRLSCAASGFTFSSNGIHWVRQAPGK GLEWVAVIWSDGSNKFYADSVKGRFTISRDNSKNTLYLQMNSL RAEDTAVYYCARASGSGSYYNFFDYWGQGTLVTVSSASTKGPS VFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVH TFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSNTKVD KTVERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTC VVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTFRVVS VLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQ VYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHN HYTQKSLSLSPG**GGGGSGGGGSGGGGS**CDLPQTHSLGSRRTL MLLAQMRKISLFSCLKDRHDFGFPQEEFGNQFQKAETIPVLHEMI QQIFNLFSTKDSSAAWDETLLDKFYTELYQQLNDLEACVIQGVG VTETPLMKEDSILAVRKYFQRITLYLKEKKYSPCAWEVVRAEIM RSFSLSTNLQESLRSKE
antiCD40_hIgG2 dK_HC--(G4S)4--IFNα2a (SEQ ID NO 74)	QVQLVESGGGVVQPGKSLRLSCAASGFTFSSNGIHWVRQAPGK GLEWVAVIWSDGSNKFYADSVKGRFTISRDNSKNTLYLQMNSL RAEDTAVYYCARASGSGSYYNFFDYWGQGTLVTVSSASTKGPS VFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVH TFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSNTKVD KTVERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTC VVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTFRVVS VLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQ VYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHN HYTQKSLSLSPG**GGGGSGGGGSGGGGSGGGGS**CDLPQTHSLG SRRTLMLLAQMRKISLFSCLKDRHDFGFPQEEFGNQFQKAETIPV

	LHEMIQQIFNLFSTKDSSAAWDETLLDKFYTELYQQLNDLEACV IQGVGVTETPLMKEDSILAVRKYFQRITLYLKEKKYSPCAWEVV RAEIMRSFSLSTNLQESLRSKE
antiCD40_hIgG2 dK_HC--HL-- IFNα2a (SEQ ID NO 75)	QVQLVESGGGVVQPGKSLRLSCAASGFTFSSNGIHWVRQAPGK GLEWVAVIWSDGSNKFYADSVKGRFTISRDNSKNTLYLQMNSL RAEDTAVYYCARASGSGSYYNFFDYWGQGTLVTVSSASTKGPS VFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVH TFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSNTKVD KTVERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTC VVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTFRVVS VLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQ VYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHN HYTQKSLSLSPG**AEAAAKEAAAKA**CDLPQTHSLGSRRTLMLLA QMRKISLFSCLKDRHDFGFPQEEFGNQFQKAETIPVLHEMIQQIF NLFSTKDSSAAWDETLLDKFYTELYQQLNDLEACVIQGVGVTET PLMKEDSILAVRKYFQRITLYLKEKKYSPCAWEVVRAEIMRSFS LSTNLQESLRSKE

[00194] In preferred embodiments, the interferon-associated antigen binding proteins described herein are interferon-fused antigen binding proteins comprising polypeptides derived from those specified in **Table 9,** in particular **Table 9A** or **Table 9B**, more particularly **Table 9A** below, and especially from the polypeptides of SEQ ID NO 38, SEQ ID NO 39, SEQ ID NO 40, SEQ ID NO 41, SEQ ID NO 42 or SEQ ID NO 43 above. In preferred embodiments, the interferon-associated antigen binding proteins described herein are interferon-fused antigen binding proteins consisting of polypeptides derived from those specified in **Table 9,** in particular **Table 9A** or **Table 9B**, more particularly **Table 9A** below, and especially from the polypeptides of SEQ ID NO 38, SEQ ID NO 39, SEQ ID NO 40, SEQ ID NO 41, SEQ ID NO 42 or SEQ ID NO 43 above. In more preferred embodiments, the interferon-fused antibody comprises the sequences as set forth in SEQ ID NO 38 and

SEQ ID NO 3. In other more preferred embodiments, the interferon-fused antibody comprises the sequences as set forth in SEQ ID NO 39 and SEQ ID NO 3. In other more preferred embodiments, the interferon-fused antibody comprises the sequences as set forth in SEQ ID NO 40 and SEQ ID NO 3. In other more preferred embodiments, the interferon-fused antibody comprises the sequences as set forth in SEQ ID NO 41 and SEQ ID NO 9. In other more preferred embodiments, the interferon-fused antibody comprises the sequences as set forth in SEQ ID NO 42 and SEQ ID NO 9. In other more preferred embodiments, the interferon-fused antibody comprises the sequences as set forth in SEQ ID NO 43 and SEQ ID NO 9.

Table 9. *Polypeptide combinations found in preferred interferon-fused antigen binding proteins of the invention based on the antiCD40 antibody CP870,893, their mean EC_{50} values with regard to the activation of CD40 and IFN-pathways and their productivity (i.e., yield per liter culture). Each sequence combination as indicated is comprised twice in the respective IFA.* SN: supernatant.

A

Interferon-fused Antibody (IFA)	**Sequence combination**	CD40 EC_{50} (ng/mL)	IFNβ EC_{50} (ng/mL)	IFNα EC_{50} (ng/mL)	productivity (mg/L)
IFA1	(SEQ ID NO 28) + (SEQ ID NO 9)	74,1	1,64		16,7
IFA2	(SEQ ID NO 29) + (SEQ ID NO 9)	111	0,14		17,8
IFA8	(SEQ ID NO 30) + (SEQ ID NO 3)	39,7	2,9		6,45
IFA9	(SEQ ID NO 31) + (SEQ ID NO 3)	42,6	0,7		3,4
IFA10	(SEQ ID NO 32) + (SEQ ID NO 3)	26,5	4,5		6,9
IFA11	(SEQ ID NO 33) + (SEQ ID NO 3)	42,8	1,78		5,1
IFA12	(SEQ ID NO 34) + (SEQ ID NO 9)	105	3,64		21,2
IFA13	(SEQ ID NO 35) + (SEQ ID NO 9)	192	0,7		11,5

IFA19	(SEQ ID NO 36) + (SEQ ID NO 9)	110	1,3		5,6
IFA20	(SEQ ID NO 37) + (SEQ ID NO 9)	182	2,34		4,2
IFA25	(SEQ ID NO 38) + (SEQ ID NO 3)	13,3		5,1	21
IFA26	(SEQ ID NO 39) + (SEQ ID NO 3)	15,35		4	8,6
IFA27	(SEQ ID NO 40) + (SEQ ID NO 3)	17		2,4	9,3
IFA28	(SEQ ID NO 41) + (SEQ ID NO 9)	12,8		4,5	75
IFA29	(SEQ ID NO 42) + (SEQ ID NO 9)	11,1		2	56,6
IFA30	(SEQ ID NO 43) + (SEQ ID NO 9)	11,3		1,6	46,6
IFA34	(SEQ ID NO 44) + (SEQ ID NO 49)	active (SN)	active (SN)		no significant production
IFA35	(SEQ ID NO 45) + (SEQ ID NO 49)	active (SN)	active (SN)		no significant production
IFA36	(SEQ ID NO 46) + (SEQ ID NO 3)	active (SN)	active (SN)		no significant production
IFA37	(SEQ ID NO 47) + (SEQ ID NO 3)	active (SN)	active (SN)		no significant production

B

Interferon-fused Antibody (IFA)	**Sequence combination**	CD40 EC_{50} (ng/mL)	IFNα EC_{50} (ng/mL)	IFNλ EC_{50} (ng/mL)	IFNγ EC_{50} (ng/mL)	IFNε EC_{50} (ng/mL)	IFNω EC_{50} (ng/mL)	productivity (mg/L)
IFA38	(SEQ ID NO 81) + (SEQ ID NO 3)	22.7	3.77					1.32
IFA39	(SEQ ID NO 82) + (SEQ ID NO 9)	17.5	2.95					1.25
IFA42	(SEQ ID NO 83) + (SEQ ID NO 9)	65.6			15.4			0.72
IFA43	(SEQ ID NO 84) + (SEQ ID NO 3)	50.8			<0.001			0.55
IFA44	(SEQ ID NO 85) + (SEQ ID NO 9)	41.4		0.153				0.91

IFA45	(SEQ ID NO 86) + (SEQ ID NO 3)	25.8		<0.001				1.09
IFA46	(SEQ ID NO 87) + (SEQ ID NO 9)	86.3					0.493	0.89
IFA49	(SEQ ID NO 88) + (SEQ ID NO 3)	65.8				78.2		0.61
IFA50	(SEQ ID NO 41) + (SEQ ID NO 50)	128	1.36					0.57
IFA51	(SEQ ID NO 42) + (SEQ ID NO 50)	123	1.43					0.48

[00195] In other preferred embodiments, the interferon-associated antigen binding proteins described herein are interferon-fused antigen binding proteins comprising polypeptides derived from those specified in **Table 10** below. In preferred embodiments, the interferon-associated antigen binding proteins described herein are interferon-fused antigen binding proteins consisting of polypeptides derived from those specified in **Table 10** below.

Table 10. *Polypeptide combinations found in preferred interferon-fused antigen binding proteins of the invention based on the antiCD40 antibody 3G5, their mean EC_{50} values with regard to the activation of CD40 and IFN-pathways. Each sequence combination as indicated is comprised twice in the respective IFA.* SN: supernatant.

Interferon - fused Antibody (IFA)	**Sequence combination**	CD40 EC_{50} (ng/mL)	IFNβ EC_{50} (ng/mL)	IFNα EC_{50} (ng/mL)	productivity mg/L
IFA106	(seq ID NO 66) + (seq ID NO 59)	190,5	10,30		0,36
IFA107	(seq ID NO 67) + (seq ID NO 59)	141,5	2,03		0,28
IFA108	(seq ID NO 68) + (seq ID NO 59)	37,3	1,27		0,59
IFA109	(seq ID NO 69) + (seq ID NO 59)	30	0,45		0,4
IFA114	(seq ID NO 70) + (seq ID NO 61)	active (SN)	active (SN)		no significant production

IFA115	(seq ID NO 71) + (seq ID NO 61)	active (SN)	active (SN)		no significant production
IFA121	(seq ID NO 72) + (seq ID NO 59)	14,2		0,12	22,6
IFA122	(seq ID NO 73) + (seq ID NO 59)	11,74		0,07	16,8
IFA123	(seq ID NO 74) + (seq ID NO 59)	12,85		0,05	17,2
IFA124	(seq ID NO 75) + (seq ID NO 59)	12,14		0,04	21,6

Nucleic Acids and Expression Vectors

[00196] In one aspect, a combination of polynucleotides encoding an interferon-associated antigen binding protein is provided. Methods of making an interferon-associated antigen binding protein comprising expressing these polynucleotides are also provided.

[00197] In some embodiments, a nucleic acid encoding an IFN or a functional fragment thereof being fused to an agonistic anti-CD40 antibody or an agonistic antigen binding fragment thereof, as disclosed herein is provided. In certain exemplary embodiments, the nucleic acid is encoding an IFN or a functional fragment thereof fused to an agonistic anti-CD40 antibody or an agonistic antigen binding fragment thereof according to any of the sequences set forth in SEQ ID NOs 81 to 88, or a nucleic acid sequence at least 80%, at least 85%, at least 90%, at least 95%, at least 98% or at least 99% identical to a nucleic acid encoding any of these sequences. In certain exemplary embodiments, said nucleic acid is at least 95%, at least 98% or at least 99% identical to a nucleic acid encoding any of SEQ ID NOs 81 to 88. In preferred embodiments, the nucleic acid is encoding an IFN or a functional fragment thereof fused to an agonistic anti-CD40 antibody or an agonistic antigen binding fragment thereof according to any of the sequences set forth in SEQ ID NOs 28 to 47, or a nucleic acid sequence at least 80%, at least 85%, at least 90%, at least 95%, at least 98% or at least 99% identical to a nucleic acid encoding any of these sequences. In even more specific embodiments, said nucleic acid is at least 95%, at least 98% or at least 99% identical to a nucleic acid encoding any of SEQ ID NOs 28

to 47. In other preferred embodiments, the nucleic acid is encoding an IFN or a functional fragment thereof fused to an agonistic anti-CD40 antibody or an agonistic antigen binding fragment thereof according to any of the sequences set forth in SEQ ID NOs 66 to 75, or a nucleic acid sequence at least 80%, at least 85%, at least 90%, at least 95%, at least 98% or at least 99% identical to a nucleic acid encoding any of these sequences. In even more specific embodiments, said nucleic acid is at least 95%, at least 98% or at least 99% identical to a nucleic acid encoding any of SEQ ID NOs 66 to 75.

[00198] In those embodiments wherein a nucleic acid encodes an IFN or a functional fragment thereof being fused to a light chain of the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof, the nucleic acid may further encode a heavy chain of the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof. In more specific embodiments, the heavy chain of the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof comprises a sequence as set forth in SEQ ID NO 6, SEQ ID NO 7, SEQ ID NO 8, SEQ ID NO 9, SEQ ID NO 10, SEQ ID NO 11, SEQ ID NO 12, SEQ ID NO 13, SEQ ID NO 48, SEQ ID NO 49, or SEQ ID NO 50, or a nucleic acid sequence at least 80%, at least 85%, at least 90%, at least 95%, at least 98% or at least 99% identical to a nucleic acid encoding any of these sequences. In even more specific embodiments, said nucleic acid is at least 95%, at least 98% or at least 99% identical to a nucleic acid encoding SEQ ID NO 6, SEQ ID NO 7, SEQ ID NO 8, SEQ ID NO 9, SEQ ID NO 10, SEQ ID NO 11, SEQ ID NO 12, SEQ ID NO 13, SEQ ID NO 48, SEQ ID NO 49, or SEQ ID NO 50. In other more specific embodiments, the heavy chain of the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof comprises a sequence as set forth in SEQ ID NO 61, SEQ ID NO 62, SEQ ID NO 63, SEQ ID NO 64 or SEQ ID NO 65, or a nucleic acid sequence at least at least 80%, at least 85%, at least 90%, at least 95%, at least 98% or at least 99% identical to a nucleic acid encoding any of these sequences. In such other even more specific embodiments, said nucleic acid is at least 95%, at least 98% or at least 99% identical to a nucleic acid encoding SEQ ID NO 61, SEQ ID NO 62, SEQ ID NO 63, SEQ ID NO 64 or SEQ ID NO 65.

[00199] In those embodiments where a nucleic acid encodes an IFN or a functional fragment thereof being fused to the heavy chain of the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof, the nucleic acid may further encode a light chain of the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof. In more specific embodiments, the light chain of the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof comprises a sequence as set forth in SEQ ID NO 3, SEQ ID NO 4 or SEQ ID NO 5, or a nucleic acid sequence at least 80%, at least 85%, at least 90%, at least 95%, at least 98% or at least 99% identical to a nucleic acid encoding any of these sequences. In even more specific embodiments, said nucleic acid is at least 95%, at least 98% or at least 99% identical to a nucleic acid encoding SEQ ID NO 3, SEQ ID NO 4 or SEQ ID NO 5. In other more specific embodiments, the light chain of the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof comprises a sequence as set forth in SEQ ID NO 59 or SEQ ID NO 60, or a nucleic acid sequence at least at least 80%, at least 85%, at least 90%, at least 95%, at least 98% or at least 99% identical to a nucleic acid encoding any of these sequences. In even more specific embodiments, said nucleic acid is at least 95%, at least 98% or at least 99% identical to a nucleic acid encoding SEQ ID NO 59 or SEQ ID NO 60.

[00200] In certain embodiments, the nucleic acids described herein may comprise a sequence encoding a sequence to increase the yield (e.g. a solubility tag) or facilitate purification of the expressed proteins (i.e., a purification tag). Purification tags are known to a person skilled in the art and may be selected from glutathione *S*-transferase (GST) tags, maltose binding protein (MBP) tags, calmodulin binding peptide (CBP) tags, intein-chitin binding domain (intein-CBD) tags, Streptavidin/Biotin-based tags (such as biotinylation signal peptide (BCCP) tags, Streptavidin-binding peptide (SBP) tags, His-patch ThioFusion tags, tandem affinity purification (TAP) tags, Small ubiquitin-like modifier (SUMO) tags, HaloTag® (Promega), Profinity eXact™ system (Bio-Rad). In some embodiments, the purification tag may be a polyhistidine tag (e.g., a His_6-, His_7-, His_8-, His_9- or His_{10}-tag). In other embodiments, the purification tag may be a Strep-tag (e.g., a Strep-tag® or a Strep-tag II®; IBA Life Sciences). In yet other embodiments, the purification tag may be a maltose binding protein (MBP) tag.

[00201] In some embodiments, the nucleic acid sequence may further comprise a sequence encoding a cleavage site for removal of the purification tag. Such cleavage sequences are known to a person skilled in the art and may be selected from a sequence recognized and cleaved by an endoprotease or an exoprotease. In some embodiments, an endoprotease for the removal of a purification tag may be selected from: Enteropeptidase, Thrombin, Factor Xa, TEV protease or Rhinovirus 3C protease. In some embodiments, an exoprotease for the removal of a purification tag may be selected from: Carboxypeptidase A, Carboxypeptidase B or DAPase. In preferred embodiments, the protease for the removal of a purification tag is TEV protease. In a more specific preferred embodiment, the nucleic acid comprises a sequence encoding a His_6-tag and a TEV cleavage site. In an even more specific preferred embodiment, said nucleic acid comprises a sequence encoding a sequence as set forth in SEQ ID NO 27.

[00202] The nucleic acid molecules of the invention may also comprise a sequence encoding a signal peptide. The skilled person is aware of the various signal peptides available to direct the expressed protein to the desired site of folding, assembly and/or maturation as well as to effect secretion of the final protein into the medium to facilitate downstream processing. Thus, in some embodiments, the signal peptide is a secretory signal peptide. The encoded signal peptide may comprise a sequence as set forth in SEQ ID NO: 1 or SEQ ID NO: 2. In some embodiments, the signal peptide comprises the sequence as set forth in SEQ ID NO: 1. In other embodiments, the signal peptide comprises the sequence as set forth in SEQ ID NO: 2.

[00203] Signal peptide 1 (SEQ ID NO 1) was used for synthesis of the polypeptide sequences as set forth in SEQ ID NO 28, SEQ ID NO 29, SEQ ID NO 30, SEQ ID NO 31, SEQ ID NO 32, SEQ ID NO 33, SEQ ID NO 34, SEQ ID NO 35, SEQ ID 36, SEQ ID NO 37, SEQ ID NO 44, SEQ ID NO 45, SEQ ID NO 46, SEQ ID NO 47, SEQ ID NO 50, SEQ ID NO 65, SEQ ID NO 66, SEQ ID NO 67, SEQ ID NO 68, SEQ ID NO 69, SEQ ID NO 70, SEQ ID NO 71, SEQ ID NO 72, SEQ ID NO 73, SEQ ID NO 74 and SEQ ID NO 75. Such signal peptide that is initially present at the N-terminus of the respective sequence of the polypeptide is cleaved during synthesis.

[00204] Signal peptide 2 (SEQ ID NO 2) was used for synthesis of the polypeptide sequences as set forth in SEQ ID NO 38, SEQ ID NO 39, SEQ ID NO 40, SEQ ID NO 41, SEQ ID NO 42 and SEQ ID NO 43. Such signal peptide that is initially present at the N-terminus of the respective sequence of the polypeptide is cleaved during synthesis.

[00205] For the synthesis of the polypeptide sequences as set forth in SEQ ID NO 81, SEQ ID NO 82, SEQ ID NO 83, SEQ ID NO 84, SEQ ID NO 85, SEQ ID NO 86, SEQ ID 87 and SEQ ID NO 88 the signal peptide MGWSCIILFLVATATGVHS (SEQ ID NO 1) was used. Such signal peptide that is initially present at the N-terminus of the respective sequence of the polypeptide is cleaved during synthesis.

[00206] Polynucleotides encoding an IFN or a functional fragment thereof being fused to the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof as disclosed herein are typically inserted in an expression vector for introduction into host cells that may be used to produce the desired quantity of the claimed interferon-associated antigen binding proteins. Accordingly, in certain aspects, the invention provides expression vectors comprising polynucleotides disclosed herein and host cells comprising these vectors and polynucleotides.

[00207] The term **"vector" or "expression vector**" is used herein for the purposes of the specification and claims, to mean vectors used in accordance with the present invention as a vehicle for introducing into and expressing a desired gene in a cell. As known to those skilled in the art, such vectors may easily be selected from the group consisting of plasmids, phages, viruses and retroviruses. In general, vectors compatible with the present invention will comprise a selection marker, appropriate restriction sites to facilitate cloning of the desired gene and the ability to enter and/or replicate in eukaryotic or prokaryotic cells.

[00208] Numerous expression **vector systems** may be employed for the purposes of this invention. For example, one class of vector utilizes DNA elements which are derived from animal viruses such as bovine papilloma virus, polyoma virus, adenovirus, vaccinia virus, baculovirus, retroviruses (RSV, MMTV or MOMLV), or SV40 virus. Others involve the use of polycistronic systems with internal ribosome binding sites. Additionally, cells which have integrated the DNA into their chromosomes may be selected by introducing one or more markers which allow

selection of transfected host cells. The marker may provide for prototrophy to an auxotrophic host, biocide resistance (e.g., antibiotics) or resistance to heavy metals such as copper. The selectable marker gene can either be directly linked to the DNA sequences to be expressed, or introduced into the same cell by co-transformation. Additional elements may also be needed for optimal synthesis of mRNA. These elements may include signal sequences, splice signals, as well as transcriptional promoters, enhancers, and termination signals. In some embodiments the cloned variable region genes, one of them fused with a gene encoding an IFN or a functional fragment thereof, are inserted into an expression vector along with the heavy and light chain constant region genes (such as human genes) synthesized as discussed above.

[00209] In other embodiments, a vector system of the invention may comprise more than one vector. In some embodiments, a vector system may comprise a first vector for the expression of an IFN or a functional fragment thereof fused to a light chain of the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof and a second vector for expression of a heavy chain of the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof. Alternatively, such a vector system may comprise a first vector for the expression of an IFN or a functional fragment thereof fused to a heavy chain of the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof and a second vector for expression of a light chain of the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof.

[00210] In other embodiments, an interferon-associated antigen binding protein as described herein may be expressed using polycistronic constructs. In such expression systems, multiple gene products of interest such as those encoding an IFN or a functional fragment thereof being fused to a heavy chain of an agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof and encoding a light chain of said antibody, or those encoding an IFN or a functional fragment thereof being fused to a light chain of an agonistic anti-CD40 antibody or an agonistic antigen binding fragment thereof and encoding a heavy chain of said antibody or an agonistic antigen binding fragment thereof may be produced from a single polycistronic construct. These systems advantageously use an internal ribosome entry site (IRES)

to provide relatively high levels of polypeptides in eukaryotic host cells. Compatible IRES sequences are disclosed in U.S. Pat. No. 6,193,980, which is incorporated by reference herein. Those skilled in the art will appreciate that such expression systems may be used to effectively produce the full range of polypeptides disclosed in the instant application.

[00211] More generally, once a vector or a DNA sequence encoding an interferon-associated antigen binding protein of the present invention has been prepared, the expression vector may be introduced into an appropriate host cell. That is, the host cell may be transformed. Introduction of a plasmid into the host cell can be accomplished by various techniques well known to those of skill in the art. These include, but are not limited to, transfection (including electrophoresis and electroporation), protoplast fusion, calcium phosphate precipitation, cell fusion with enveloped DNA, microinjection, and infection with intact virus. See, e.g., Ridgway, A. A. G. "Mammalian Expression Vectors" Chapter 24.2, pp. 470-472 Vectors, Rodriguez and Denhardt, Eds. (Butterworths, Boston, MA 1988). The transformed cells are grown under conditions appropriate to the production of the light chains and heavy chains, and assayed for heavy and/or light chain protein synthesis. Exemplary assay techniques include enzyme-linked immunosorbent assay (ELISA), radioimmunoassay (RIA), or fluorescence-activated cell sorter analysis (FACS), immunohistochemistry and the like.

[00212] As used herein, the term "**transformation**" shall be used in a broad sense to refer to the introduction of DNA into a recipient host cell that changes the genotype and consequently results in a change in the recipient cell.

[00213] Along those same lines, "**host cells**" refer to cells that have been transformed with vectors constructed using recombinant DNA techniques and encoding at least one heterologous gene. In descriptions of processes for isolation of polypeptides from recombinant hosts, the terms "**cell**" and "**cell culture**" are used interchangeably to denote the source of the interferon-associated antigen binding protein unless it is clearly specified otherwise. In other words, recovery of polypeptide from the "**cells**" may mean either from spun down whole cells, or from the cell culture containing both the medium and the suspended cells.

[00214] In one embodiment, the **host cell line** used for expression of an interferon-associated antigen binding protein is of eukaryotic or prokaryotic origin. As used herein, the term "expression" may include the transcription and translation of more than one polypeptide chain (such as a heavy and a light chain of the antibody moiety of an interferon-associated antigen binding protein), which associate to form the final interferon-associated antigen binding protein. In one embodiment, the host cell line used for expression of an interferon-associated antigen binding protein is of bacterial origin. In one embodiment, the host cell line used for expression of an interferon-associated antigen binding protein is of mammalian origin; those skilled in the art can determine particular host cell lines which are best suited for the desired gene product to be expressed therein. Exemplary host cell lines include, but are not limited to, CHO K1 GS knockout from Horizon, DG44 and DUXB11 (Chinese Hamster Ovary lines, DHFR minus), HELA (human cervical carcinoma), CVI (monkey kidney line), COS (a derivative of CVI with SV40 T antigen), R1610 (Chinese hamster fibroblast) BALBC/3T3 (mouse fibroblast), HAK (hamster kidney line), SP2/O (mouse myeloma), BFA-1c1BPT (bovine endothelial cells), RAJI (human lymphocyte), HEK 293 (human kidney). In a preferred embodiment, HEK FS S11/ 254 cells may be used. In another preferred embodiment, CHO K1 GS from Horizon may be used. In one embodiment, the cell line provides for altered glycosylation, e.g., afucosylation, of the antibody expressed therefrom (e.g., PER.C6® (Crucell) or FUT8-knock-out CHO cell lines (POTELLIGENT^{TM} cells) (Biowa, Princeton, NJ)). In one embodiment NS0 cells may be used. Host cell lines are typically available from commercial services, the American Tissue Culture Collection or from published literature.

[00215] In one embodiment, the **host** used for expression of an interferon-associated antigen binding protein is a non-human transgenic animal or transgenic plant.

[00216] Interferon-associated antigen binding proteins of the invention can also be produced transgenically through the generation of a non-human animal (e.g., mammal) or plant that is transgenic for the sequences of interest and production of the interferon-associated antigen binding protein in a recoverable form therefrom. In connection with the transgenic production in mammals, interferon-associated antigen binding proteins can be produced in, and recovered from, the milk of goats, cows, or

other mammals. See, e.g., US. Patent Nos 5,827,690, 5,756,687, 5,750,172, and 5,741,957. Exemplary plant hosts are Nicotiana, Arabidopsis, duckweed, corn, wheat, potato, etc. Methods for expressing antibodies in plants, including a description of promoters and vectors, as well as transformation of plants is known in the art. See, e.g., United States Patent 6,517,529, herein incorporated by reference. In some embodiments, non-human transgenic animals or plants are produced by introducing one or more nucleic acid molecules encoding an interferon-associated antigen binding protein of the invention into the animal or plant by standard transgenic techniques. See Hogan and United States Patent 6,417,429. The transgenic cells used for making the transgenic animal can be embryonic stem cells or somatic cells. The transgenic non-human organisms can be chimeric, nonchimeric heterozygotes, and nonchimeric homozygotes. See, e.g., Hogan et al., Manipulating the Mouse Embryo: A Laboratory Manual 2nd ed., Cold Spring Harbor Press (1999); Jackson et al., Mouse Genetics and Transgenics: A Practical Approach, Oxford University Press (2000); and Pinkert, Transgenic Animal Technology: A Laboratory Handbook, Academic Press (1999). In some embodiments, the transgenic non-human animals have a targeted disruption and replacement by a targeting construct that encodes the sequence(s) of interest. The interferon-associated antigen binding proteins may be made in any transgenic animal. In a preferred embodiment, the non-human animals are mice, rats, sheep, pigs, goats, cattle or horses. The non-human transgenic animal expresses said interferon-associated antigen binding proteins in blood, milk, urine, saliva, tears, mucus and other bodily fluids.

[00217] *In vitro* production allows scale-up to give large amounts of the desired interferon-associated antigen binding proteins. Techniques for mammalian cell cultivation under tissue culture conditions are known in the art and include homogeneous suspension culture, e.g., in an airlift reactor or in a continuous stirrer reactor, or immobilized or entrapped cell culture, e.g., in hollow fibers, microcapsules, on agarose microbeads or ceramic cartridges. If necessary and/or desired, a solution of an interferon-associated antigen binding protein, can be purified by the customary chromatography methods, for example gel filtration, ion-exchange chromatography, chromatography over DEAE-cellulose and/or (immuno-) affinity chromatography.

[00218] One or more genes encoding an interferon-associated antigen binding protein can also be expressed in non-mammalian cells such as bacteria or yeast or plant cells. In this regard it will be appreciated that various unicellular non-mammalian microorganisms such as bacteria can also be transformed; i.e. those capable of being grown in cultures or fermentation. Bacteria, which are susceptible to transformation, include members of the enterobacteriaceae, such as strains of *Escherichia coli* or *Salmonella*; *Bacillaceae*, such as *Bacillus subtilis*; *Pneumococcus*; *Streptococcus*, and *Haemophilus influenzae*. It will further be appreciated that, when expressed in bacteria, interferon-associated antigen binding proteins according to the invention or components thereof (i.e., agonistic anti-CD40 antibodies or agonistic antigen binding fragments thereof, and IFNs or functional fragments of IFNs) can become part of inclusion bodies. The desired interferon-associated antigen binding proteins may then need to be isolated, optionally also refolded, and purified.

[00219] In addition to prokaryotes, eukaryotic microbes may also be used. *Saccharomyces cerevisiae*, or common baker's yeast, is the most commonly used among eukaryotic microorganisms although a number of other strains are commonly available. For expression in *Saccharomyces*, the plasmid YRp7, for example, (Stinchcomb *et al.*, Nature, 282:39 (1979); Kingsman *et al.*, Gene, 7:141 (1979); Tschemper *et al.*, Gene, 10:157 (1980)) is commonly used. This plasmid already contains the TRP1 gene, which provides a selection marker for a mutant strain of yeast lacking the ability to grow in tryptophan, for example ATCC No. 44076 or PEP4-1 (Jones, Genetics, 85:12 (1977)). The presence of the trp1 lesion as a characteristic of the yeast host cell genome then provides an effective environment for detecting transformation by growth in the absence of tryptophan.

Therapeutic Vectors

[00220] A nucleic acid sequence encoding an interferon-associated antigen binding protein can be inserted into a vector and used as a therapeutic vector, e.g., a vector that expresses an interferon-associated antigen binding protein of the invention. The construction of suitable, functional expression constructs and therapeutic expression vectors is known to one of ordinary skill in the art. Thus, in certain embodiments, the interferon-associated antigen binding protein may be administered to a subject by

means of genetic delivery with RNA or DNA sequences, a vector or vector system encoding the interferon-associated antigen binding protein.

[00221] Therapeutic vectors can be delivered to a subject by, for example, intravenous injection, local administration (see U.S. Pat. No. 5,328,470) or by stereotactic injection (see, e.g., Chen et al., PNAS 91:3054-3057 (1994)). The pharmaceutical preparation of a therapeutic vector can include the vector in an acceptable diluent.

[00222] An interferon-associated antigen binding protein encoding nucleic acid, or nucleic acids, can be incorporated into a gene construct to be used as a part of a therapy protocol to deliver nucleic acids encoding an interferon-associated antigen binding protein. Expression vectors for *in vivo* transfection and expression of an interferon-associated antigen binding protein are provided.

[00223] Expression constructs of such components may be administered in any biologically effective carrier, e.g., any formulation or composition capable of effectively delivering the component nucleic acid sequence to cells *in vivo*, as are known to one of ordinary skill in the art. Approaches include, but are not limited to, insertion of the subject nucleic acid sequence(s) in viral vectors including, but not limited to, recombinant retroviruses, adenovirus, adeno-associated virus and herpes simplex virus-1, recombinant bacterial or eukaryotic plasmids and the like.

[00224] Retrovirus vectors and adeno-associated viral vectors can be used as a recombinant delivery system for the transfer of exogenous nucleic acid sequences *in vivo*, particularly into humans. Such vectors provide efficient delivery of genes into cells, and the transferred nucleic acids can be stably integrated into the chromosomal DNA of the host.

[00225] The development of specialized cell lines (termed "**packaging cells**") which produce only replication-defective retroviruses has increased the utility of retroviruses for gene therapy, and defective retroviruses are characterized for use in gene transfer for gene therapy purposes (for a review see, e.g., Miller, Blood 76:271-78 (1990)). A replication-defective retrovirus can be packaged into virions, which can be used to infect a target cell through the use of a helper virus by standard techniques. Protocols for producing recombinant retroviruses and for infecting cells in vitro or in vivo with such viruses can be found in Current Protocols in Molecular Biology, Ausubel, et al., (eds.) Greene Publishing Associates, (1989), Sections 9.10-

9.14, and other standard laboratory manuals. Non-limiting examples of suitable retroviruses include pLJ, pZIP, pWE and pEM, which are known to those of ordinary skill in the art. Examples of suitable packaging virus lines include *Crip, *Cre, *2 and *Am. (See, for example, Eglitis, et al., Science 230:1395-1398 (1985); Danos and Mulligan, Proc. Natl. Acad. Sci. USA 85:6460-6464 (1988); Wilson, et al., Proc. Natl. Acad. Sci. USA 85:3014-3018 (1988); Armentano, et al., Proc. Natl. Acad. Sci. USA 87:6141-6145 (1990); Huber, et al., Proc. Natl. Acad. Sci. USA 88:8039-8043 (1991); Ferry, et al., Proc. Natl. Acad. Sci. USA 88:8377-8381 (1991); Chowdhury, et al., Science 254:1802-1805 (1991); van Beusechem, et al., Proc. Natl. Acad. Sci. USA 89:7640-7644 (1992); Kay, et al., Human Gene Therapy 3:641-647 (1992); Dai, et al., Proc. Natl. Acad. Sci. USA 89:10892-10895 (1992); Hwu, et al., J. Immunol. 150:4104-4115 (1993); U.S. Pat. No. 4,868,116; U.S. Pat. No. 4,980,286; PCT Application WO 89/07136; PCT Application WO 89/02468; PCT Application WO 89/05345; and PCT Application WO 92/07573).

[00226] In another embodiment, adenovirus-derived delivery vectors are provided. The genome of an adenovirus can be manipulated such that it encodes and expresses a gene product of interest but is inactivated in terms of its ability to replicate in a normal lytic viral life cycle. See, for example, Berkner, et al., BioTechniques 6:616 (1988); Rosenfeld, et al., Science 252:431-434 (1991); and Rosenfeld, et al., Cell 68:143-155 (1992). Suitable adenoviral vectors derived from the adenovirus strain Ad type 5 d1324 or other strains of adenovirus (e.g., Ad2, Ad3, Ad7 etc.) are known to those of ordinary skill in the art. Recombinant adenoviruses can be advantageous in certain circumstances in that they are not capable of infecting non-dividing cells and can be used to infect a wide variety of cell types, including epithelial cells (Rosenfeld, et al. (1992), supra). Furthermore, the virus particle is relatively stable and amenable to purification and concentration and, as above, can be modified so as to affect the spectrum of infectivity. Additionally, introduced adenoviral DNA (and foreign DNA contained therein) is not integrated into the genome of a host cell, but remains episomal, thereby avoiding potential problems that can occur as a result of insertional mutagenesis *in situ* where introduced DNA becomes integrated into the host genome (e.g., retroviral DNA). Moreover, the carrying capacity of the adenoviral genome for foreign DNA is large (up to 8 kilobases) relative to other

delivery vectors (Berkner, et al. (1998), supra; Haj-Ahmand and Graham, J. Virol. 57:267 (1986)).

[00227] Yet another viral vector system useful for delivery of a nucleic acid sequence encoding an interferon-associated antigen binding protein, is the adeno-associated virus (AAV). AAV is a naturally occurring defective virus that requires another virus, such as an adenovirus or a herpes virus, as a helper virus for efficient replication and a productive life cycle. (For a review see Muzyczka, et al., Curr. Topics in Micro. and Immunol. 158:97-129 (1992)). It is also one of the few viruses that may integrate its DNA into non-dividing cells, and exhibits a high frequency of stable integration (see for example Flotte, et al., Am. J. Respir. Cell. Mol. Biol. 7:349-356 (1992); Samulski, et al., J. Virol. 63:3822-3828 (1989); and McLaughlin, et al., J. Virol. 62:1963-1973 (1989)). Vectors containing as little as 300 base pairs of AAV can be packaged and can integrate. Space for exogenous DNA is limited to about 4.5 kb. An AAV vector such as that described in Tratschin, et al., Mol. Cell. Biol. 5:3251-3260 (1985) can be used to introduce DNA into cells. A variety of nucleic acids have been introduced into different cell types using AAV vectors (see for example Hermonat, et al., Proc. Natl. Acad. Sci. USA 81:6466-6470 (1984); Tratschin, et al., Mol. Cell. Biol. 4:2072-2081 (1985); Wondisford, et al., Mol. Endocrinol. 2:32-39 (1988); Tratschin, et al., J. Virol. 51:611-619 (1984); and Flotte, et al., J. Biol. Chem. 268:3781-3790 (1993)).

[00228] In addition to viral transfer methods, non-viral methods can also be employed to cause expression of a nucleic acid sequence encoding an interferon-associated antigen binding protein in the tissue of a subject. Most non-viral methods of gene transfer rely on normal mechanisms used by mammalian cells for the uptake and intracellular transport of macromolecules. In some embodiments, non-viral delivery systems rely on endocytic pathways for the uptake of the subject gene by the targeted cell. Exemplary delivery systems of this type include liposomal derived systems, poly-lysine conjugates, and artificial viral envelopes. Other embodiments include plasmid injection systems such as are described in Meuli, et al., J. Invest. Dermatol. 116 (1):131-135 (2001); Cohen, et al., Gene Ther 7 (22):1896-905 (2000); or Tam, et al., Gene Ther. 7 (21):1867-74 (2000).

[00229] In clinical settings, the delivery systems can be introduced into a subject by any of a number of methods, each of which is familiar in the art. For instance, a pharmaceutical preparation of the delivery system can be introduced systemically, e.g., by intravenous injection. Specific transduction of the protein in the target cells occurs predominantly from specificity of transfection provided by the delivery vehicle, cell-type or tissue-type expression due to the transcriptional regulatory sequences controlling expression of the receptor gene, or a combination thereof. In other embodiments, initial delivery of the recombinant gene is more limited with introduction into the animal being quite localized. For example, the delivery vehicle can be introduced by catheter (see, U.S. Pat. No. 5,328,470) or by stereotactic injection (e.g., Chen, et al., PNAS 91: 3054-3057 (1994)).

[00230] The pharmaceutical preparation of the **therapeutic construct** can consist essentially of the delivery system in an acceptable diluent, or can comprise a slow release matrix in which the delivery vehicle is imbedded. Alternatively, where the complete delivery system can be produced intact from recombinant cells, e.g., retroviral vectors, the pharmaceutical preparation can comprise one or more cells, which produce the delivery system.

Methods of Treatment

[00231] In one aspect, the invention provides methods of treating a patient in need thereof (e.g., a patient infected with HBV) comprising administering an effective amount of an interferon-associated antigen binding protein, or a nucleic acid sequence (e.g., mRNA) that encodes an interferon-associated antigen binding protein, as disclosed herein. The invention also provides for a use of an interferon-associated antigen binding protein, or a nucleic acid sequence (e.g., mRNA) that encodes an interferon-associated antigen binding protein, as disclosed herein, in the preparation of a medicament for the treatment of HBV. In certain embodiments, the present invention provides kits and methods for the treatment of disorders and/or symptoms, e.g., HBV-related disorders and/or HBV-related symptoms, in a mammalian subject in need of such treatment. In certain exemplary embodiments, the subject is a human.

[00232] The interferon-associated antigen binding proteins, or nucleic acid sequences that encode them, of the present invention are useful in a number of different applications. For example, in one embodiment, the subject interferon-associated antigen binding proteins, or nucleic acid sequences that encode them, are useful for reducing HBeAg release from an HBV-infected cell. In some embodiments, the interferon-associated antigen binding proteins of the invention reduce HBeAg release by primary hepatocytes *in vitro* by at least 10% at 1 ng/mL, at least 20% at 1 ng/mL, at least 30 % at 1 ng/mL, at least 40% at 1 ng/mL, at least 50% at 1 ng/mL, at least 60 % at 1 ng/mL, at least 70% at 1 ng/mL, at least 80% at 1 ng/mL, or at least 85% at 1 ng/mL. In some embodiments, the interferon-associated antigen binding proteins of the invention reduce HBeAg release by primary hepatocytes *in vitro* by at least 12% at 1 ng/mL. In some embodiments, the interferon-associated antigen binding proteins of the invention reduce HBeAg release by primary hepatocytes *in vitro* by up to 90% at 1 ng/mL. In related embodiments, the interferon-associated antigen binding protein reduces HBeAg release with an EC_{50} of less than 30 ng/mL, preferably with an EC_{50} of less than 10 ng/mL, more preferably with an EC_{50} of less than 1 ng/mL.

[00233] In another embodiment, the subject interferon-associated antigen binding proteins, or nucleic acid sequences that encode them, are useful for reducing pgRNA transcription of cccDNA in an HBV-infected cell.

[00234] In another embodiment, the subject interferon-associated antigen binding proteins, or nucleic acid sequences that encode them, are useful for reducing one or more symptoms and/or complications associated with HBV infection, as described herein (*infra*).

[00235] In certain embodiments, the subject interferon-associated antigen binding proteins, or nucleic acid sequences that encode them, are useful for reducing one or more disorders, symptoms and/or complications associated with chronic HBV infection, e.g., chronic inflammation of the liver (chronic hepatitis), leading to cirrhosis over a period of several years; hepatocellular carcinoma (HCC); development of membranous glomerulonephritis (MGN); risk of death; acute necrotizing vasculitis (polyarteritis nodosa), membranous glomerulonephritis, and papular acrodermatitis of childhood (Gianotti–Crosti syndrome); HBV-associated

nephropathy (e.g., membranous glomerulonephritis); immune-mediated hematological disorders (e.g., essential mixed cryoglobulinemia, aplastic anemia); and the like.

[00236] In certain embodiments, the subject interferon-associated antigen binding proteins, or nucleic acid sequences that encode them, are useful for reducing one or more symptoms and/or complications associated with acute HBV infection, e.g., acute viral hepatitis (which begins with general ill-health, loss of appetite, nausea, vomiting, body aches, mild fever, and dark urine, and then progresses to development of jaundice, fulminant hepatic failure, and/or serum-sickness-like syndrome); loss of appetite; joint and muscle pain; low-grade fever; stomach pain; nausea; vomiting; jaundice; bloated stomach; and the like.

[00237] Accordingly, this invention also relates to a method of treating one or more disorders, symptoms and/or complications associated with HBV infection in a human or other animal by administering to such human or animal an effective, non-toxic amount of an interferon-associated antigen binding protein, or a nucleic acid sequence that encodes it. One skilled in the art would be able, by routine experimentation, to determine what an effective, non-toxic amount of an interferon-associated antigen binding protein, or a nucleic acid sequence that encodes it, would be for the purpose of treating HBV infection.

[00238] For example, a "**therapeutically active amount**" of an interferon-associated antigen binding protein of the present invention may vary according to factors such as the disease stage (e.g., acute vs. chronic), age, sex, medical complications (e.g., HIV co-infection, immunosuppressed conditions or diseases) and weight of the subject, and the ability of the interferon-associated antigen binding protein to elicit a desired response in the subject. The dosage regimen may be adjusted to provide the optimum therapeutic response. For example, several divided doses may be administered daily, or the dose may be proportionally reduced as indicated by the exigencies of the therapeutic situation.

[00239] In general, the compositions provided in the current invention may be used to prophylactically treat non-infected cells or therapeutically treat any HBV-infected cells comprising an antigenic marker that allows for the targeting of the HBV-infected cells by an interferon-associated antigen binding protein.

Pharmaceutical Compositions and Administration Thereof

[00240] In certain embodiments, the interferon-associated antigen binding proteins of the invention or nucleic acid sequences (including vectors or vector systems) that encode them are comprised in a pharmaceutical composition. Methods of preparing and administering interferon-associated antigen binding proteins, or nucleic acid sequences that encode them, of the current invention to a subject are well known to or can be readily determined by those skilled in the art using this specification and the knowledge in the art as a guide. The route of administration of the interferon-associated antigen binding proteins, or nucleic acid sequences that encode them, of the current invention may be oral, parenteral, by inhalation or topical. The term "**parenteral**", as used herein, includes intravenous, intraarterial, intraperitoneal, intramuscular, subcutaneous, rectal or vaginal administration. While all these forms of administration are clearly contemplated as being within the scope of the current invention, a form for administration would be a solution for injection, in particular for intravenous or intraarterial injection or drip. Usually, a suitable pharmaceutical composition for injection may comprise a buffering agent (e.g. acetate, phosphate or citrate buffer), a surfactant (e.g. polysorbate), optionally a stabilizing agent (e.g. human albumin), etc. In some embodiments, the buffering agent is acetate. In another embodiment, the buffering agent is formate. In yet another embodiment, the buffering agent is citrate. In related embodiments, the surfactant may be selected from the list comprising pluronics, PEG, sorbitan esters, polysorbates, triton, tromethamine, lecithin, cholesterol and tyloxapal. In preferred embodiments, the surfactant is polysorbate. In more preferred embodiments, the surfactant is polysorbate 20, polysorbate 40, polysorbate 60, polysorbate 80 or polysorbate 100, preferably polysorbate 20 or polysorbate 80.

[00241] In some embodiments, the interferon-associated antigen binding proteins, or nucleic acid sequences that encode them, can be delivered directly to the site of the adverse cellular population (e.g., the liver) thereby increasing the exposure of the diseased tissue to the therapeutic agent.

[00242] Preparations for parenteral administration include sterile aqueous or non-aqueous solutions, suspensions, and emulsions. Examples of non-aqueous solvents are propylene glycol, polyethylene glycol, vegetable oils such as olive oil, and injectable organic esters such as ethyl oleate. Aqueous carriers include water, alcoholic/aqueous solutions, emulsions or suspensions, including saline and buffered media. In the compositions and methods of the current invention, pharmaceutically acceptable carriers include, but are not limited to, 0.01-0.1 M, e.g., 0.05 M phosphate buffer, or 0.8% saline. Other common parenteral vehicles include sodium phosphate solutions, Ringer's dextrose, dextrose and sodium chloride, lactated Ringer's, or fixed oils. Intravenous vehicles include fluid and nutrient replenishers, electrolyte replenishers, such as those based on Ringer's dextrose, and the like. Preservatives and other additives may also be present such as for example, antimicrobials, antioxidants, chelating agents, and inert gases and the like. More particularly, pharmaceutical compositions suitable for injectable use include sterile aqueous solutions (where water-soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersions. In such cases, the composition must be sterile and should be fluid to the extent that easy syringability exists. It should be stable under the conditions of manufacture and storage and will typically be preserved against the contaminating action of microorganisms, such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (e.g., glycerol, propylene glycol, and liquid polyethylene glycol, and the like), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants.

[00243] Prevention of the action of microorganisms can be achieved by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid, thimerosal and the like. In many cases, isotonic agents will be included, for example, sugars, polyalcohols, such as mannitol, sorbitol, or sodium chloride in the composition. Prolonged absorption of the injectable compositions can be brought about by including in the composition an agent which delays absorption, for example, aluminum monostearate and gelatin.

[00244] In any case, sterile injectable solutions can be prepared by incorporating an active compound such as an interferon-associated antigen binding protein, or a nucleic acid sequence encoding said interferon-associated antigen binding protein, of the present invention by itself or in combination with other active agents in the required amount in an appropriate solvent with one or a combination of ingredients enumerated herein, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the active compound into a sterile vehicle, which contains a basic dispersion medium and the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, exemplary methods of preparation include vacuum drying and freeze-drying, which yields a powder of an active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof. The preparations for injections are processed, filled into containers such as ampules, bags, bottles, syringes or vials, and sealed under aseptic conditions according to methods known in the art. Further, the preparations may be packaged and sold in the form of a kit. Such articles of manufacture will typically have labels or package inserts indicating that the associated compositions are useful for treating a subject suffering from HBV infection.

[00245] Effective doses of the compositions of the present invention, for the treatment of the above described HBV infection-related conditions vary depending upon many different factors, including means of administration, target site, physiological state of the patient, whether the patient is human or an animal, other medications administered, and whether treatment is prophylactic or therapeutic. Usually, the patient is a human, but non-human mammals including transgenic mammals, in particular non-human primates, can also be treated. Treatment dosages may be titrated using routine methods known to those of skill in the art to optimize safety and efficacy.

[00246] For treatment with an interferon-associated antigen binding protein, the dosage can range, e.g., from about 0.0001 to about 100 mg/kg, and more usually about 0.01 to about 5 mg/kg (e.g., about 0.02 mg/kg, about 0.25 mg/kg, about 0.5 mg/kg, about 0.75 mg/kg, about 1 mg/kg, about 2 mg/kg, etc.), of the host body weight. For example, dosages can be about 1 mg/kg body weight or about 10 mg/kg

body weight or within the range of about 1 to about 10 mg/kg, e.g., at least about 1 mg/kg. Doses intermediate in the above ranges are also intended to be within the scope of the current invention. Subjects can be administered such doses daily, on alternative days, weekly or according to any other schedule determined by empirical analysis. An exemplary treatment entails administration in multiple dosages over a prolonged period, for example, of at least six months. Additional exemplary treatment regimens entail administration about once per every two weeks or about once a month or about once every 3 to 6 months. Exemplary dosage schedules include about 1 to about 10 mg/kg or about 15 mg/kg on consecutive days, about 30 mg/kg on alternate days or about 60 mg/kg weekly.

[00247] Interferon-associated antigen binding proteins, or nucleic acid sequences expressing any of these, can be administered on multiple occasions. Intervals between single dosages can be weekly, monthly or yearly. Intervals can also be irregular as indicated by measuring blood levels of interferon-associated antigen binding proteins of components thereof in the patient. Alternatively, interferon-associated antigen binding proteins, or nucleic acid sequences expressing any of these can be administered as a sustained release formulation, in which case less frequent administration is required. Dosage and frequency vary depending on the half-life of the interferon-associated antigen binding proteins in the patient.

[00248] The term "**half-life**" or "$t_{1/2}$", as referred to herein, relates to the stability and/or the rate of excretion of a compound, such as the interferon-associated antigen binding proteins of the invention. In practice, the half-life of a compound is usually measured in the serum and denotes the time after administration that the serum concentration is 50% of the serum concentration at the time of administration. The interferon-associated antigen binding proteins of the invention are characterized by a long serum half-life in mice. In some embodiments, the half-life of the interferon-associated antigen binding protein is at least 50 h, at least 60 h, at least 70 h, at least 80 h, at least 90 h or at least 100 h. In some embodiments, the half-life of the interferon-associated antigen binding protein is at least 100 h. In preferred embodiments, the half-life of the interferon-associated antigen binding protein in mice ranges from 116 to 158 h.

[00249] The half-life of a protein is related to its clearance. The term "**clearance**" or "**clearance rate**", as used herein, refers to the volume of plasma cleared of the protein per unit time. Clearance of the interferon-associated antigen binding proteins of the invention is low. In some embodiments, clearance of the interferon-associated antigen binding protein is below 10 mL/h/kg, below 5 mL/h/kg, below 2.5 mL/h/kg, below 1 mL/h/kg, or below 0.5 mL/h/kg. In some embodiments, clearance of the interferon-associated antigen binding protein is below 5 mL/h/kg. In some embodiments, clearance of the interferon-associated antigen binding protein is below 1 mL/h/kg. In some embodiments, clearance of the interferon-associated antigen binding protein in mice ranges from 0.28 to 0.49 mL/h/kg.

[00250] The terms "**volume of distribution**", "V_D", "V_{SS}" or "**apparent volume of distribution**" as used herein refer to the theoretical volume that would be necessary to contain the total amount of an administered compound such as the interferon-associated antigen binding protein of the invention at the same concentration that it is observed in the blood plasma and relates to the distribution of said compound between plasma and the rest of the body after oral or parenteral dosing. In certain embodiments, the volume of distribution Vss of the interferon-associated antigen binding protein is below 500 mL/kg, below 400 mL/kg, below 300 mL/kg, below 200 mL/kg, or below 100 mL/kg. In some embodiments, the volume of distribution Vss of the interferon-associated antigen binding protein is below 100 mL/kg. In some embodiments, the volume of distribution Vss of the interferon-associated antigen binding protein in mice ranges from 50 to 98 mL/kg.

[00251] Another related pharmacokinetic parameter is the systemic exposure. As used herein, the terms "**systemic exposure**", "**AUC**" or "**area under the curve**" refer to the integral of the concentration-time curve. Systemic exposure might be represented by plasma (serum or blood) concentrations or the AUCs of parent compound and/or metabolite(s). The interferon-associated antigen binding proteins of the invention circulate in the blood with higher systemic exposure (AUC (0-inf)) than their parental antibody. In some embodiments, the parental antibody is CP870,893. In other embodiments, the parental antibody is 3G5. In some embodiments, the systemic exposure of the interferon-associated antigen binding protein is at least 600 µg*h/mL, at least 700 µg*h/mL, at least 800 µg*h/mL, at least 900 µg*h/mL or at

least 1000 μg*h/mL, preferably at least 1000 μg*h/mL. In some embodiments, the systemic exposure of the interferon-associated antigen binding protein in mice ranges from 1033 μg*h/mL to 1793 μg*h/mL.

[00252] As previously discussed, an interferon-associated antigen binding protein of the present invention may be administered in a pharmaceutically effective amount for the *in vivo* treatment of mammalian disorders. In this regard, it will be appreciated that as disclosed an interferon-associated antigen binding protein, will be formulated to facilitate administration and promote stability of the active agent.

[00253] A pharmaceutical composition in accordance with the present invention can comprise a pharmaceutically acceptable, non-toxic, sterile carrier such as physiological saline, nontoxic buffers, preservatives and the like. A pharmaceutically effective amount of an interferon-associated antigen binding protein typically is an amount sufficient to mediate one or more of: a reduction of HBeAg release from an HBV-infected cell; a reduction of pgRNA transcription in an HBV-infected cell; and a stimulation of the IFN signaling pathway in an infected cell. Of course, the pharmaceutical compositions of the present invention may be administered in single or multiple doses to provide for a pharmaceutically effective amount of the interferon-associated antigen binding protein.

[00254] In keeping with the scope of the present invention, interferon-associated antigen binding proteins, or nucleic acid sequences expressing any of them, may be administered to a human or other animal in accordance with the aforementioned methods of treatment in an amount sufficient to produce a therapeutic effect. The interferon-associated antigen binding proteins, or nucleic acid sequences expressing any of them, can be administered to such human or other animal in a conventional dosage form prepared by combining the interferon-associated antigen binding proteins, or nucleic acid sequences expressing any of them, with a conventional pharmaceutically acceptable carrier or diluent according to known techniques. It will be recognized by one of skill in the art that the form and character of the pharmaceutically acceptable carrier or diluent is dictated by the amount of active ingredient with which it is to be combined, the route of administration and other well-known variables. Those skilled in the art will further appreciate that a cocktail comprising one or more species of interferon-associated antigen binding proteins, or

nucleic acid sequences expressing any of them, described in the current invention may prove to be effective.

[00255] It is to be understood that the methods described in this invention are not limited to particular methods and experimental conditions disclosed herein as such methods and conditions may vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to be limiting.

[00256] Furthermore, the experiments described herein, unless otherwise indicated, use conventional molecular and cellular biological and immunological techniques within the skill of the art. Such techniques are well known to the skilled worker, and are explained fully in the literature. See, e.g., Ausubel, et al., ed., Current Protocols in Molecular Biology, John Wiley & Sons, Inc., NY, N.Y. (1987-2008), including all supplements, Molecular Cloning: A Laboratory Manual (Fourth Edition) by MR Green and J. Sambrook and Harlow et al., Antibodies: A Laboratory Manual, Chapter 14, Cold Spring Harbor Laboratory, Cold Spring Harbor (2013, 2nd edition).

[00257] Unless otherwise defined, scientific and technical terms used herein have the meanings that are commonly understood by those of ordinary skill in the art. In the event of any latent ambiguity, definitions provided herein take precedent over any dictionary or extrinsic definition. Unless otherwise required by context, singular terms shall include pluralities and plural terms shall include the singular. The use of "or" means "and/or" unless stated otherwise. The use of the term "including", as well as other forms, such as "includes" and "included," is not limiting. The use of the term "comprising" shall include the term "consisting of" unless stated otherwise.

[00258] Generally, nomenclature used in connection with cell and tissue culture, molecular biology, immunology, microbiology, genetics and protein and nucleic acid chemistry and hybridization described herein is well-known and commonly used in the art. The methods and techniques provided herein are generally performed according to conventional methods well known in the art and as described in various general and more specific references that are cited and discussed throughout the present specification unless otherwise indicated. Enzymatic reactions and purification techniques are performed according to manufacturer's specifications, as commonly accomplished in the art or as described herein. The nomenclatures used

in connection with, and the laboratory procedures and techniques of, analytical chemistry, synthetic organic chemistry, and medicinal and pharmaceutical chemistry described herein are those well-known and commonly used in the art. Standard techniques are used for chemical syntheses, chemical analyses, pharmaceutical preparation, formulation, and delivery, and treatment of patients.

[00259] The section headings used herein are for organizational purposes only and are not to be construed as limiting the subject matter described. The contents of the articles, patents, and patent applications, and all other documents and electronically available information mentioned or cited herein, are hereby incorporated by reference in their entirety to the same extent as if each individual publication was specifically and individually indicated to be incorporated by reference. Applicants reserve the right to physically incorporate into this application any and all materials and information from any such articles, patents, patent applications, or other physical and electronic documents.

[00260] While the present invention has been described with reference to the specific embodiments thereof, it should be understood by those skilled in the art that various changes may be made and equivalents may be substituted without departing from the true spirit and scope of the invention using this disclosure as a guide. Having now described certain embodiments in detail, the same will be more clearly understood by reference to the following examples, which are included for purposes of illustration only and are not intended to be limiting.

EXAMPLES

EXAMPLE I

Generation of Interferon-Fused Antibodies (IFA) based on agonistic anti-CD40 antibody CP870,893 and characterization on reporter cells

I.a - IFA design

[00261] The sequence combinations of exemplary IFAs, designed with CP870,893 agonistic anti-CD40 antibody as backbone antibody, with the location of IFNs and the nature of the linkers are listed in **Table 7** and **Table 9.** IFN was fused via a linker at the N- or the C-terminal part of the Light Chain (LC) or the Heavy Chain (HC), as indicated in **Table 7**. Nucleic acids encoding the HC, the LC or the fusions were synthesized with optimized mammalian expression codons and cloned into a eukaryotic expression vector such as pcDNA3.1 (Invitrogen). **Fig. 2A** depicts an exemplary map of a pcDNA3.1 plasmid encoding Seq ID NO 32 under the control of the pCMV promoter.

I.b - IFA production

[00262] The Freestyle 293-F cells (Invitrogen) were transiently cotransfected with plasmids encoding both HC and LC at a HC/LC ratio of 4/6. Six days after transfection, the supernatant was collected, centrifuged and filtered through 0.22 µm filters. Purification process was performed in two purification steps, on AktaExpress chromatography system (GE Healthcare) using Protein A MabSelect Sure 5mL 1.6/2.5 cm column (GE Healthcare) at a Flow rate of 5 mL/min. Sample binding was done in D-PBS1X pH 7.5 buffer, and elution with Glycine/HCl 0.1 M pH 3.0 buffer. Elution peak was stored in a loop then injected on HiTrap desalting 26/10 column (GE Healthcare) with a flow rate of 10 mL/min in D-PBS1XpH 7.5 buffer. Elution peak was collected on a 96-well microplate (2 mL fractions). Pool was performed according to the UV peak profile. After filtration on 0.22 µm filters (Sartorius MiniSart), quality control was performed including Bacterial Endotoxins using

Endosafe® nexgen-PTS™ (Charles River), size exclusion Chromatography: using SEC 200 Increase 10/300 column (GE Healthcare) to determine purity and oligomers and SDS-PAGE under reducing and non-reducing conditions on NuPAGE gel System (Invitrogen) in MES SDS running buffer. The production yield is indicated in **Table 9**. For some IFAs, the production yield was very low. In that case, the agonistic CD40 activity and the IFN activity were assessed directly using the supernatant containing IFAs without any further purification.

[00263] Reduced SDS-PAGE analysis of purified IFAs indicated the presence of two major bands corresponding to the HC and the LC. When the IFN (whatever the IFN family member) was fused to the HC, a shift of its molecular weight was observed and the same phenomenon was observed for the LCs fused with any IFN **(Fig. 2B).**

I.c - IFA characterization on reporter cells

[00264] HEK-Blue™ CD40L cells (InvivoGen Cat. #: hkb-cd40) or HEK-Blue™ IFN-α/β cells (InvivoGen, Cat. #: hkb-ifnαβ), were used to monitor, respectively, the activation of the NFκB pathway by CD40 agonists or of the IFN pathway induced by type I-IFN.

[00265] HEK-Blue™ CD40L cells were generated by stable transfection of HEK293 cells with the human CD40 gene and a NFκB-inducible Secreted Embryonic Alkaline Phosphatase (SEAP) construct (Invivogen) to measure the bioactivity of CD40 agonists. Stimulation of CD40 leads to NFκB induction and then production of SEAP, which is detected in the supernatant using QUANTI-Blue™ (Invivogen, Cat. # rep-qbs2).

[00266] HEK-Blue™ IFN-cells are designed to monitor the activation of the JAK/STAT/ISGF3 pathways induced by type I-IFNs. Activation of this pathway induces the production and release of SEAP. Levels of SEAP are readily assessable in the supernatant using QUANTI-Blue™.

[00267] HEK-Blue™ IFN-α/β are used to monitor the activity of human IFNα or IFNβ.

[00268] Cells were seeded in 96-well plates (50,000 cells per well) and stimulated with the indicated concentration for each IFA or controls and incubated at 37 °C for

24 h. Supernatants were then collected and levels of SEAP were quantified after incubation of the supernatant for about 30 min with QuantiBlue™ and Optical Density (O.D.) assessment at 620 nm on an Ensight plate reader or PheraStar (Lab Biotech).

[00269] HEK-Blue™ Dual IFN-γ cells (InvivoGen, Cat. #: hkb-ifng) or HEK-Blue™ IFN-λ (InvivoGen, Cat. #: hkb-ifnl) may be used to respectively monitor the activity of type II- and type III-IFNs. HEK-Blue™ IFN-λ cells are designed to monitor the activity of IFNλ. HEK-Blue™ Dual IFN-γ cells allow the detection of bioactive human IFNγ.

I.d - Functional activities of IFNα/β-based IFAs on reporter cells

[00270] **Fig. 3** shows examples of dose responses of IFAs, where IFNβ or a mutated version thereof as specified in **Tables 7** was fused to the HC as indicated in **Table 7**, on HEK-Blue™ **CD40L** (**Figs. 3A-3B**) and HEK-Blue™ IFN-α/β cells (**Figs. 3C-3D**). Agonistic anti-CD40 activities of IFAs are summarized in **Table 9** and examples are shown in **Fig. 3A** and **Fig. 3B**. Results indicate that all tested IFAs are functional to activate both the CD40 pathway and the IFN-α/β pathway in a dose dependent manner. For fusions to the C-terminus of the HC or LC, the EC_{50} values for agonistic CD40 are ranging from 11.1 ng/mL to 192 ng/mL (**Table 9**). The mean EC_{50} value for the parental antibody is 48ng/mL and 57ng/mL in the experiment shown in **Fig. 3.** IFAs with the IFN fused to the N-terminus of the HC or the LC were also able to activate the CD40 pathway, but the precise EC_{50} values could not be determined for these IFAs since the activity was directly determined from the supernatant and not using purified proteins (**Fig. 3B**).

[00271] The IFN activity of various IFAs is summarized in **Table 9** and examples are shown in **Figs. 3C** to **3D**. For fusions of IFNβ or mutated IFNβ (as specified in **Table 7**) to the C-terminus of the HC or LC, the IFN activity is variable depending on the linker sequence with EC_{50} values ranging from 0.14 ng/mL to 4.5 ng/mL (**Fig. 3C** and **Table 9**). **Fig. 3D** shows that IFAs with IFNβ fused to the N-terminal part exhibit high IFN activity. The parental antibody used as negative control did not show any activity, whereas recombinant IFNβ did show a strong dose-dependent response.

Altogether, these results demonstrate that fusion of IFNβ or a mutated version thereof as specified in **Table 7** to an antibody, regardless the location, maintain both biological functions, although with differences in terms of potencies.

[00272] Fig. 4 shows examples of dose responses of IFAs, where IFNα was fused to the HC or the LC as indicated in **Table 7**, on HEK-Blue™ CD40L (**Fig. 4A** and **Fig.4 C**) and HEK-Blue™ IFN-α/β cells (**Fig. 4B** and **Fig. 4D**). Results indicate that all tested IFAs are functional to activate both the CD40 pathway and the IFNα/β pathway in a dose-dependent manner. Surprisingly, for all the IFNα-based IFAs, the potency on CD40 pathway was reproducibly higher than that of the parental antibody. The EC_{50} values for IFNα-based IFAs ranged from 11.1 ng/mL to 22.7 ng/mL and the EC_{50} for CP870,893 ranged from 30 ng/mL to 80 ng/mL (mean EC_{50} value: 48 ng/mL).

[00273] The IFN activity of IFAs is variable depending on the linker sequence with EC_{50} values ranging from 1.6 ng/mL to 5.1 ng/mL. In the same assay, PEGylated IFNα2a (Pegasys®) was also active in a dose-dependent manner with an EC_{50} value of around 1 ng/mL.

I.e – Generation and characterization of IFAs without the Fc region

[00274] Suitable constructs according to the invention can also be interferon-associated antigen binding proteins without an Fc region. A construct encoding the heavy chain of the fab fragment of CP870,893 fused to a TEV-His tag was designed (SEQ ID NO 50) and cloned into the expression plasmid pcDNA3.1. This construct is cotransfected in HEK cells as described earlier, with LCs fused via different linkers to different IFNs such as SEQ ID NO 28, SEQ ID NO 29, SEQ ID NO 34, SEQ ID NO 35, SEQ ID NO 36, SEQ ID NO 37, SEQ ID NO 41, SEQ ID NO 42, or SEQ ID NO 43. Proteins and/or supernatants are evaluated in reporter cells and/or their effect on HBV infection in PHHs. It will be understood by one of skill in the art that constructs for use in therapy will no longer contain the TEV-His tag. These constructs are likewise embodiments of the invention. Interferon-associated antigen binding proteins without the Fc part will be active against HBV infection. Two IFAs were then produced and their functional characterization is described in Example V:

IFA50: (SEQ ID NO 41) + (SEQ ID NO 50) and IFA51: (SEQ ID NO 42) + (SEQ ID NO 50).

EXAMPLE II

Effect of IFAs on HBV infected primary hepatocytes

II.a - Effect of IFAs on HBV infection in primary human hepatocytes

[00275] The effect of IFAs on HBV infection in primary human hepatocytes (PHHs) was investigated. PHH cells were plated in 96-well plates (70,000 cells/well) in William's E GlutaMAX media (32551-020, Gibco) supplemented with 10% fetal calf serum (FCS) (SH30066.02, Hyclone), insulin (19278-5ML, Sigma), hydrocortisone (H2270-100MG, Sigma) and Penicillin/Streptomycin (15140, Gibco). Four hours later, cells were rinsed and media was replaced. The next day, media was replaced by matrigel-containing media (0.25mg/mL; 356231, Corning). Cells were infected 48 hours after plating with a MOI (Multiplicity Of Infection) of 500 to 1,000 vge/cell (viral genome equivalent) in InVitroGRO HI medium (Z99009, Bioreclamation IVT) supplemented with 5% FCS, 4% PEG 8000 (81268, Sigma), 2% DMSO (DMSO-100ML, Sigma) and 1% Penicillin/Streptomycin. Sixteen hours post-infection, cells were washed three times with PBS. Four days after infection, cells were kept untreated or treated with serially diluted IFAs as indicated in the figures. Three days after treatment, culture supernatants were collected and kept at -80 °C for further protein detection.

II.b. - HBV e-antigen (HBeAg) release Assessment

[00276] HBV e-antigen (HBeAg) levels in the cell culture supernatant were measured using ELISA as described by the manufacturer and results expressed in PEI Units (HBeAg CLIA 96T/K: CL0312-2; Autobio) or in luminescence.

II.c. - HBV s-antigen (HBsAg) release Assessment

[00277] Quantification of the HBsAg in the supernatant was carried out by following the protocol of the AutoBio HBsAg CLIA kit (# CL0310-2), the main steps were: first the samples were diluted 1/5 in 1X PBS. Then 50 µL of standards, controls, and diluted samples were placed in the wells. 50 µL of "Enzyme conjugate" solution were added to each well, followed by an incubation of one hour at 37 °C. Subsequently, the plates were washed 6 times with 300 µL of washing solution from the kit using the plate washer. Then 50 µL of "Substrate Solution" (volume-to-volume mix in reagents A and B) was added in each well and an incubation of 10 minutes in the dark was carried out. The plates were then read on a PHERASTAR microplate reader (BMG Labtech) in Luminescence mode.

II.d. - pgRNA quantification

[00278] The qPCR technique was used to compare the level of expression of pgRNA from infected cells treated with test compounds. pgRNA quantification from infected cells was done in 96-well plates with the QuantStudio 12K Flex. The cDNA was obtained by RT, followed by qPCR with TaqMan Fast Virus assay in one step (ThermoFisher cat# 4444434). The results were processed by the ΔΔCt method and normalized with the housekeeping gene GUSB in duplex. The pgRNA was amplified using the following primers and probe: (forward: CCTCACCATACTGCACTCA, reverse: GAGGGAGTTCTTCTTCTAGG, AGTGTGGATTCGCACTCCTCCAGC as a probe). The GUSB gene was amplified using the TaqMan assay from Thermo Fisher (Hs99999908-m1).

II.e. - CXCL10 release

[00279] CXCL10 release was assessed using an ELISA kit according to the manufacturer's instruction (BioLegend 439904). Samples were diluted 1/50 and luminescence was assessed on an EnSight microplate reader at 450nm.

II.f - Effect of IFNα/β based IFAs on HBV infection

[00280] Several IFAs were tested for their abilities to reduce HBeAg secretion after infection of PHH with HBV. In **Fig. 5**, IFAs with IFNβ or a mutated version thereof fused at the C-terminus of the LC were used. Results indicate that all the tested IFAs strongly reduce HBeAg release. Indeed, even at the lowest concentration tested (1 ng/mL), depending on the IFA, 70% to 90% inhibition of HBeAg release was observed, demonstrating that they are endowed with potent anti-viral effect. It is noteworthy that 100% inhibition could not be reached in this experiment, since treatment started four days after infection and at that time an existing pool of HBeAg (mRNA and protein) is already present in the cell and continue to be produced thereafter.

[00281] The effect of IFAs fused to IFNα were also tested in HBV-infected PHHs. **Fig. 6** shows that these IFAs are very potent on HBV infection with EC_{50} values ranging from 0.06 ng/mL to 0.2 ng/mL for IFAs with IFNα2a fused at the C-terminus of the HC (IFA25: 0.16 ng/mL, IFA26: 0.1 ng/mL; IFA27: 0.06 ng/mL; and IFA38: ~0.2 ng/mL (~2.2 pM); **Fig. 6A** and **Fig. 6C**) and from 0.15 ng/mL to 0.36 ng/mL for IFAs with IFNα2a fused at the C-terminus of the LC (IFA28: 0.36 ng/mL; IFA29: 0.15 ng/mL; IFA30: 0.31 ng/mL; and IFA39: ~0.3 ng/mL (~3 pM); **Fig. 6B** and **Fig. 6C**). To compare the antiviral effect of Pegasys to IFA38 and IFA39, results are expressed in pM and indicate that EC_{50} for Pegasys is ~250 pM in comparison to ~2.2 pM for IFA38 and ~3 pM for IFA39, indicating that IFAs are much more potent than Pegasys.

II.g - Short terms treatment is sufficient to induce potent anti-viral activity

[00282] To assess the effect of short term IFA treatment of primary hepatocytes infected with HBV, cells were infected and incubated for 4 days, treated with IFA25, IFA27, IFA28, IFA30 or with Pegasys in a dose dependent manner for 24h, washed and then incubated with fresh medium without any treatment. After 3 days, supernatants were collected to assess the level of HBeAG (**Fig. 6E**), HBsAG (**Fig. 6F**) and CXCL10 (**Fig. 6H**) release and cells were lysed and RNA extracted for the quantification of pgRNA (**Fig. 6G**). Results indicate that all tested IFAs were able to

inhibit HbeAG and HBsAG release as well as pgRNA expression in a dose dependent manner. Pegasys alone was only able to inhibit HBeAG release and reduce pgRNA levels. In this respect, IFAs are at least 2 logs more active than Pegasys on viral parameters. Surprisingly, although all tested IFAs showed a dose dependent inhibition of HBsAg release, no reduction was observed with Pegasys even at the highest concentration. Analysis of CXCL10, a biomarker of the IFN pathway, showed that IFAs are also much more potent than Pegasys.

EXAMPLE III

Cytokine Release

III.a - Cytokine Release Assessment (CRA) from human Whole blood cells

[00283] Whole blood cells (WBC) *ex vivo* stimulation assay was used to investigate release of cytokines following IFA stimulation. WBC were collected from four healthy donors, diluted 1/3 in RPMI1640 (72400-021, Gibco) and distributed in sterile reaction tubes (300 µl). Cells were left unstimulated, stimulated with LPS (LipoPolySaccharide) K12 (tlrl-eklps, Invivogen) at 10 ng/mL as a positive control or with IFAs at 1 µg/mL and incubated for 24 h at 37 °C. Supernatants were then collected and frozen at -20 °C until the day of analysis.

[00284] Human pro-inflammatory cytokines were analyzed using multiplexing MSD assay (K15067L-4) which measures Tumor Necrosis Factor (TNF)-α, Interleukin (IL)-1β, IL-2, IL-6, IL-8, IL-10, IL-12/IL-23p40 and IFNγ. MSD plates were analyzed on the 1300 MESO QuickPlex SQ120 apparatus (MSD).

[00285] Fig. 7 depicts exemplary results from an *in vitro* Cytokine Release Assessment of Human WBC either non-stimulated, treated with LPS or with IFA1.

[00286] [0021] Further results from testing IFNβ- /mutated IFNβ- and IFNα- based IFAs are summarized in **Tables 11a and 11b**. Results show that for all donors, LPS induces very high level of the inflammatory cytokines (IL-1β, TNF-α, IL-6, IL-12p40 and IFNγ). It also induced IP10 (CXCL10) which is a biomarker of the IFN pathway and moderate level of IL-10. Two IFNβ- (**Table 11a**) and six IFNα- (**Table 11b**)

based IFAs were tested. All of them induced the biomarker IP10. However, they did not induce IL-10, IL-1β and IL-2, and they induced only very low to moderate level of IFNγ, IL-6 and TNF-α, thus suggesting a favorable safety profile with regard to the induction of inflammatory cytokines.

EXAMPLE IV

Pharmacokinetic studies

IV.a - ELISA assay development for IFA quantifications

[00287] For the ELISA quantification 96-wells plates (PLATES 96 wells Maxisorp, THERMO Scientifique; 442404) were coated overnight at 4 °C with 100 µl of recombinant human CD40/TNFRSF5 Fc Chimera Protein, consisting of the extracellular domain of human CD40 fused to the Fc part of human IgG1 (CD40-Fc; R&D Systems; 1493-CDB-050) at 0.5 µg/mL in Sodium Carbonate (0.05 M, pH 9.6, C-3041, Sigma). After emptying by flipping, plates were then incubated for 1 hour at 37 °C with PBS - 0.05% Tween20 – 1% Milk (SIGMA; 70166-500g) followed by washing with PBS-0.05% Tween20. Samples and controls (100 µl of 1/2 serial dilutions) were then incubated for 90 minutes at 37 °C followed by three washes (PBS - 0.05% Tween20) and incubation with a secondary anti-IgG2-conjugate HRP (1/5000, ab99779, Abcam) antibody or anti-IFNα conjugate HRP (1/1000, eBIOSCIENCE/ Invitrogen; BMS216MST) in PBS - 0.05% Tween20 - 1% Milk. After three washes with PBS, 0.05% Tween2, TMB (Tetramethylbenzidin, Tebu Bio; TMBW-1000-01) was added and the plates incubated for 20 minutes in the dark. The reaction was stopped by adding 1M HCl. Plates were read at 450-650 nm with an Ensight plate reader (Perkin Elmer). Quantification of Pegasys was assessed using similar protocol steps but using human IFNα matched antibody pairs from eBioscience/Invitrogen. Capture was performed using 100 µL of human anti-IFNα antibody (eBioscience/Invitrogen; BMS216MST), at 1 µg/mL in sodium carbonate (0.05 M,pH 9.6, C-3041, Sigma). For the detection, a secondary anti-IFNα conjugate

HRP antibody (1/1000, Affymetrix eBioscience/BMS216MST; 15501707) in PBS - 0.05% Tween20 - 1% Milk was applied.

IV.b - in vivo Bioavailability in mice

[00288] To determine the PK parameters, CP870,893, IFA25, IFA26, IFA27, IFA28, IFA29 and IFA30 were administrated at 0.5 mg/kg and Pegasys at 0.3 mg/kg i.v. bolus to male CD1-Swiss mice and blood samples were collected at different time points. Examples of quantification of circulating molecules using the ELISA approach described above and revealed with anti-IFNα-conjugated HRP are shown in **Fig. 8A** and **8B**, while examples of quantification revealed with anti-IgG2-conjugated HRP are shown in **Fig. 8C**; Pegasys quantification is shown in **Fig. 8D**. In one set of experiments summarized in **Table 12A**, PK parameters for CP870,893 were explored in a 7-day experiment and those for IFA27, IFA29 and IFA30 in 10-day experiments (quantification for IFA27 was performed using 2 different ELISA approaches). In another set of experiments summarized in **Table 12B**, the PK parameters for CP870,893 and IFA25, IFA26, IFA28 and Pegasys were explored in 21-day experiments (quantification for IFA25 was performed using 2 different ELISA approaches).

[00289] After a short distribution phase, the pharmacokinetic profiles of IFAs are characterized by a long serum half-life ranging from 116 to 218 h **(Table 12A and Table 12B)**. Very similar PK profiles were obtained for the 6 tested IFAs with high circulating level even ten days after single dose administration. The pharmacokinetic parameters summarized in **Table 12A/B** indicate that these IFAs surprisingly circulate in the blood with higher systemic exposure (AUC (0-inf)) ranging from 1033 µg.h/mL to 2552 µg.h/mL for IFAs in comparison to 590 or 797 µg.h/mL, respectively, for the parental antibody CP870,893 (up to 3.2 fold), also reflecting lower clearance values for IFAs. The volume of distribution Vss was low and ranked from 50 to 105 mL/kg, slightly higher than the plasma vascular volume (50 mL/kg) in this species. For all IFAs, the clearance was ranked as low (0.28 to 0.49 mL/h/kg). Interestingly, the clearance of Pegasys (1.4 mL/hr/kg) is up to 7 fold higher than clearance of IFAs (e.g., 0.2 mL/hr/kg for IFA27) demonstrating a higher systemic exposure of IFAs.

Example V

V.a - Functional activities of IFAs without Fc region on reporter cells and HBV infection

[00290] To determine whether the Fc part of IFAs is needed for activity, fusions of IFNα to the C-terminal part of the LC associated with a Fab fragment of the HC were designed and produced. IFNα was linked to the LC part with a (G4S)2 (IFA50) or (G4S)3 (IFA51) linker.

[00291] Evaluation on HEK-Blue™ CD40L cells demonstrated that such IFAs still exhibit agonistic CD40 activity (**Fig. 9A**) and activate the CD40 pathway with an EC_{50} value of about 128 ng/ml (IFA 50) and 123 ng/mL (IFA51), respectively.

[00292] Evaluation of the IFN activity on HEK-Blue™ IFN-α/β cells showed that both tested IFAs exhibit IFN activity (**Fig. 9B**). EC_{50} values are reported in **Table 9B** and are about 1.36 ng/ml for IFA50 and 1.43 ng/mL for IFA51.

[00293] Both IFAs were tested on HBV infection as described earlier and both IFAs exhibit potent anti-viral activity with EC_{50} values of about 4.1 pM (IFA50) and 2.7 pM (IFA51), respectively.

V.b - Functional activities of IFNε based IFAs on reporter cells and on HBV infection

[00294] Fusions of CP870,893 to a third type I interferon (IFN epsilon; IFNε) have also been designed and produced. Such IFAs were tested on HEK-Blue™ CD40L cells and it could be demonstrated that they maintain agonistic CD40 activity. Results for one such IFA (IFA49) are shown in **Fig. 10A**. Evaluation on HEK-Blue™ hIFN-α/β cells (which are in fact activated by any type I interferon) showed that IFA49 is also able to activate the IFN-I-pathways (**Fig. 10B**). EC_{50} values are reported in **Table 9B**. In addition, IFA49 was also tested on HBV infection in primary hepatocytes and showed similar activity to Pegasys (**Fig. 10C**).

[00295] These results demonstrate that IFAs with IFNε maintain both IFN and agonistic CD40 activity (i.e., are bifunctional) and have antiviral activity.

V.c - Functional activities of IFNω based IFAs on reporter cells and on HBV infection

[00296] Fusions of CP870,893 to a fourth type I interferon (IFN omega; IFNω) have also been designed and produced. Such IFAs were tested on HEK-Blue™ CD40L cells and results demonstrated that they maintain agonistic CD40 activity. Results for one such IFA (IFA46) are shown in **Fig. 11A**. Evaluation on HEK-Blue™ hIFN-α/β cells (which are in fact activated by any type I interferon) showed that IFA46 is also able to activate the IFN-I-pathways (**Fig. 11B**). EC_{50} values are reported in **Table 9B**. In addition, IFA46 was also tested on HBV infection in primary hepatocytes and showed similar activity to Pegasys (**Fig. 11C**).

[00297] These results demonstrate that IFAs with IFNω maintain both IFN and agonistic CD40 activity (i.e., are bifunctional) and have antiviral activity.

V.d - Functional activities of IFNγ based IFAs on reporter cells on HBV infection

[00298] Fusions of CP870,893 to type II Interferon (IFN gamma; IFNγ) have also been designed and produced. Evaluation of these IFAs on HEK-Blue™ CD40L cells demonstrate that they maintain agonistic CD40 activity, regardless of whether IFNγ is linked to the C-terminal part of the LC (IFA42) or of the HC (IFA43) (**Fig. 12A**). Evaluation of these IFAs on HEK-Blue™-IFNγ cells (**Fig. 12B**) showed that they are also able to activate the IFNγ-pathway. IFNγ activity differed somewhat between IFA42 (EC_{50}: 15 ng/ml) and IFA43 (EC_{50}: < 0.01 ng/ml). EC_{50} values are reported in **Table 9B**. In addition, IFA42 and IFA43 were tested in a dose dependent manner on HBV infection in primary hepatocytes as described earlier. Results indicate that both IFAs reduce HbeAg release in a dose dependent manner (**Fig. 12C**), indicating that IFAs with type II-IFN are active on HBV infection.

[00299] Taken together, these results demonstrate that IFAs with IFNγ maintain both IFN and agonistic CD40 activity (i.e., are bifunctional) and have anti-viral activity.

V.e - Functional activities of IFNλ based IFAs on reporter cells and on HBV infection

[00300] Fusions of CP870,893 to type III Interferon (IFN lambda; IFNλ) have also been designed and produced. These IFAs were tested on HEK-Blue™ CD40L cells and results demonstrated that they also maintain agonistic CD40 activity, regardless

of whether IFNλ is linked to the C-terminal part of the LC (IFA44) or of the HC (IFA45) (**Fig. 13A**). Evaluation of these IFAs on HEK-Blue™-IFNλ cells showed that they are also able to activate the IFNλ-pathway (**Fig. 13B**). EC_{50} values are reported in **Table 9B**. These results also demonstrate that IFAs with IFNλ maintain both IFN and agonistic CD40 activity (i.e., are bifunctional).

[00301] IFA44 and IFA45 were tested in a single dose in comparison to Pegasys on HBV infection in primary hepatocytes as described earlier. Results indicate that both types of IFAs reduce HbeAg release by 65% and 78%, respectively. Under these condition Pegasys inhibited HbeAg release by 81%. These results indicate that IFAs with type III IFN are active on HBV infection with EC_{50} values for both tested IFAs < 10 nM (**Fig. 13C**).

Example VI

Generation of Interferon-Fused Antibodies (IFA) based on anti-CD40 antibody 3G5 and characterization on reporter cells

VI.a - IFA design

[00302] The sequence combinations of exemplary IFAs, designed with 3G5 anti-CD40 antibody (Celldex) as backbone antibody, with the location of IFNs and the nature of the linkers are listed in **Table 7** and **Table 10.** IFN was fused via a linker at the C-terminal part of the Light Chain (LC) or the Heavy Chain (HC), as indicated in **Table 7**. Nucleic acids encoding the HC, the LC or the fusions were synthesized with optimized mammalian expression codons and cloned into a eukaryotic expression vector such as pcDNA3.1 (Invitrogen).

VI.b - IFA production

[00303] IFA production was performed as described earlier and the production yield is indicated in **Table 10**. For some IFAs, the production yield was very low, mainly for the fusion of IFNβ to the C-terminal part of the LC. For these IFAs, the agonistic

CD40 and the IFN activities were assessed directly using the supernatant containing IFAs without any further purification. Reduced SDS-PAGE analysis of purified IFAs indicated the presence of two major bands corresponding to the HC and LC. When IFN was fused to the HC, a shift of its molecular weight was observed. (**Fig. 14**).

VI.c- Functional activities of IFNα/β-based IFAs on reporter cells

[00304] Characterization of 3G5 IFAs on reporter cells was done on HEK-Blue™ CD40L (**Fig. 15A-B, and Fig. 16A**) and HEK-Blue™ IFN-α/β cells (**Fig. 15C-D, and Fig. 16B**) as previously described **(see I.c)**.

VI.c.1. IFNβ based IFAs

[00305] Fig. 15- shows examples of dose responses of IFAs, where IFNβ was fused to the HC or the LC of 3G5, on HEK-Blue™ CD40L and HEK-Blue™ IFN-α/β cells (**Fig. 15**). Results summarized in **Table 10** indicate that all tested IFNβ-based IFAs are functional and able to activate both the CD40 pathway and the IFNα/β pathway in a dose-dependent manner.

[00306] Examples of CD40 activity are shown in **Fig. 15A and Fig. 15B**. Fusion of IFNβ to the C-terminal part of the HC demonstrates high variable anti-CD40 activity and in all cases lower than the parental antibody with EC_{50} values ranging from 30 ng/mL to 190.5 ng/mL (**Fig. 15A** and **Table 10**). The mean EC_{50} value for the parental 3G5 antibody is 9.3 ng/mL.

[00307] For fusions on the C-terminal part the LC, the production yield was very low and the activity was assessed using supernatant-containing IFAs after overexpression in HEK-cells. Evaluation of these supernatants on HEK-Blue™ CD40L (**Fig. 15B**) demonstrates that these IFAs are active on CD40 pathway. For 3G5, the agonistic anti-CD40 activity is still detected when supernatant was diluted 300 times. Conversely, a 1/10 dilution was needed for the IFAs-containing supernatants to observe an activity (**Fig. 15B**).

[00308] The IFN activity of IFAs were tested on HEK-Blue™ IFN-α/β cells and results are summarized in **Table 10.** Examples are shown in **Fig. 15C-D**. For fusions of IFNβ at the C-terminal part of the HC, the IFN activity is variable depending on the linker sequence with EC_{50} values ranging from 0.45 ng/mL to 10,3 ng/mL (**Fig. 15C**). For IFAs with IFNβ fusion at C-terminal part of the LC-containing supernatant, IFN activity is still detected even after a 10000-fold dilution of the supernatant (**Fig. 15D**).

VI.c.2. IFNα based IFAs

[00309] Fig. 16 shows examples of dose responses of IFAs, where IFNα was fused to the HC of 3G5, on HEK-Blue™ CD40L (**Fig. 16A**) and HEK-Blue™ IFNα/β cells (**Fig. 16B**).

[00310] Results indicate that all IFAs display a functional activation of both the CD40 pathway and the IFNα/β pathway in a dose-dependent manner (mean EC_{50} values are reported in **Table 10**).

[00311] For all the IFNα-based IFAs, the potency on CD40 pathway was similar to the parental antibody with the mean EC_{50} values ranging from 11.74 ng/mL to 14.2 ng/mL (**Fig. 16A and Table 10**). The mean EC_{50} value for the parental 3G5 antibody is 9.3ng/mL.

[00312] The IFN activities of IFNα-based IFAs were tested on HEK-Blue™ IFN-α/β cells and demonstrate very high activity. The mean EC_{50} values for the IFN activity of these IFAs ranged from 0.04 ng/mL to 0.12 ng/mL (**Fig. 16B and Table 10**).

VI.d – Generation and characterization of IFAs without the Fc region

[00313] Suitable constructs according to the invention can also be interferon-associated antigen binding proteins without an Fc region. A construct encoding the heavy chain of the Fab fragment of 3G5 fused to a TEV-His tag was designed (SEQ ID NO 65) and cloned into the expression plasmid pcDNA3.1. This construct is cotransfected in HEK cells as described earlier, with LCs fused via different linkers to IFNs such as SEQ ID NO 70, or SEQ ID NO 71. Proteins and/or supernatants are evaluated in reporter cells and/or their effect on HBV infection in PHHs. It will be

understood by one of skill in the art that constructs for use in therapy will no longer contain the TEV-His tag. These constructs are likewise embodiments of the invention. Interferon-associated antigen binding proteins without the Fc part will be active against HBV infection.

Example VII

VII.a - Effect of IFNα/β based IFAs on HBV infection

VII.a.1. IFNβ based IFAs

[00314] IFAs fused to IFNβ were tested for their ability to reduce HBeAg release after infection of PHHs with HBV as described earlier and examples are shown in **Fig. 17A**. Results indicate that these IFAs are active on HBV infection. For all tested IFAs, a dose-dependent inhibition is observed with 12% to 52% of reduction obtained at 1 ng/mL and a maximum reduction of about 85% observed with IFA109 at 100 ng/mL. 100% inhibition could not be reached since treatment started four days after infection and at that time, an existing pool of HBeAg (mRNA and protein) is already present in the cell and continue to be produced thereafter.

VII.a.2. IFNα based IFAs

[00315] IFAs fused to IFNα were also tested for their ability to reduce HBeAg release after infection of PHH with HBV as described earlier and examples are shown in **Fig. 17B**. Results indicate that these IFNα-based IFAs are very potent on HBV infection. For all tested IFAs, a dose-dependent inhibition was also observed with a 61% to 80% reduction obtained at 1 ng/mL and a maximal reduction (between 85% and 92%) was almost reached at 100 ng/mL for all IFAs. These demonstrate that IFNα-based IFAs are very potent anti-HBV antiviral molecules.

Example VIII

Cytokine Release Assay (CRA) from human Whole blood cells

[00316] A WBC ex vivo stimulation assay was used to investigate release of cytokines following IFA stimulation as described previously **(see III.a)**. An example with IFA109 is shown in **Fig. 18** and **Table 13**. The results indicate that all IFAs induce CXCL10 release. They did not induce IL-10, IL-1β and IL-2, and they induced only very low to moderate level of IFNγ, IL-6 and TNF-α, thus suggesting a favorable safety profile with regard to the induction of inflammatory cytokines.

Equivalents

[00317] The invention may be embodied in other specific forms without departing from the spirit or essential characteristics thereof. The foregoing embodiments are therefore to be considered in all respects illustrative rather than limiting of the invention. Scope of the invention is thus indicated by the appended claims rather than by the foregoing description, and all changes that come within the meaning and range of equivalency of the claims are therefore intended to be embraced herein.

Items

[00318] In view of the above, it will be appreciated that the present invention also relates to the following **items**:

1. An interferon-associated antigen binding protein comprising
(I) an agonistic anti-CD40 antibody or an agonistic antigen binding fragment thereof, and
(II) an Interferon (IFN) or a functional fragment thereof
for use in treating hepatitis B virus (HBV) infection.

2. The interferon-associated antigen binding protein for the use of item 1, wherein the agonistic anti-CD40 antibody, or the agonistic antigen binding fragment thereof, comprises three light chain complementarity determining regions (CDRs) that are at least 90% identical to the CDRL1, CDRL2 and CDRL3 sequences within SEQ ID NO 3; and three heavy chain CDRs that are at least 90% identical to the CDRH1, CDRH2 and CDRH3 sequences within SEQ ID NO 6.

3. The interferon-associated antigen binding protein for the use of item 1 or 2, wherein the agonistic anti-CD40 antibody, or the agonistic antigen binding fragment thereof, comprises three light chain complementarity determining regions (CDRs) that are identical to the CDRL1, CDRL2 and CDRL3 sequences within SEQ ID NO 3; and three heavy chain CDRs that are identical to the CDRH1, CDRH2 and CDRH3 sequences within SEQ ID NO 6.

4. The interferon-associated antigen binding protein for the use of items 2 or 3, wherein each CDR is defined in accordance with the Kabat definition, the Chothia definition, the AbM definition, or the contact definition of CDR; preferably wherein each CDR is defined in accordance with the CDR definition of Kabat or the CDR definition of Chothia.

5. The interferon-associated antigen binding protein for the use of item 1, wherein the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof comprises
(a) a heavy chain or a fragment thereof comprising a complementarity determining region (CDR) CDRH1 that is at least 90% identical to SEQ ID NO 56, a CDRH2 that is at least 90% identical to SEQ ID NO 57, and a CDRH3 that is at least 90% identical to SEQ ID NO 58; and

(b) a light chain or a fragment thereof comprising a CDRL1 that is at least 90% identical to SEQ ID NO 52, a CDRL2 that is at least 90% identical to SEQ ID NO 53, and a CDRL3 that is at least 90% identical to SEQ ID NO 54.

6. The interferon-associated antigen binding protein for the use of item 1, wherein the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof comprises
(a) a heavy chain or a fragment thereof comprising a complementarity determining region (CDR) CDRH1 that is identical to SEQ ID NO 56, a CDRH2 that is identical to SEQ ID NO 57, and a CDRH3 that is identical to SEQ ID NO 58; and
(b) a light chain or a fragment thereof comprising a CDRL1 that is identical to SEQ ID NO 52, a CDRL2 that is identical to SEQ ID NO 53, and a CDRL3 that is identical to SEQ ID NO 54.

7. The interferon-associated antigen binding protein for the use of any one of the preceding items, wherein the agonistic anti-CD40 antibody, or the agonistic antigen binding fragment thereof, comprises a light chain variable region V_L comprising the sequence as set forth in SEQ ID NO 51, or a sequence at least 90% identical thereto; and/or a heavy chain variable region V_H comprising the sequence as set forth in SEQ ID NO 55, or a sequence at least 90% identical thereto.

8. The interferon-associated antigen binding protein for the use of any one of the preceding items, wherein a heavy chain of the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof, comprises a Fab region heavy chain comprising an amino acid sequence as set forth in SEQ ID NO 12, or a sequence at least 90% identical thereto.

9. The interferon-associated antigen binding protein for the use of any one of the preceding items, wherein the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof comprises a light chain (LC) that comprises a sequence as set forth in SEQ ID NO 3, or a sequence at least 90% identical thereto; and/or a heavy chain (HC) that comprises a sequence selected from the group consisting of SEQ ID NO 6, SEQ ID NO 9, SEQ ID NO 49 and SEQ ID NO 48, or a sequence at least 90% identical thereto.

10. The interferon-associated antigen binding protein for the use of item 9, wherein the HC comprises the sequence as set forth in SEQ ID NO 6, or a sequence at least 90% identical thereto.

11. The interferon-associated antigen binding protein for the use of item 9, wherein the HC comprises the sequence as set forth in SEQ ID NO 9, or a sequence at least 90% identical thereto.

12. The interferon-associated antigen binding protein for the use of item 9, wherein the HC comprises the sequence as set forth in SEQ ID NO 49, or a sequence at least 90% identical thereto.

13. The interferon-associated antigen binding protein for the use of item 9, wherein the HC comprises the sequence as set forth in SEQ ID NO 48, or a sequence at least 90% identical thereto.

14. The interferon-associated antigen binding protein for the use of any one of the preceding items, wherein the IFN or the functional fragment thereof is a human interferon.

15. The interferon-associated antigen binding protein for the use of any one of the preceding items, wherein the IFN or the functional fragment thereof is selected from the group consisting of a Type I IFN, a Type II IFN and a Type III IFN, or a functional fragment thereof.

16. The interferon-associated antigen binding protein for the use of any one of the preceding items, wherein the IFN or the functional fragment thereof is a Type I IFN, or a functional fragment thereof.

17. The interferon-associated antigen binding protein for the use of item 16, wherein the type I IFN or the functional fragment thereof is IFNα, IFNβ, IFNω, or IFNε, or a functional fragment thereof.

18. The interferon-associated antigen binding protein for the use of item 16, wherein the type I IFN or the functional fragment thereof is IFNα or IFNβ, or a functional fragment thereof.

19. The interferon-associated antigen binding protein for the use of item 16, wherein the type I IFN or the functional fragment thereof is IFNω, or a functional fragment thereof.

20. The interferon-associated antigen binding protein for the use of item 16, wherein the type I IFN or the functional fragment thereof is IFNε, or a functional fragment thereof.

21. The interferon-associated antigen binding protein for the use of any of the items 1 to 14, wherein the IFN or the functional fragment thereof is IFNα, IFNβ, IFNγ, IFNλ, IFNω or IFNε, or a functional fragment thereof.

22. The interferon-associated antigen binding protein for the use of item 21, wherein the IFN or the functional fragment thereof is IFNα or IFNβ, or a functional fragment thereof.

23. The interferon-associated antigen binding protein for the use of item 22, wherein the IFN or the functional fragment thereof is IFNα, or a functional fragment thereof.

24. The interferon-associated antigen binding protein for the use of item 23, wherein the IFN or functional fragment thereof is IFNα2a, or a functional fragment thereof.

25. The interferon-associated antigen binding protein for the use of item 24, wherein the IFNα2a comprises the sequence as set forth in SEQ ID NO 17, or a sequence at least 90% identical thereto.

26. The interferon-associated antigen binding protein for the use of item 22, wherein the IFN or the functional fragment thereof is IFNβ, or a functional fragment thereof.

27. The interferon-associated antigen binding protein for the use of item 26, wherein the IFNβ comprises the sequence as set forth in SEQ ID NO 14, or a sequence at least 90% identical thereto.

28. The interferon-associated antigen binding protein for the use of item 26, wherein the IFNβ or the functional fragment thereof comprises one or two amino acid substitution(s) relative to SEQ ID NO 14, selected from C17S and N80Q.

29. The interferon-associated antigen binding protein for the use of item 28, wherein the IFNβ or the functional fragment thereof comprises the amino acid substitution C17S relative to SEQ ID NO 14.

30. The interferon-associated antigen binding protein for the use of item 29, wherein the IFNβ comprises the amino acid sequence as set forth in SEQ ID NO 15.

31. The interferon-associated antigen binding protein for the use of item 28, wherein the IFNβ or the functional fragment thereof comprises the amino acid substitutions C17S and N80Q relative to SEQ ID NO 14.

32. The interferon-associated antigen binding protein for the use of item 31, wherein the IFNβ comprises the amino acid sequence as set forth in SEQ ID NO 16.

33. The interferon-associated antigen binding protein for the use of item 21, wherein the IFN or a functional fragment thereof is IFNγ or IFNλ, or a functional fragment thereof.

34. The interferon-associated antigen binding protein for the use of item 33, wherein the IFN or a functional fragment thereof is IFNγ, or a functional fragment thereof.

35. The interferon-associated antigen binding protein for the use of item 34, wherein the IFNγ comprises the sequence as set forth in SEQ ID NO 19, or a sequence at least 90% identical thereto.

36. The interferon-associated antigen binding protein for the use of item 33, wherein the IFN or a functional fragment thereof is IFNλ, or a functional fragment thereof.

37. The interferon-associated antigen binding protein for the use of item 36, wherein the IFNλ or the functional fragment thereof is IFNλ2, or a functional fragment thereof.

38. The interferon-associated antigen binding protein for the use of item 37, wherein the IFNλ2 comprises the sequence as set forth in SEQ ID NO 18, or a sequence at least 90% identical thereto.

39. The interferon-associated antigen binding protein for the use of any one of the preceding items, wherein the IFN or the functional fragment thereof is non-covalently associated with the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof.

40. The interferon-associated antigen binding protein for the use of item 39, wherein the IFN or the functional fragment thereof is non-covalently associated with the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof via ionic, Van-der-Waal, and/or hydrogen bond interactions.

41. The interferon-associated antigen binding protein for the use of any one of items 1 to 38, wherein the IFN or the functional fragment thereof is covalently associated with the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof.

42. The interferon-associated antigen binding protein for the use of item 41, wherein the IFN or the functional fragment thereof is fused to the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof.

43. The interferon-associated antigen binding protein for the use of item 42, wherein the IFN or the functional fragment thereof is fused to a light chain of the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof.

44. The interferon-associated antigen binding protein for the use of item 43, wherein the IFN or the functional fragment thereof is fused to the N-terminus of the light chain of the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof.

45. The interferon-associated antigen binding protein for the use of item 43, wherein the IFN or the functional fragment thereof is fused to the C-terminus of the light chain of the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof.

46. The interferon-associated antigen binding protein for the use of item 42, wherein the IFN or the functional fragment thereof is fused to a heavy chain of the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof.

47. The interferon-associated antigen binding protein for the use of item 46, wherein the IFN or the functional fragment thereof is fused to the N-terminus of the heavy chain of the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof.

48. The interferon-associated antigen binding protein for the use of item 46, wherein the IFN or the functional fragment thereof is fused to the C-terminus of the heavy chain of the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof.

49. The interferon-associated antigen binding protein for the use of any one of items 42 to 48, wherein the agonistic anti-CD40 antibody or an agonistic antigen binding fragment thereof, and the IFN or the functional fragment thereof are fused to each other via a linker.

50. The interferon-associated antigen binding protein for the use of item 49, wherein the interferon-associated antigen binding protein comprises no amino acids other than those forming (I) said agonistic anti-CD40 antibody, or agonistic antigen binding fragment thereof, (II) said IFN or functional fragment thereof and (III) said linker.

51. The interferon-associated antigen binding protein for the use of any one of items 1 to 49, wherein the interferon-associated antigen binding protein comprises no amino acids other than those forming (I) said agonistic anti-CD40 antibody, or agonistic antigen binding fragment thereof and (II) said IFN or functional fragment thereof.

52. The interferon-associated antigen binding protein for the use of any one of items 49 to 50, wherein the linker is a peptide linker.

53. The interferon-associated antigen binding protein for the use of item 52, wherein the linker comprises at least 1, at least 2, at least 3, at least 4, or at least 5 amino acids.

54. The interferon-associated antigen binding protein for the use of item 53, wherein the linker comprises at least 4 amino acids.

55. The interferon-associated antigen binding protein for the use of item 53, wherein the linker comprises at least 11 amino acids.

56. The interferon-associated antigen binding protein for the use of item 53, wherein the linker comprises at least 12 amino acids.

57. The interferon-associated antigen binding protein for the use of item 53, wherein the linker comprises at least 13 amino acids.

58. The interferon-associated antigen binding protein for the use of item 53, wherein the linker comprises at least 15 amino acids.

59. The interferon-associated antigen binding protein for the use of item 53, wherein the linker comprises at least 20 amino acids.

60. The interferon-associated antigen binding protein for the use of item 53, wherein the linker comprises at least 21 amino acids.

61. The interferon-associated antigen binding protein for the use of item 53, wherein the linker comprises at least 24 amino acids.

62. The interferon-associated antigen binding protein for the use of item 52, wherein the linker comprises up to 10, up to 20, up to 30, up to 40, up to 50, up to 60, up to 70, up to 80, up to 90, or up to 100 amino acids.

63. The interferon-associated antigen binding protein for the use of item 62, wherein the linker comprises up to 80 amino acids.

64. The interferon-associated antigen binding protein for the use of item 62, wherein the linker comprises up to 40 amino acids.

65. The interferon-associated antigen binding protein for the use of item 62, wherein the linker comprises up to 24 amino acids.

66. The interferon-associated antigen binding protein for the use of item 62, wherein the linker comprises up to 21 amino acids.

67. The interferon-associated antigen binding protein for the use of item 62, wherein the linker comprises up to 20 amino acids.

68. The interferon-associated antigen binding protein for the use of item 62, wherein the linker comprises up to 15 amino acids.

69. The interferon-associated antigen binding protein for the use of item 62, wherein the linker comprises up to 13 amino acids.

70. The interferon-associated antigen binding protein for the use of item 62, wherein the linker comprises up to 12 amino acids.

71. The interferon-associated antigen binding protein for the use of item 62, wherein the linker comprises up to 11 amino acids.

72. The interferon-associated antigen binding protein for the use of item 62, wherein the linker comprises up to 4 amino acids.

73. The interferon-associated antigen binding protein for the use of any one of items 52 to 72, wherein the linker is selected from the group comprising acidic, basic and neutral linkers.

74. The interferon-associated antigen binding protein for the use of item 73, wherein the linker is an acidic linker.

75. The interferon-associated antigen binding protein for the use of item 73 or 74, wherein the linker comprises a sequence as set forth in SEQ ID NO 22 or SEQ ID NO 23.

76. The interferon-associated antigen binding protein for the use of item 73, wherein the linker is a basic linker.

77. The interferon-associated antigen binding protein for the use of item 73, wherein the linker is a neutral linker.

78. The interferon-associated antigen binding protein for the use of item 73 or 77, wherein the linker comprises a sequence as set forth in SEQ ID NO 20, SEQ ID NO 21, SEQ ID NO 24, SEQ ID NO 25 or SEQ ID NO 26.

79. The interferon-associated antigen binding protein for the use of any one of items 52 to 78, wherein the linker is selected from the group comprising rigid, flexible and helix-forming linkers.

80. The interferon-associated antigen binding protein for the use of item 79, wherein the linker is a rigid linker.

81. The interferon-associated antigen binding protein for the use of item 79 or 80, wherein the linker comprises a sequence as set forth in SEQ ID NO 20, SEQ ID NO 22 or SEQ ID NO 23.

82. The interferon-associated antigen binding protein for the use of item 79, wherein the linker is a flexible linker.

83. The interferon-associated antigen binding protein for the use of item 79 or 82, wherein the linker comprises a sequence as set forth in SEQ ID NO 21, SEQ ID NO 24, SEQ ID NO 25 or SEQ ID NO 26.

84. The interferon-associated antigen binding protein for the use of item 79, wherein the linker is a helix-forming linker.

85. The interferon-associated antigen binding protein for the use of item 79 or 84, wherein the linker comprises a sequence as set forth in SEQ ID NO 22 or SEQ ID NO 23.

86. The interferon-associated antigen binding protein for the use of any one of items 52 to 74, 76, 77, 79, 80, 82 or 84, wherein the linker comprises the amino acids glycine and serine.

87. The interferon-associated antigen binding protein for the use of item 86, wherein the linker comprises the sequence as set forth in SEQ ID NO 21, SEQ ID NO 24, SEQ ID NO 25, or SEQ ID NO 26.

88. The interferon-associated antigen binding protein for the use of item 86, wherein the linker further comprises the amino acid threonine.

89. The interferon-associated antigen binding protein for the use of item 88, wherein the linker comprises the sequence as set forth in SEQ ID NO 21.

90. The interferon-associated antigen binding protein for the use of item 52, wherein the linker comprises a sequence selected from the sequences as set forth in SEQ ID NOs 20 to 26.

91. The interferon-associated antigen binding protein for the use of item 90, wherein the linker comprises a sequence selected from the sequences as set forth in SEQ ID NO 24, SEQ ID NO 25 or SEQ ID NO 26.

92. The interferon-associated antigen binding protein for the use of item 91, wherein the linker comprises a sequence as set forth in SEQ ID NO 24.

93. The interferon-associated antigen binding protein for the use of item 91, wherein the linker comprises a sequence as set forth in SEQ ID NO 25.

94. The interferon-associated antigen binding protein for the use of item 91, wherein the linker comprises a sequence as set forth in SEQ ID NO 26.

95. The interferon-associated antigen binding protein for the use of any one of items 49, 50 or 52 to 94, wherein the IFN or a functional fragment thereof is fused to the C-terminus of a heavy chain of the agonistic anti-CD40 antibody, or the agonistic antigen binding fragment thereof, via the linker as set forth in Table 3, in particular Table 3A or Table 3B, more particularly Table 3A.

96. The interferon-associated antigen binding protein for the use of item 95, wherein the heavy chain of the agonistic anti-CD40 antibody, or the agonistic antigen binding fragment thereof, comprises a sequence as set forth in SEQ ID NO 6, SEQ ID NO 9, SEQ ID NO 12, SEQ ID NO 48 or SEQ ID NO 49.

97. The interferon-associated antigen binding protein for the use of items 95 or 96, wherein the IFNα2a comprises the sequence as set forth in SEQ ID NO 17.

98. The interferon-associated antigen binding protein for the use of items 95 or 96, wherein the IFNβ comprises the sequence as set forth in SEQ ID NO 14, SEQ ID NO 15 or SEQ ID NO 16.

99. The interferon-associated antigen binding protein for the use of item 98, wherein the IFNβ comprises the sequence as set forth in SEQ ID NO 14.

100. The interferon-associated antigen binding protein for the use of item 98, wherein the IFNβ comprises the sequence as set forth in SEQ ID NO 15.

101. The interferon-associated antigen binding protein for the use of item 98, wherein the IFNβ comprises the sequence as set forth in SEQ ID NO 16.

102. The interferon-associated antigen binding protein for the use of item 95 or 96, wherein the IFNγ comprises the sequence as set forth in SEQ ID NO 19.

103. The interferon-associated antigen binding protein for the use of item 95 or 96, wherein the IFNλ2 comprises the sequence as set forth in SEQ ID NO 18.

104. The interferon-associated antigen binding protein for the use of any one of items 95 to 103, wherein the interferon-associated antigen binding protein

further comprises a light chain of an agonistic anti-CD40 antibody, or an agonistic antigen binding fragment thereof.

105. The interferon-associated antigen binding protein for the use of item 104, wherein the light chain comprises a sequence as set forth in SEQ ID NO 3.

106. The interferon-associated antigen binding protein for the use of any one of items 49, 50 or 52 to 94, wherein the IFN or a functional fragment thereof is fused to the N-terminus of a heavy chain of the agonistic anti-CD40 antibody, or the agonistic antigen binding fragment thereof, via the linker as set forth in Table 4, in particular Table 4A or Table 4B, more particularly Table 4A.

107. The interferon-associated antigen binding protein for the use of item 106, wherein the heavy chain of the agonistic anti-CD40 antibody, or the agonistic antigen binding fragment thereof, comprises a sequence as set forth in SEQ ID NO 6, SEQ ID NO 9, SEQ ID NO 49, SEQ ID NO 48, or SEQ ID NO 12.

108. The interferon-associated antigen binding protein for the use of items 106 or 107, wherein the IFNα2a comprises the sequence as set forth in SEQ ID NO 17.

109. The interferon-associated antigen binding protein for the use of items 106 or 107, wherein the IFNβ comprises the sequence as set forth in SEQ ID NO 14, SEQ ID NO 15 or SEQ ID NO 16.

110. The interferon-associated antigen binding protein for the use of item 109, wherein the IFNβ comprises the sequence as set forth in SEQ ID NO 14.

111. The interferon-associated antigen binding protein for the use of item 109, wherein the IFNβ comprises the sequence as set forth in SEQ ID NO 15.

112. The interferon-associated antigen binding protein for the use of item 109, wherein the IFNβ comprises the sequence as set forth in SEQ ID NO 16.

113. The interferon-associated antigen binding protein for the use of items 106 or 107, wherein the IFNγ comprises the sequence as set forth in SEQ ID NO 19.

114. The interferon-associated antigen binding protein for the use of items 106 or 107, wherein the IFNλ2 comprises the sequence as set forth in SEQ ID NO 18.

115. The interferon-associated antigen binding protein for the use of any one of items 106 to 114, wherein the interferon-associated antigen binding protein further comprises a light chain of an agonistic anti-CD40 antibody, or an agonistic antigen binding fragment thereof.

116. The interferon-associated antigen binding protein for the use of item 115, wherein the light chain comprises a sequence as set forth in SEQ ID NO 3.

117. The interferon-associated antigen binding protein for the use of any one of items 49, 50 or 52 to 94, wherein the IFN or a functional fragment thereof is fused to the C-terminus of a light chain of the agonistic anti-CD40 antibody, or the agonistic antigen binding fragment thereof, via the linker as set forth in Table 5, in particular Table 5A or Table 5B, more particularly Table 5A.

118. The interferon-associated antigen binding protein for the use of item 117, wherein the light chain of the agonistic anti-CD40 antibody, or the agonistic antigen binding fragment thereof, comprises a sequence as set forth in SEQ ID NO 3.

119. The interferon-associated antigen binding protein for the use of items 117 or 118, wherein the IFNα2a comprises the sequence as set forth in SEQ ID NO 17.

120. The interferon-associated antigen binding protein for the use of items 117 or 118, wherein the IFNβ comprises the sequence as set forth in SEQ ID NO 14, SEQ ID NO 15 or SEQ ID NO 16.

121. The interferon-associated antigen binding protein for the use of item 120, wherein the IFNβ comprises the sequence as set forth in SEQ ID NO 14.

122. The interferon-associated antigen binding protein for the use of item 120, wherein the IFNβ comprises the sequence as set forth in SEQ ID NO 15.

123. The interferon-associated antigen binding protein for the use of item 120, wherein the IFNβ comprises the sequence as set forth in SEQ ID NO 16.

124. The interferon-associated antigen binding protein for the use of items 117 or 118, wherein the IFNγ comprises the sequence as set forth in SEQ ID NO 19.

125. The interferon-associated antigen binding protein for the use of items 117 or 118, wherein the IFNλ2 comprises the sequence as set forth in SEQ ID NO 18.

126. The interferon-associated antigen binding protein for the use of any one of items 117 to 125, wherein the interferon-associated antigen binding protein further comprises a heavy chain of an agonistic anti-CD40 antibody, or an agonistic antigen binding fragment thereof.

127. The interferon-associated antigen binding protein for the use of item 126, wherein the heavy chain of the agonistic anti-CD40 antibody comprises a sequence as set forth in SEQ ID NO 6, SEQ ID NO 9, SEQ ID NO 49, SEQ ID NO 48, or SEQ ID NO 12.

128. The interferon-associated antigen binding protein for the use of any one of items 49, 50 or 52 to 94, wherein the IFN is fused to the N-terminus of a light chain of the agonistic anti-CD40 antibody, or the agonistic antigen binding fragment thereof, via the linker as set forth in Table 6, in particular Table 6A or Table 6B, more particularly Table 6A.

129. The interferon-associated antigen binding protein for the use of item 128, wherein the light chain of the agonistic anti-CD40 antibody, or the agonistic antigen binding fragment thereof, comprises a sequence as set forth in SEQ ID NO 3.

130. The interferon-associated antigen binding protein for the use of items 128 or 129, wherein the IFNα2a comprises the sequence as set forth in SEQ ID NO 17.

131. The interferon-associated antigen binding protein for the use of items 128 or 129, wherein the IFNβ comprises the sequence as set forth in SEQ ID NO 14, SEQ ID NO 15 or SEQ ID NO 16.

132. The interferon-associated antigen binding protein for the use of item 131, wherein the IFNβ comprises the sequence as set forth in SEQ ID NO 14.

133. The interferon-associated antigen binding protein for the use of item 131, wherein the IFNβ comprises the sequence as set forth in SEQ ID NO 15.

134. The interferon-associated antigen binding protein for the use of item 131, wherein the IFNβ comprises the sequence as set forth in SEQ ID NO 16.

135. The interferon-associated antigen binding protein for the use of items 128 or 129, wherein the IFNγ comprises the sequence as set forth in SEQ ID NO 19.

136. The interferon-associated antigen binding protein for the use of items 128 or 129, wherein the IFNλ2 comprises the sequence as set forth in SEQ ID NO 18.

137. The interferon-associated antigen binding protein for the use of any one of items 128 to 136, wherein the interferon-associated antigen binding protein further comprises a heavy chain of an anti-CD40 antibody, or an agonistic antigen binding fragment thereof.

138. The interferon-associated antigen binding protein for the use of item 137, wherein the heavy chain of the agonistic anti-CD40 antibody comprises a sequence as set forth in SEQ ID NO 6, SEQ ID NO 9, SEQ ID NO 49, SEQ ID NO 48, or SEQ ID NO 12.

139. The interferon-associated antigen binding protein for the use of any one of items 1 to 138, wherein the interferon-associated antigen binding protein comprises a sequence selected from SEQ ID NO 28, SEQ ID NO 29, SEQ ID NO 30, SEQ ID NO 31, SEQ ID NO 32, SEQ ID NO 33, SEQ ID NO 34, SEQ ID NO 35, SEQ ID NO 36, SEQ ID NO 37, SEQ ID NO 38, SEQ ID NO 39, SEQ ID NO 40, SEQ ID NO 41, SEQ ID NO 42, SEQ ID NO 43, SEQ ID NO 44, SEQ ID NO 45, SEQ ID NO 46 and SEQ ID NO 47.

140. The interferon-associated antigen binding protein for the use of item 139, wherein the interferon-associated antigen binding protein comprises a sequence selected from SEQ ID NO 38, SEQ ID NO 39, SEQ ID NO 40, SEQ ID NO 41, SEQ ID NO 42 or SEQ ID NO 43.

141. The interferon-associated antigen binding protein for the use of items 139 or 140, wherein the interferon-associated antigen binding protein is an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic antigen binding fragment thereof comprising one of the sequence combinations disclosed in Table 9, in particular Table 9A or Table 9B, more particularly Table 9A.

142. The interferon-associated antigen binding protein for the use of item 141, wherein the interferon-associated antigen binding protein is an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic antigen binding fragment thereof comprising the sequences as set forth in SEQ ID NO 38 and SEQ ID NO 3.

143. The interferon-associated antigen binding protein for the use of item 141, wherein the interferon-associated antigen binding protein is an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic antigen binding fragment thereof comprising the sequences as set forth in SEQ ID NO 39 and SEQ ID NO 3.

144. The interferon-associated antigen binding protein for the use of item 141, wherein the interferon-associated antigen binding protein is an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic antigen binding fragment thereof comprising the sequences as set forth in SEQ ID NO 40 and SEQ ID NO 3.

145. The interferon-associated antigen binding protein for the use of item 141, wherein the interferon-associated antigen binding protein is an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic antigen binding fragment thereof comprising the sequences as set forth in SEQ ID NO 41 and SEQ ID NO 9.

146. The interferon-associated antigen binding protein for the use of item 141, wherein the interferon-associated antigen binding protein is an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic antigen binding fragment thereof comprising the sequences as set forth in SEQ ID NO 42 and SEQ ID NO 9.

147. The interferon-associated antigen binding protein for the use of item 141, wherein the interferon-associated antigen binding protein is an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic antigen binding fragment thereof comprising the sequences as set forth in SEQ ID NO 43 and SEQ ID NO 9.

148. The interferon-associated antigen binding protein for the use of any one of items 1 to 147, wherein the interferon-associated antigen binding protein activates both the CD40 and an IFN pathway.

149. The interferon-associated antigen binding protein for the use of item 148, wherein CD40 activity is determined using a whole blood surface molecule upregulation assay or an in vitro reporter cell assay.

150. The interferon-associated antigen binding protein for the use of item 149, wherein CD40 activity is determined using an in vitro reporter cell assay, optionally using HEK-Blue™ CD40L cells.

151. The interferon-associated antigen binding protein for the use of any one of items 148 to 150, wherein the interferon-associated antigen binding protein activates the CD40 pathway with an EC_{50} of less than 400, 300, 200, 150, 100, 70, 60, 50, 40, 30, 25, 20, or 15 ng/mL.

152. The interferon-associated antigen binding protein for the use of item 151, wherein the interferon-associated antigen binding protein activates the CD40 pathway with an EC_{50} ranging from 10 to 200 ng/mL.

153. The interferon-associated antigen binding protein for the use of item 152, wherein the interferon-associated antigen binding protein activates the CD40 pathway with an EC_{50} ranging from 10 to 50 ng/mL, preferably 10 to 30 ng/mL.

154. The interferon-associated antigen binding protein for the use of any one of items 148 to 153, wherein the interferon-associated antigen binding protein activates the IFN pathway with an EC_{50} of less than 100, 60, 50, 40, 30, 20, 10, or 1 ng/mL.

155. The interferon-associated antigen binding protein for the use of any one of items 148 to 154, wherein the interferon-associated antigen binding protein activates the IFN pathway with an EC_{50} of less than 11 ng/mL, preferably less than 6 ng/mL.

156. The interferon-associated antigen binding protein for the use of any one of items 148 to 155, wherein the IFN pathway is the IFNα, IFNβ, IFNε, IFNγ, IFNω or IFNλ pathway.

157. The interferon-associated antigen binding protein for the use of item 156, wherein IFNβ activity is determined using an in vitro reporter cell assay, optionally using HEK-Blue™ IFN-α/β cells.

158. The interferon-associated antigen binding protein for the use of item 156, wherein IFNα activity is determined using an in vitro reporter cell assay, optionally using HEK-Blue™ IFN-α/β cells.

159. The interferon-associated antigen binding protein for the use of item 156, wherein IFNγ activity is determined using an in vitro reporter cell assay, optionally using HEK-Blue™ Dual IFN-γ cells.

160. The interferon-associated antigen binding protein for the use of item 156, wherein IFNλ activity is determined using an in vitro reporter cell assay, optionally using HEK-Blue™ IFN-λ cells.

161. The interferon-associated antigen binding protein for the use of any one of the preceding items, wherein the interferon-associated antigen binding protein reduces HBeAg release by primary hepatocytes *in vitro* by at least 12% at 1 ng/mL.

162. The interferon-associated antigen binding protein for the use of item 161, wherein the interferon-associated antigen binding protein reduces HBeAg release by primary hepatocytes *in vitro* by up to 90% at 1 ng/mL.

163. The interferon-associated antigen binding protein for the use of item 161, wherein the interferon-associated antigen binding protein reduces HBeAg release with an EC_{50} of less than 30 ng/mL.

164. The interferon-associated antigen binding protein for the use of item 163, wherein the interferon-associated antigen binding protein reduces HBeAg release with an EC_{50} of less than 10 ng/mL.

165. The interferon-associated antigen binding protein for the use of item 164, wherein the interferon-associated antigen binding protein reduces HBeAg release with an EC_{50} of less than 1 ng/mL.

166. The interferon-associated antigen binding protein for the use of item 164, wherein the interferon-associated antigen binding protein reduces HBeAg release with an EC_{50} of less than 0.1 ng/mL.

167. The interferon-associated antigen binding protein for the use of any one of the preceding items, in particular items 148 to 165, wherein the expression level of one or more IFN pathway biomarkers is upregulated in an HBV-infected

cell upon treatment with the interferon-associated antigen binding protein, preferably at least 1.5-fold, more preferably at least 2-fold, most preferably at least 3-fold.

168. The interferon-associated antigen binding protein for the use of item 167, wherein the IFN pathway biomarker is a chemokine.

169. The interferon-associated antigen binding protein for the use of item 168, wherein the IFN pathway biomarker is the interferon stimulated gene ISG20.

170. The interferon-associated antigen binding protein for the use of item 168, wherein the IFN pathway biomarker is a C-X-C chemokine, selected from the group consisting of CXCL9, CXCL10 and CXCL11.

171. The interferon-associated antigen binding protein for the use of item 170, wherein the IFN pathway biomarker is CXCL10.

172. The interferon-associated antigen binding protein for the use of any one of the preceding items, in particular items 148 to 171, wherein the expression level of one or more of IL10, IL1β and IL2 is not significantly upregulated in an HBV-infected cell upon treatment with the interferon-associated antigen binding protein.

173. The interferon-associated antigen binding protein for the use of any one of the preceding items, wherein the systemic exposure of the interferon-associated antigen binding protein is increased compared to antibody CP870,893, preferably by at least 10%, more preferably by at least 15%, most preferably by at least 25%.

174. The interferon-associated antigen binding protein for the use of any one of the preceding items, wherein the systemic exposure of the interferon-associated antigen binding protein is at least 1000 µg*h/mL.

175. The interferon-associated antigen binding protein for the use of item 174, wherein the systemic exposure of the interferon-associated antigen binding protein ranges from 1033 µg*h/mL to 1793 µg*h/mL.

176. The interferon-associated antigen binding protein for the use of any one of the preceding items, wherein the half-life of the interferon-associated antigen binding protein is at least 100 h.

177. The interferon-associated antigen binding protein for the use of item 176, wherein the half-life of the interferon-associated antigen binding protein ranges from 116 to 158 h.

178. The interferon-associated antigen binding protein for the use of any one of the preceding items, wherein the clearance rate of the interferon-associated antigen binding protein is below 0.5 mL/h/kg.

179. The interferon-associated antigen binding protein for the use of item 178, wherein the clearance of the interferon-associated antigen binding protein ranges from 0.28 to 0.49 mL/h/kg.

180. The interferon-associated antigen binding protein for the use of any one of items 1 to 179, wherein the volume of distribution Vss of the interferon-associated antigen binding protein is below 100 mL/kg.

181. The interferon-associated antigen binding protein for the use of item 180, wherein the volume of distribution Vss of the interferon-associated antigen binding protein ranges from 50 to 98 mL/kg.

182. The interferon-associated antigen binding protein for the use of any one of the preceding items, wherein the use comprises administering the interferon-associated antigen binding protein to a subject in need thereof by means of genetic delivery with RNA or DNA sequences encoding the interferon-associated antigen binding protein, or a vector or vector system encoding the interferon-associated antigen binding protein.

183. The interferon-associated antigen binding protein for the use of any one of items 1 to 182, wherein the interferon-associated antigen binding protein is comprised in a pharmaceutical composition.

184. The interferon-associated antigen binding protein for the use of item 183, wherein the pharmaceutical composition is suitable for oral, parenteral, or topical administration or for administration by inhalation.

185. The interferon-associated antigen binding protein for the use of item 184, wherein the pharmaceutical composition is suitable for oral administration.

186. The interferon-associated antigen binding protein for the use of item 184, wherein the pharmaceutical composition is suitable for topical administration.

187. The interferon-associated antigen binding protein for the use of item 184, wherein the pharmaceutical composition is suitable for administration by inhalation.

188. The interferon-associated antigen binding protein for the use of item 184, wherein the pharmaceutical composition is suitable for parenteral administration.

189. The interferon-associated antigen binding protein for the use of item 188, wherein the pharmaceutical composition is suitable for intravenous, intraarterial, intraperitoneal, intramuscular, subcutaneous, rectal or vaginal administration.

190. The interferon-associated antigen binding protein for the use of item 189, wherein the pharmaceutical composition is suitable for injection, preferably for intravenous or intraarterial injection or drip.

191. The interferon-associated antigen binding protein for the use of any one of items 183 to 190, wherein the pharmaceutical composition comprises at least one buffering agent.

192. The interferon-associated antigen binding protein for the use of item 191, wherein the buffering agent is acetate, formate or citrate.

193. The interferon-associated antigen binding protein for the use of item 192, wherein the buffering agent is acetate.

194. The interferon-associated antigen binding protein for the use of item 192, wherein the buffering agent is formate.

195. The interferon-associated antigen binding protein for the use of item 192, wherein the buffering agent is citrate.

196. The interferon-associated antigen binding protein for the use of any one of items 183 to 195, wherein the pharmaceutical composition comprises a surfactant.

197. The interferon-associated antigen binding protein for the use of item 196, wherein the surfactant is selected from the list comprising pluronics, PEG,

sorbitan esters, polysorbates, triton, tromethamine, lecithin, cholesterol and tyloxapal.

198. The interferon-associated antigen binding protein for the use of item 197, wherein the surfactant is polysorbate.

199. The interferon-associated antigen binding protein for the use of item 198, wherein the surfactant is polysorbate 20, polysorbate 40, polysorbate 60, polysorbate 80 or polysorbate 100.

200. The interferon-associated antigen binding protein for the use of item 199, wherein the surfactant is polysorbate 20.

201. The interferon-associated antigen binding protein for the use of item 199, wherein the surfactant is polysorbate 80.

202. The interferon-associated antigen binding protein for the use of any one of items 183 to 201, wherein the pharmaceutical composition comprises a stabilizing agent, optionally wherein the stabilizing agent is albumin

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Table 11a: IFN-β-based IFAs		IFN-γ	IL10	IL12p40	IL1β	IL2	IL6	IP10	TFNα
NT	donor 1	nd	nd	nd	nd	nd	nd	457,0	nd
	donor 2	nd	nd	101,4	nd	nd	nd	672,7	4,6
	donor 3	nd	nd	nd	nd	nd	nd	302,3	nd
	donor 4	nd	nd	104,0	nd	nd	nd	648,2	nd
LPS	donor 1	2023,0	148,0	7757,1	5116,0	nd	20709,6	6646,7	1706,3
	donor 2	4675,6	57,2	6265,6	6263,7	20,7	11070,1	39539,4	2987,1
	donor 3	1537,3	192,9	1750,0	3137,6	nd	16837,7	6141,0	944,9
	donor 4	2360,7	299,7	1676,5	6423,0	18,6	20654,0	22848,2	1107,2
IFA1	donor 1	98,1	nd	nd	nd	nd	16,3	46033,6	43,7
	donor 2	nd	nd	118,8	nd	nd	11,8	43545,5	36,6
	donor 3	nd	nd	nd	nd	nd	nd	23562,1	34,0
	donor 4	nd	nd	nd	nd	nd	nd	31922,5	57,1
IFA2	donor 1	nd	nd	nd	nd	nd	18,6	43382,3	41,0
	donor 2	nd	nd	114,2	nd	nd	17,4	43283,4	33,8
	donor 3	nd	nd	nd	nd	nd	nd	25961,4	32,2
	donor 4	109,4	nd	nd	nd	nd	nd	38445,0	66,0

Table 11b: IFN-α-based IFAs		IFN-γ	IL10	IL12p40	IL1β	IL2	IL6	IP10	TFNα
NT	donor 5	12,6	0,6	91,6	0,9	0,9	3,9	270,3	2,1
	donor 6	5,0	1,1	129,9	19,9	#DIV/0!	423,2	1052,7	16,0
	donor 7	16,5	2,0	143,7	22,1	2,1	426,9	1025,0	12,6
	donor 8	9,7	0,1	58,3	1,8	#DIV/0!	2,6	594,2	2,2
LPS	donor 5	10848,1	46,6	8463,3	8712,3	10,5	30713,2	20538,9	1738,3
	donor 6	2467,1	175,6	5364,9	6557,9	3,3	31735,5	17262,6	2583,3
	donor 7	3310,1	248,6	6814,8	9123,9	16,6	39139,8	59939,2	6270,1
	donor 8	2555,6	138,5	2942,9	6767,5	9,6	31756,7	20062,7	1265,5
IFA25	donor 5	495,5	1,5	99,5	1,9	5,5	30,5	39637,5	30,4
	donor 6	312,2	2,0	129,8	16,5	4,0	51,8	61963,8	71,4
	donor 7	271,2	2,9	130,3	9,1	4,4	75,0	133442,5	30,3
	donor 8	441,6	1,9	74,8	6,8	3,2	44,3	95647,9	87,4
IFA26	donor 5	330,4	2,0	98,1	2,1	6,4	29,3	37880,2	32,1
	donor 6	303,7	3,3	150,8	17,1	3,1	53,0	72944,8	45,7
	donor 7	180,3	2,0	135,6	9,2	4,9	75,2	154696,3	29,7
	donor 8	421,4	2,8	95,7	6,8	4,1	42,1	79768,5	89,1
IFA27	donor 5	430,7	2,2	127,8	3,1	7,1	32,9	40214,1	61,3
	donor 6	286,5	2,0	148,5	16,8	2,1	66,0	83445,0	70,1
	donor 7	350,3	4,7	117,6	9,3	4,4	73,5	195844,6	105,6
	donor 8	440,1	2,6	68,6	8,9	0,6	46,9	102676,8	43,4
IFA28	donor 5	620,1	2,7	127,3	3,4	8,7	35,0	40958,5	24,6
	donor 6	264,7	2,0	170,3	13,6	2,4	45,7	62333,3	33,0
	donor 7	289,6	2,7	144,8	13,7	3,9	77,1	176521,8	59,6
	donor 8	436,2	2,5	74,4	4,9	2,3	36,8	79217,6	37,6
IFA29	donor 5	692,7	1,3	108,7	2,3	3,7	33,9	55062,8	30,3
	donor 6	183,1	2,2	158,8	11,6	0,4	44,4	58665,4	44,3
	donor 7	235,5	2,6	127,6	9,6	2,0	65,6	136893,2	90,5
	donor 8	301,1	3,0	77,7	5,8	0,6	33,8	69226,3	48,0
IFA30	donor 5	709,7	1,2	110,6	2,9	5,5	38,0	63040,7	36,5
	donor 6	122,9	2,0	153,0	14,9	1,7	46,1	67861,2	37,4
	donor 7	64,6	1,0	114,0	10,0	2,9	75,5	149093,0	32,7
	donor 8	206,0	1,9	71,1	6,8	1,8	37,9	85986,9	40,5

Table 12A

Matrix	Compound	Dose In-life period	Method	C0 (µg/mL)	AUC (0-last) (µg.h/mL)	T_{last} (h)	AUC (0-inf) (µg.h/mL)	% extrapolation	$T_{1/2t}$ (h)	Cl (mL/hr/kg)	V_D (mL/kg)
Serum	CP870,893	0,5 mg/kg 168h	ELISA-IgG2	7,15	241	168	590	59	264 (long)	0,35 (Low)	296 (Low)
Serum	IFA27	0,5 mg/kg 240h	ELISA-IgG2	14,7	1501	240	2552	41	218 (long)	0,20 (Low)	55 (Low)
Serum	IFA27	0,5 mg/kg 240h	ELISA-IFN	16,9	1318	240	1793	26	125 (long)	0,28 (Low)	50 (Low)
Serum	IFA29	0,5 mg/kg 240h	ELISA-IFN	11,6	804	240	1033	22	116 (long)	0,49 (Low)	78 (Low)
Serum	IFA30	0,5 mg/kg 240h	ELISA-IFN	8,12	741	240	1089	31	158 (long)	0,46 (Low)	98 (Low)

Table 12B

Matrix	Compound	Dose In-life period	Method	C0 (µg/mL)	AUC (0-last) (µg.h/mL)	T_{last} (h)	AUC (0-inf) (µg.h/mL)	% extrapolation	$T_{1/2t}$ (h)	Cl (mL/hr/kg)	V_D (mL/kg)
Serum	IFA25	0,5 mg/kg 504h	ELISA-IFN	7,45	1328	504	1500	11	154 (long)	0,34 (Low)	73 (Low)
Serum	IFA26	0,5 mg/kg 504h	ELISA-IFN	8,20	988	336	1027	3,8	59 (long)	0,49 (Low)	57 (Low)
Serum	IFA28	0,5 mg/kg 504h	ELISA-IFN	9,38	1048	504	1264	17	213 (long)	0,40 (Low)	105 (Low)
Serum	Pegasys	0,3 mg/kg 504h	ELISA-IFNa specific	8,3	210	168	215	2	30 (moderate)	1,4 (Low)	62 (Low)
Serum	CP870,893	0,5 mg/kg 504h	ELISA-IgG2	11,9	527	168	797	34	116 (long)	0,63 (Low)	96 (Low)
Serum	IFA25	0,5 mg/kg 504h	ELISA-IgG2	11,8	1292	240	1971	34	155 (long)	0,26 (Low)	56 (Low)

TABLE 13

Condition	donor	IFNg	IL10	IL12p40	IL1b	IL2	IL6	IP10	TFNa
NT	D1	nd	nd	nd	nd	nd	nd	457,0	nd
	D2	nd	nd	101,4	nd	nd	nd	672,7	4,63
	D3	nd	nd	nd	nd	nd	nd	302,3	nd
	D4	nd	nd	104,0	nd	nd	nd	648,2	nd
LPS	D1	2023	148	7757	5116	nd	20710	6647	1706
	D2	4676	57	6266	6264	21	11070	39539	2987
	D3	1537	193	1750	3138	nd	16838	6141	945
	D4	2361	300	1677	6423	19	20654	22848	1107
IFA109	D1	nd	nd	nd	nd	nd	13,48	44495,49	43,63
	D2	nd	nd	116,29	nd	nd	10,6	44030,74	37,52
	D3	nd	nd	nd	nd	nd	nd	31506,88	62,17
	D4	nd	nd	103,45	nd	nd	nd	45005,31	133,02

CLAIMS

1. An interferon-associated antigen binding protein comprising
(I) an agonistic anti-CD40 antibody or an agonistic antigen binding fragment thereof, and
(II) an Interferon (IFN) or a functional fragment thereof
for use in treating hepatitis B virus (HBV) infection.

2. The interferon-associated antigen binding protein for the use of claim 1, wherein the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof comprises
(a) a heavy chain or a fragment thereof comprising a complementarity determining region (CDR) CDRH1 that is at least 90% identical to SEQ ID NO 56, a CDRH2 that is at least 90% identical to SEQ ID NO 57, and a CDRH3 that is at least 90% identical to SEQ ID NO 58; and
(b) a light chain or a fragment thereof comprising a CDRL1 that is at least 90% identical to SEQ ID NO 52, a CDRL2 that is at least 90% identical to SEQ ID NO 53, and a CDRL3 that is at least 90% identical to SEQ ID NO 54.

3. The interferon-associated antigen binding protein for the use of claim 1, wherein the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof comprises
(a) a heavy chain or a fragment thereof comprising a complementarity determining region (CDR) CDRH1 that is identical to SEQ ID NO 56, a CDRH2 that is identical to SEQ ID NO 57, and a CDRH3 that is identical to SEQ ID NO 58; and
(b) a light chain or a fragment thereof comprising a CDRL1 that is identical to SEQ ID NO 52, a CDRL2 that is identical to SEQ ID NO 53, and a CDRL3 that is identical to SEQ ID NO 54.

4. The interferon-associated antigen binding protein for the use of any one of the preceding claims, wherein the agonistic anti-CD40 antibody, or the agonistic antigen binding fragment thereof, comprises a light chain variable region V_L comprising the sequence as set forth in SEQ ID NO 51, or a sequence at least 90% identical thereto; and/or a heavy chain variable region V_H comprising the sequence as set forth in SEQ ID NO 55, or a sequence at least 90% identical thereto.

5. The interferon-associated antigen binding protein for the use of any one of the preceding claims, wherein the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof comprises a light chain (LC) that comprises a sequence as set forth in SEQ ID NO 3, or a sequence at least 90% identical thereto; and/or a heavy chain (HC) that comprises a sequence selected from the group consisting of SEQ ID NO 6, SEQ ID NO 9, SEQ ID NO 12, SEQ ID NO 49 and SEQ ID NO 48, or a sequence at least 90% identical thereto.

6. The interferon-associated antigen binding protein for the use of any one of the preceding claims, wherein the IFN or the functional fragment thereof is selected from the group consisting of a Type I IFN, a Type II IFN and a Type III IFN, or a functional fragment thereof.

7. The interferon-associated antigen binding protein for the use of claim 6, wherein the type I IFN or the functional fragment thereof is IFNα or IFNβ, or a functional fragment thereof.

8. The interferon-associated antigen binding protein for the use of any of the preceding claims, wherein the IFN or the functional fragment thereof is IFNα2a, or a functional fragment thereof, and wherein preferably the IFNα2a comprises the sequence as set forth in SEQ ID NO 17, or a sequence at least 90% identical thereto.

9. The interferon-associated antigen binding protein for the use of any of claims 1 to 7, wherein the IFN or the functional fragment thereof is IFNβ or a functional fragment thereof, and wherein preferably the IFNβ comprises the sequence as set forth in SEQ ID NO 14, or a sequence at least 90% identical thereto.

10. The interferon-associated antigen binding protein for the use of any of the preceding claims, wherein the IFN or the functional fragment thereof is fused to a light chain of the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof, preferably to the C-terminus.

11. The interferon-associated antigen binding protein for the use of any of claims 1 to 9, wherein the IFN or the functional fragment thereof is fused to a heavy chain of the agonistic anti-CD40 antibody or the agonistic antigen binding fragment thereof, preferably to the C-terminus.

12. The interferon-associated antigen binding protein for the use of any of the preceding claims, wherein the agonistic anti-CD40 antibody or an agonistic

antigen binding fragment thereof, and the IFN or the functional fragment thereof, are fused to each other via a linker, and wherein preferably the linker comprises a sequence as set forth in SEQ ID NO 20, SEQ ID NO 21, SEQ ID NO 24, SEQ ID NO 25 or SEQ ID NO 26.

13. The interferon-associated antigen binding protein for the use of any of the preceding claims, wherein the interferon-associated antigen binding protein is an interferon-fused agonistic anti-CD40 antibody or an interferon-fused agonistic antigen binding fragment thereof comprising one of the sequence combinations disclosed in Table 9, in particular Table 9A or Table 9B, more particularly Table 9A.

14. The interferon-associated antigen binding protein for the use of any one of the preceding claims, wherein the use comprises administering the interferon-associated antigen binding protein to a subject in need thereof by means of genetic delivery with RNA or DNA sequences encoding the interferon-associated antigen binding protein, or a vector or vector system encoding the interferon-associated antigen binding protein.

15. The interferon-associated antigen binding protein for the use of any one of the preceding claims, wherein the interferon-associated antigen binding protein is comprised in a pharmaceutical composition.

Fig.1

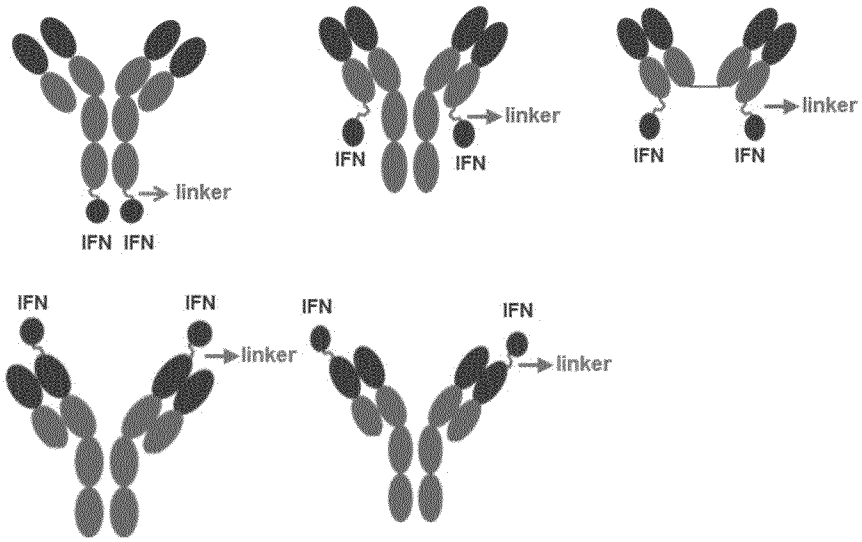
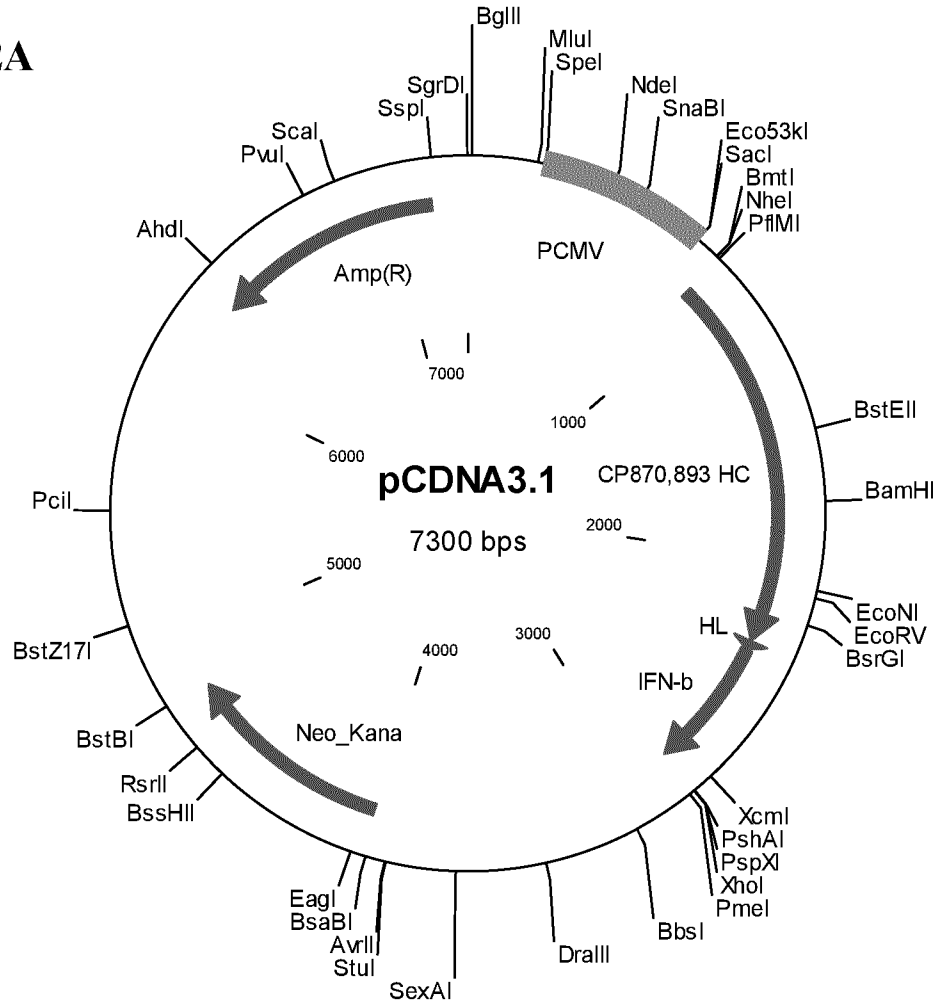

linker
IFN IFN
linker
IFN IFN
linker
IFN IFN
IFN IFN
linker
IFN IFN
linker

Fig. 2A



Nucleic acid sequence encoding seq ID NO 32

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TGGGCTGTCTGGTCAAGGACTACTTTCCTGAGCCTGTGACCGTGTCCTGGAATAGCGGAGCACTGACATCCGGCGTGCACACATT
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Fig.2B

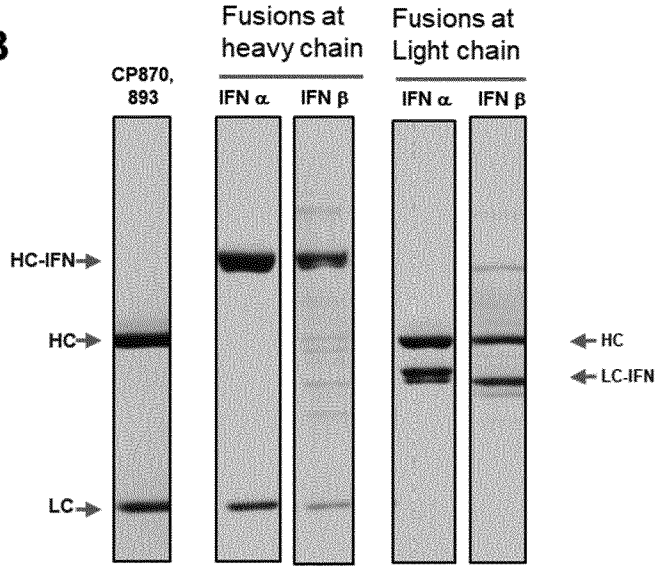
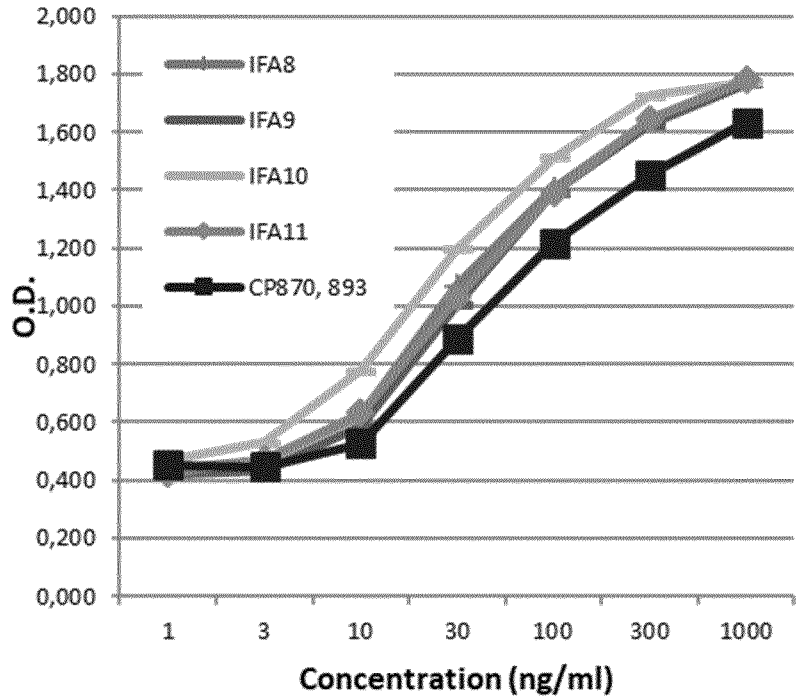

Fusions at heavy chain
Fusions at Light chain
CP870, 893
IFN α
IFN β
IFN α
IFN β
HC-IFN
HC
LC
HC
LC-IFN

Fig. 3A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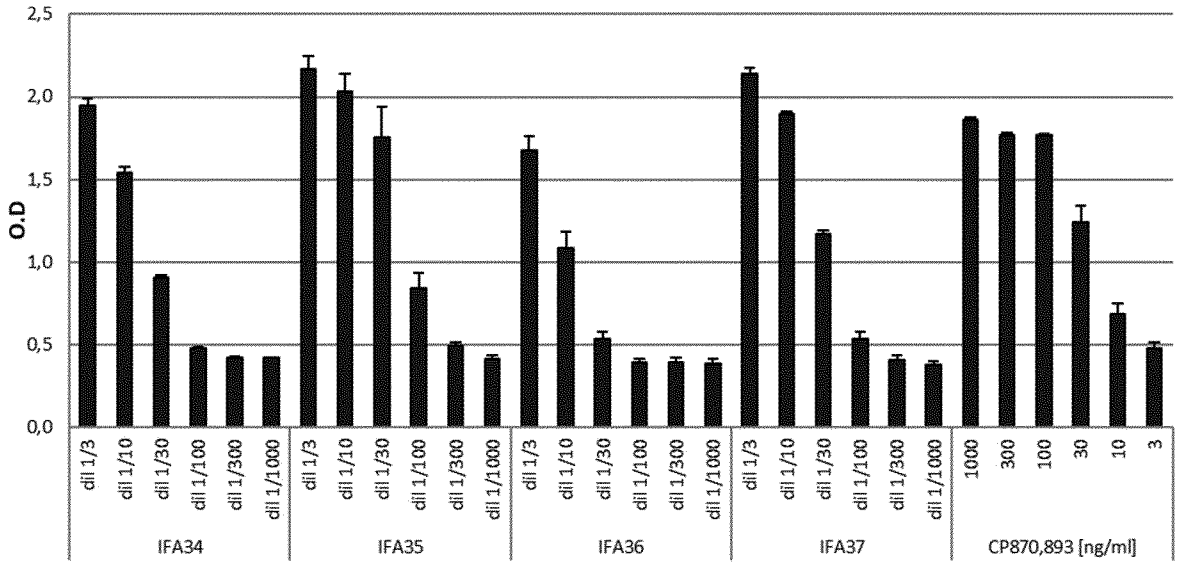
0,000
O.D.
IFA8
IFA9
IFA10
IFA11
CP870, 893
1
3
10
30
100
300
1000
Concentration (ng/ml)

Fig. 3B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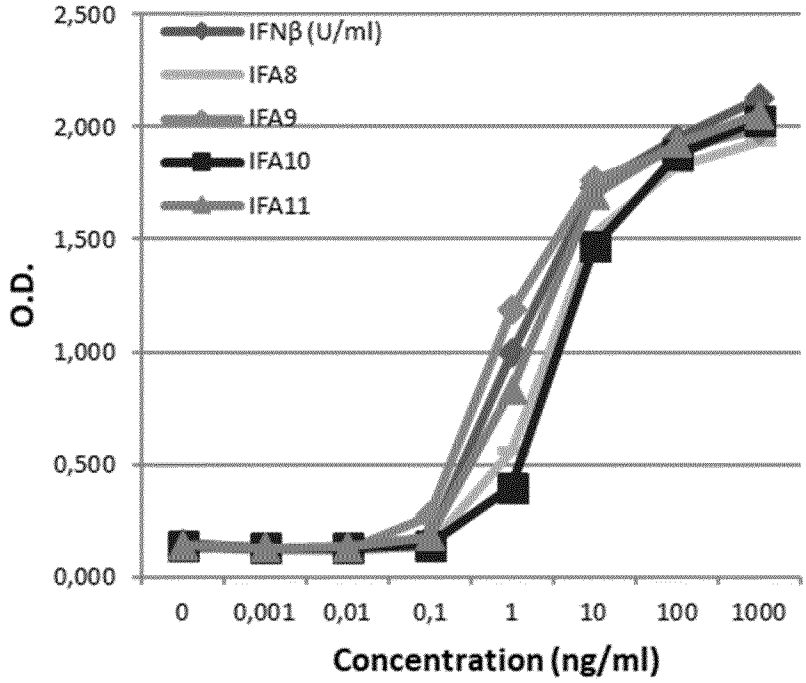
1,5
1,0
0,5
0,0
O.D
dil 1/3
dil 1/10
dil 1/30
dil 1/100
dil 1/300
dil 1/1000
IFA34
IFA35
IFA36
IFA37
1000
300
100
30
10
3
CP870,893 [ng/ml]

Fig. 3C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1,500
1,000
0,500
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O.D.
IFNβ (U/ml)
IFA8
IFA9
IFA10
IFA11
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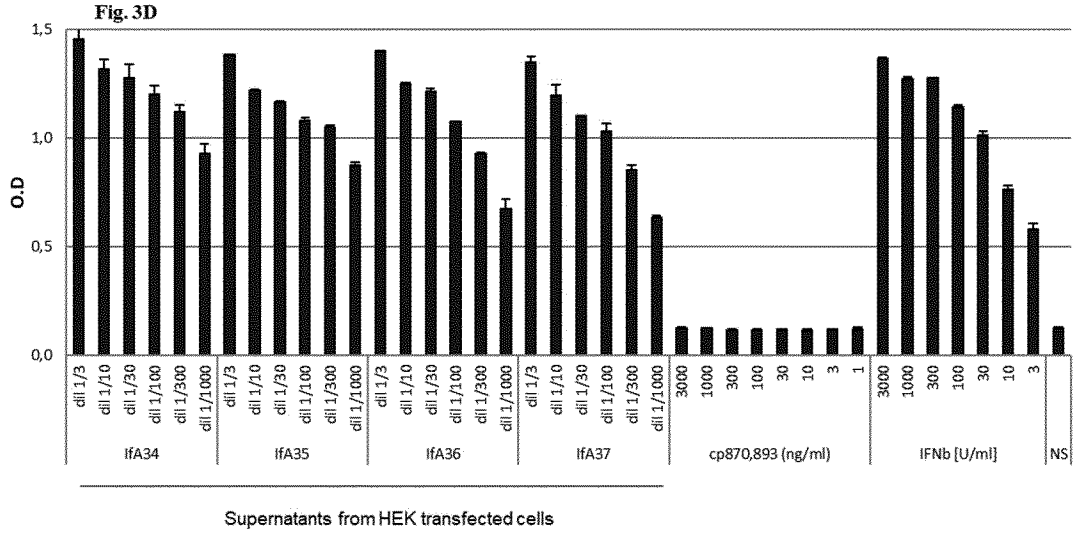
0,001
0,01
0,1
1
10
100
1000
Concentration (ng/ml)

Fig. 3D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0,0
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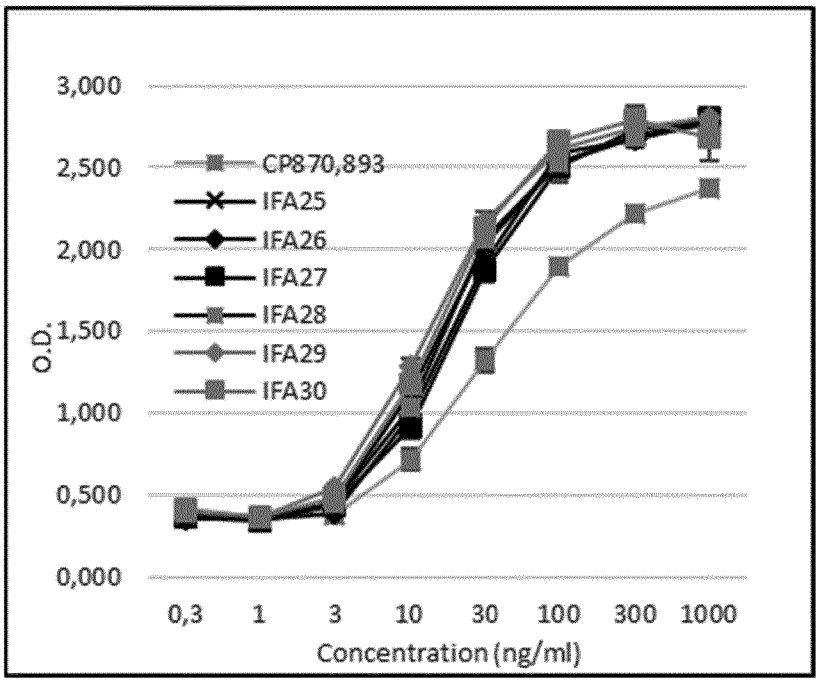
dil 1/3
dil 1/10
dil 1/30
dil 1/100
dil 1/300
dil 1/1000
IfA34
IfA35
IfA36
IfA37
3000
1000
300
100
30
10
3
1
cp870,893 (ng/ml)
IFNb [U/ml]
NS
Supernatants from HEK transfected cells

Fig. 4A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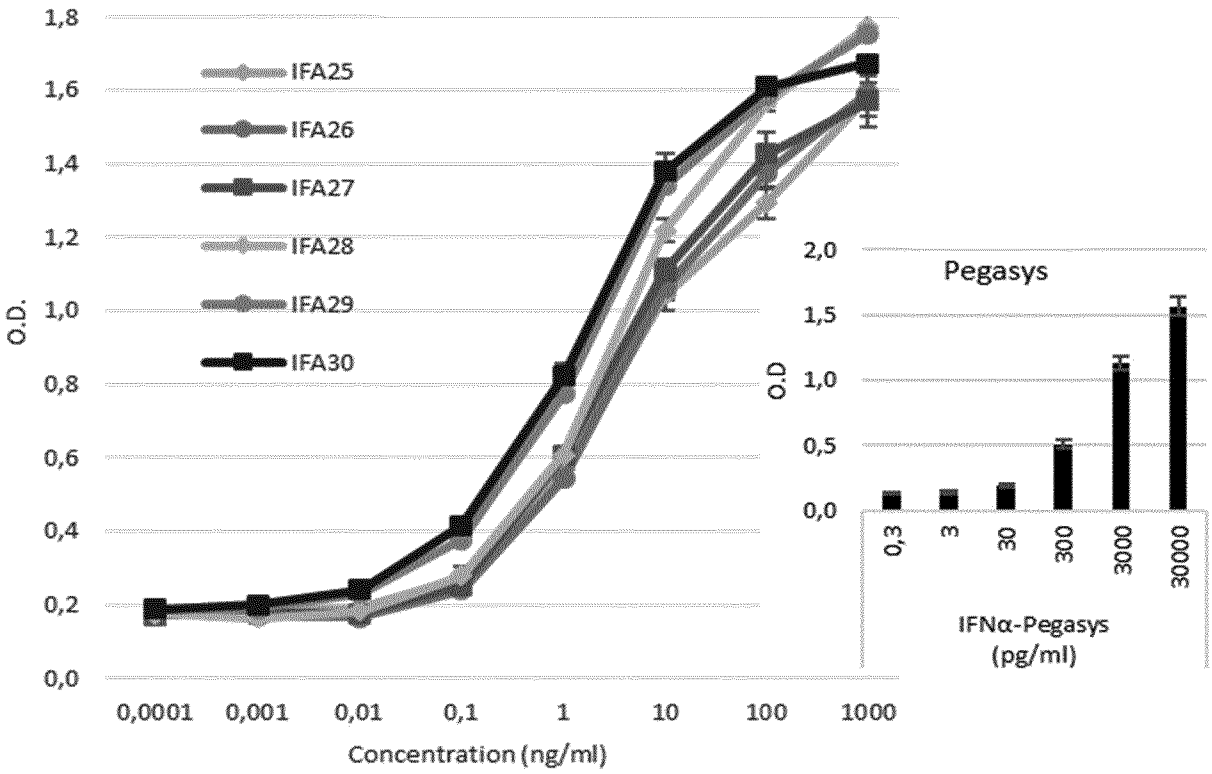
O.D.
CP870,893
IFA25
IFA26
IFA27
IFA28
IFA29
IFA30
0,3
1
3
10
30
100
300
1000
Concentration (ng/ml)

Fig. 4B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1,4
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0,8
0,6
0,4
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0,0
O.D.
IFA25
IFA26
IFA27
IFA28
IFA29
IFA30
0,0001
0,001
0,01
0,1
1
10
100
1000
Concentration (ng/ml)
Pegasys
2,0
1,5
1,0
0,5
0,0
O.D
0,3
3
30
300
3000
30000
IFNα-Pegasys
(pg/ml)

Fig. 4C

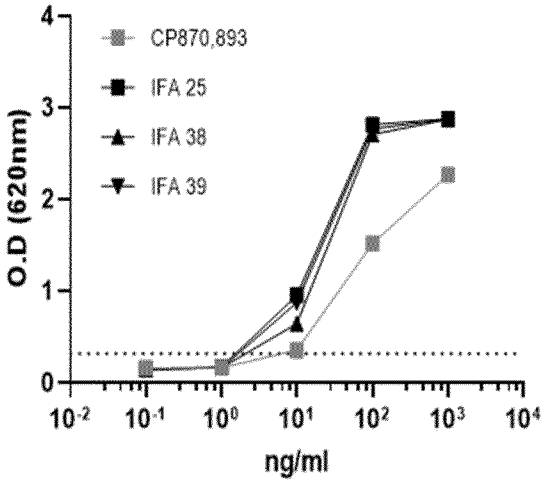

CP870,893
IFA 25
IFA 38
IFA 39
O.D (620nm)
ng/ml

Fig. 4D

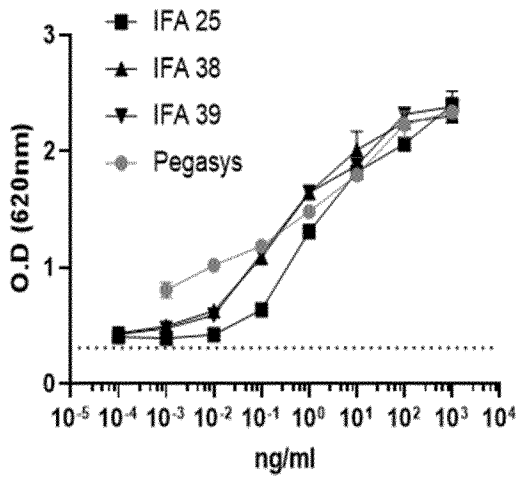

IFA 25
IFA 38
IFA 39
Pegasys
O.D (620nm)
ng/ml

Fig. 5

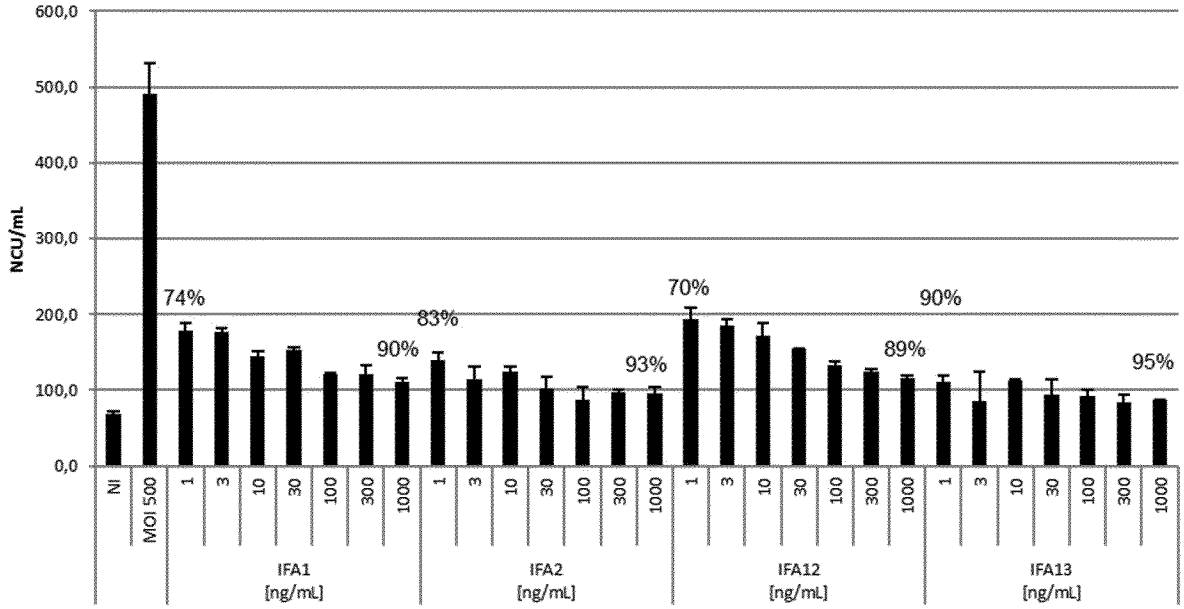

600,0
500,0
400,0
300,0
200,0
100,0
0,0
NCU/mL
74%
83%
90%
93%
70%
89%
90%
95%
NI
MOI 500
1
3
10
30
100
300
1000
IFA1 [ng/mL]
IFA2 [ng/mL]
IFA12 [ng/mL]
IFA13 [ng/mL]

Fig. 6A

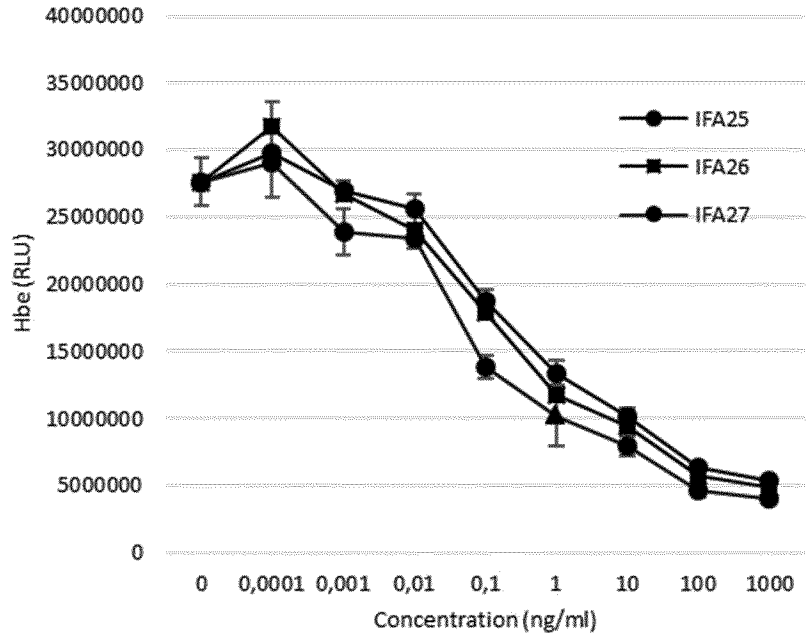

40000000
35000000
30000000
25000000
20000000
15000000
10000000
5000000
0
Hbe (RLU)
IFA25
IFA26
IFA27
0
0,0001
0,001
0,01
0,1
1
10
100
1000
Concentration (ng/ml)

Fig. 6B

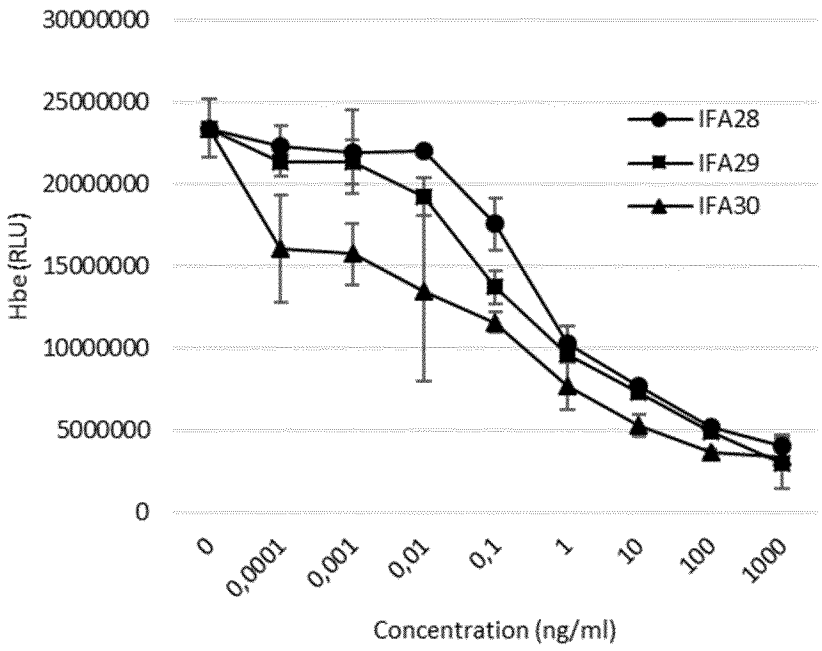

30000000
25000000
20000000
15000000
10000000
5000000
0
Hbe (RLU)
IFA28
IFA29
IFA30
0
0,0001
0,001
0,01
0,1
1
10
100
1000
Concentration (ng/ml)

Fig. 6C

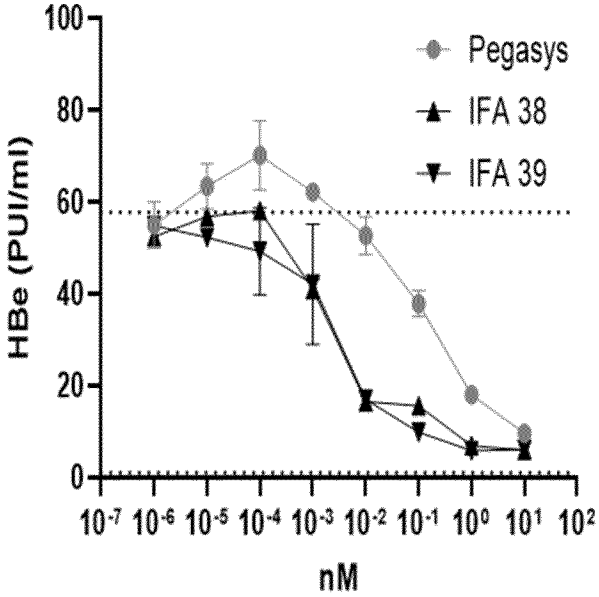

100
80
60
40
20
0
HBe (PUI/ml)
Pegasys
IFA 38
IFA 39
10-7 10-6 10-5 10-4 10-3 10-2 10-1 100 101 102
nM

Fig. 6D

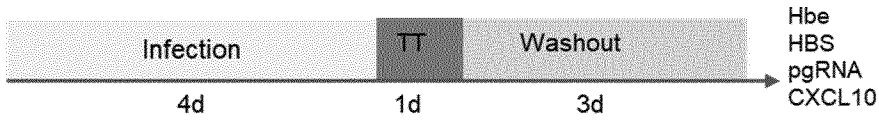


Fig. 6E HBeAg release

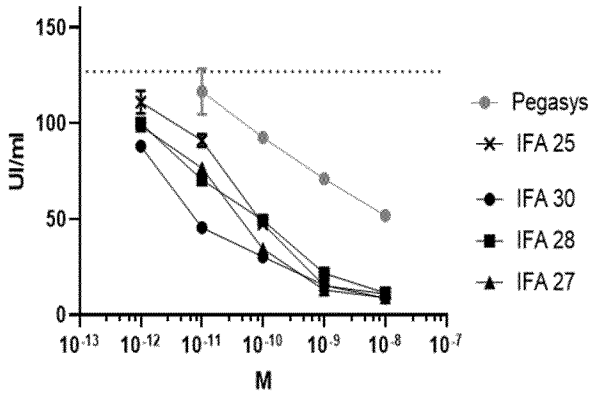


Fig. 6F HBsAg release

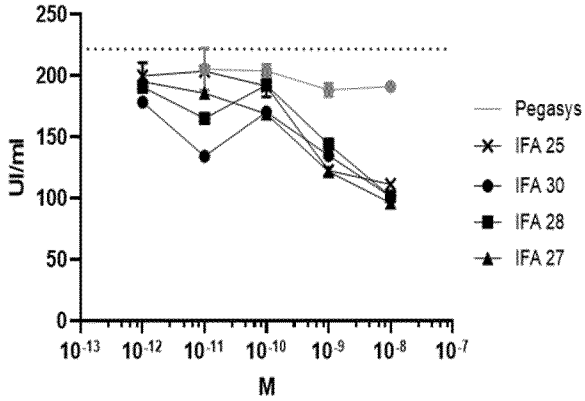


Fig. 6G pgRNA

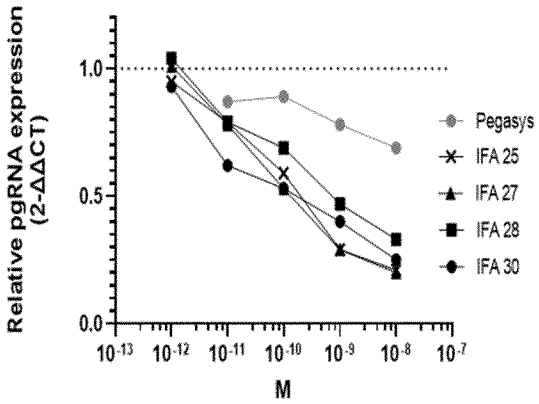


Fig. 6H CXCL10 release

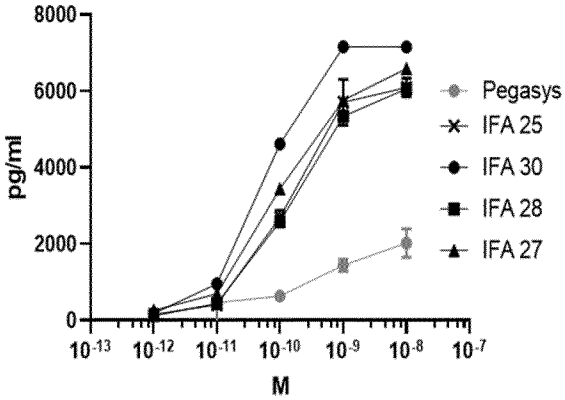
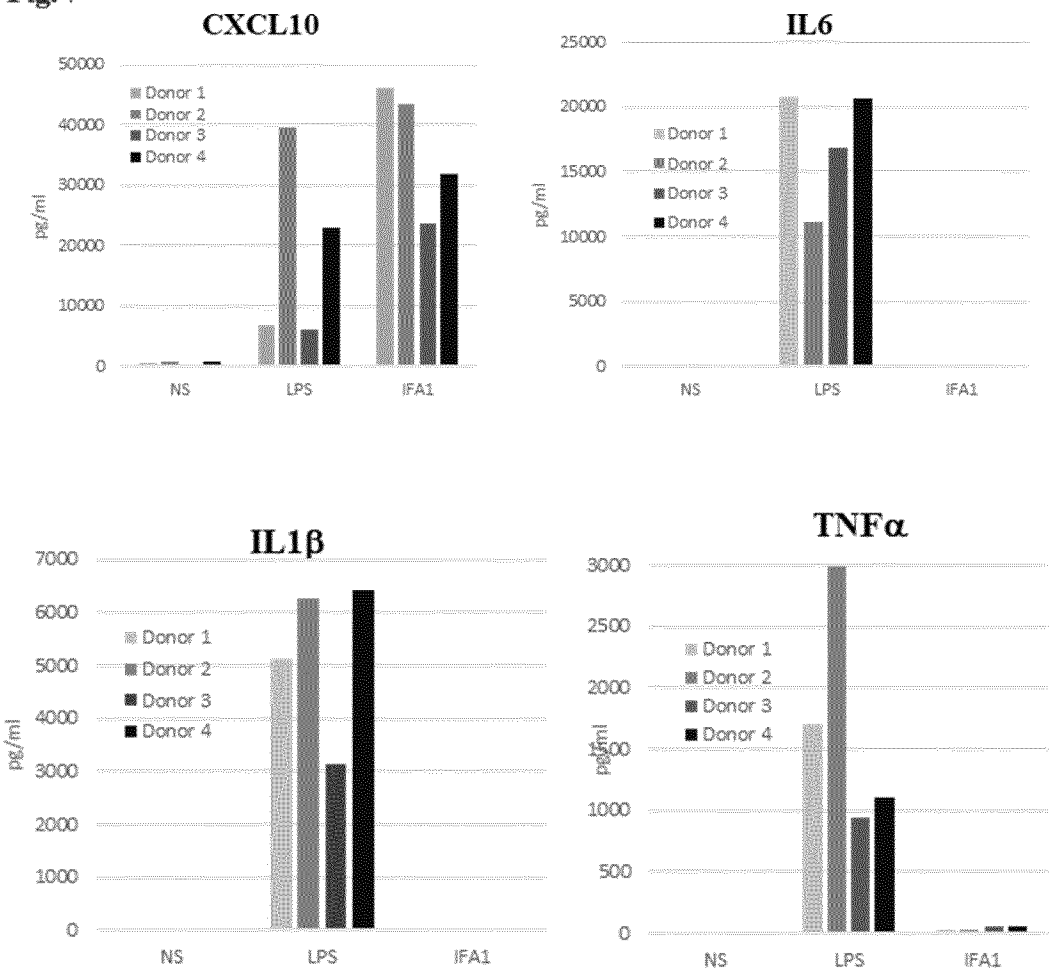


Fig. 7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50000
40000
30000
20000
10000
0
pg/ml
Donor 1
Donor 2
Donor 3
Donor 4
NS
LPS
IFA1
IL6
25000
20000
15000
10000
5000
0
pg/ml
Donor 1
Donor 2
Donor 3
Donor 4
NS
LPS
IFA1
IL1β
7000
6000
5000
4000
3000
2000
1000
0
pg/ml
Donor 1
Donor 2
Donor 3
Donor 4
NS
LPS
IFA1
TNFα
3000
2500
2000
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1000
500
0
pg/ml
Donor 1
Donor 2
Donor 3
Donor 4
NS
LPS
IFA1

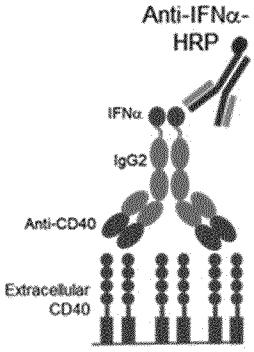


Fig. 8A

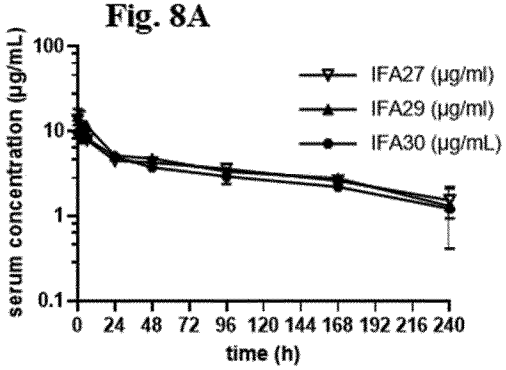
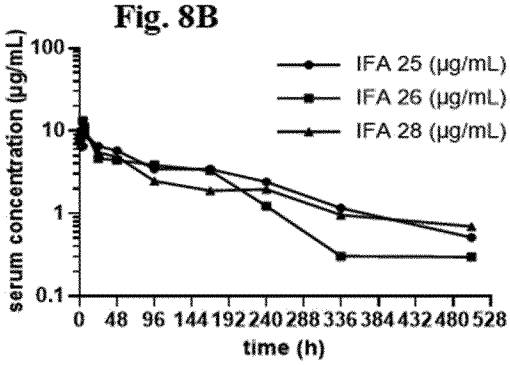


Fig. 8B



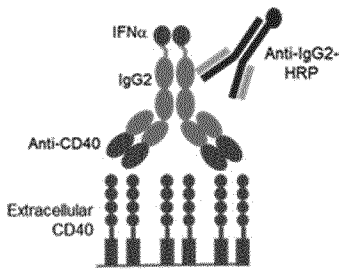


Fig. 8C

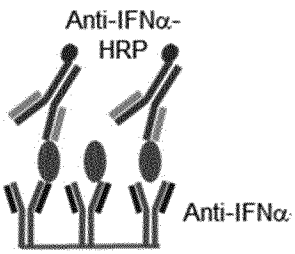
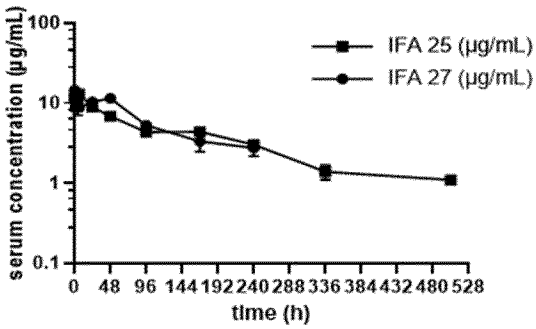


Fig. 8D



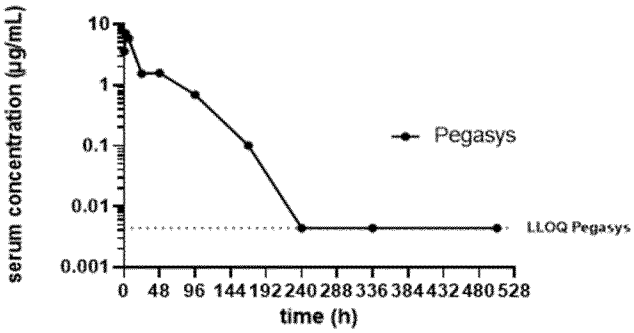


Fig. 9A

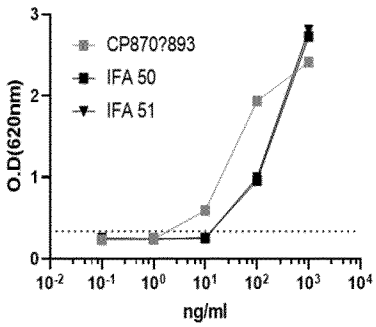


Fig. 9B

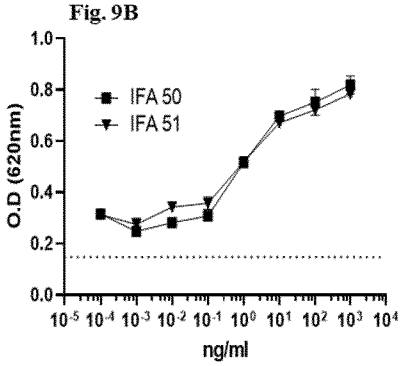


Fig. 9C

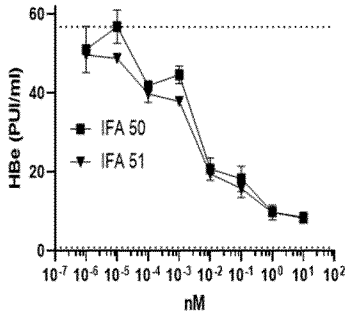


Fig. 10A

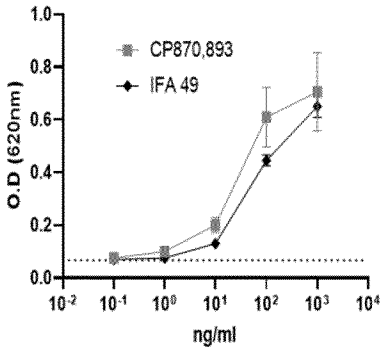


Fig. 10B

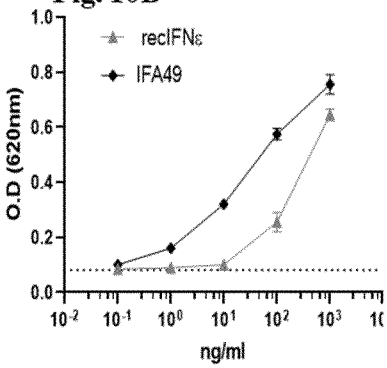


Fig. 10C

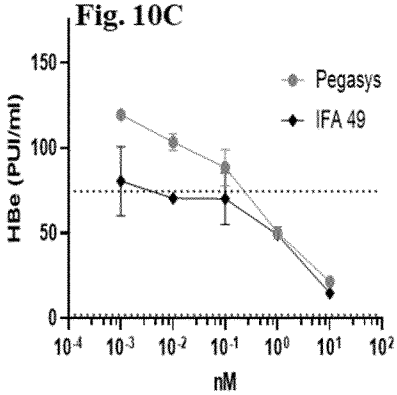


Fig. 11A

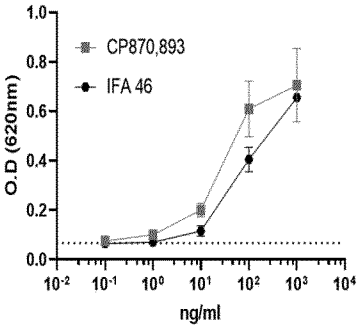


Fig. 11B

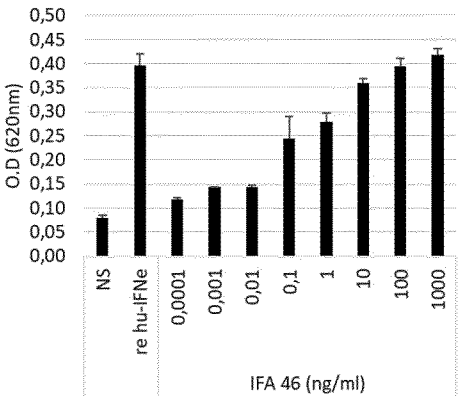


Fig. 11C

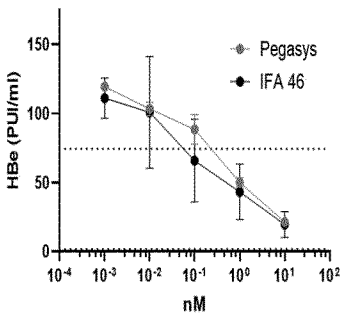


Fig. 12A

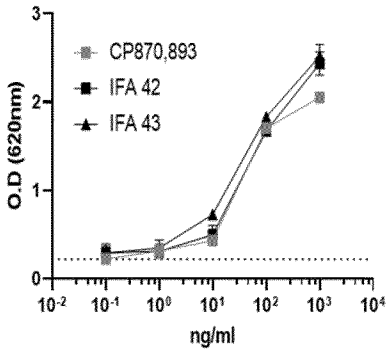


Fig. 12B

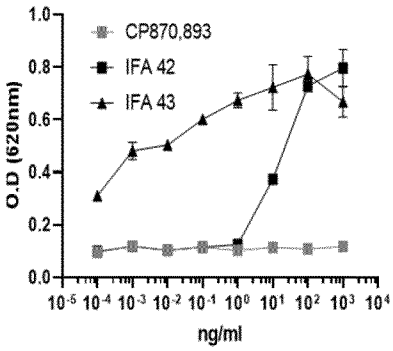


Fig. 12C

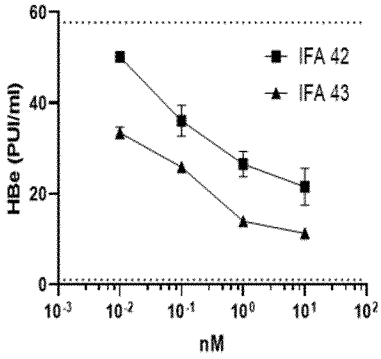


Fig. 13A

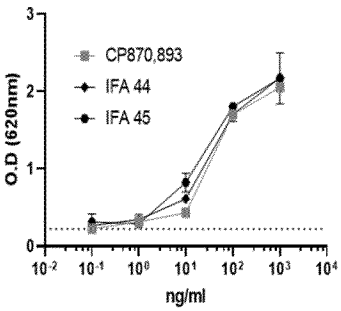


Fig. 13B

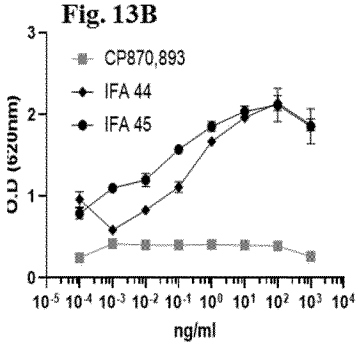


Fig. 13C

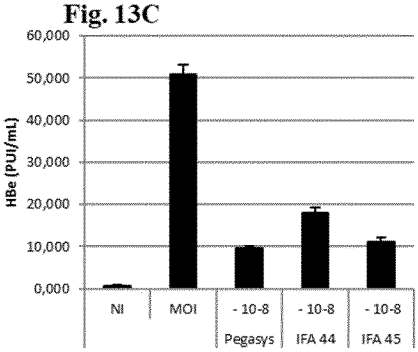


Fig. 14

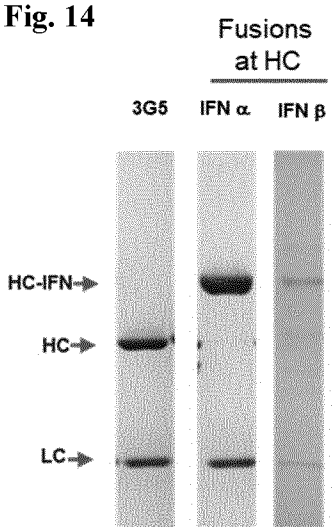


Fig. 15A

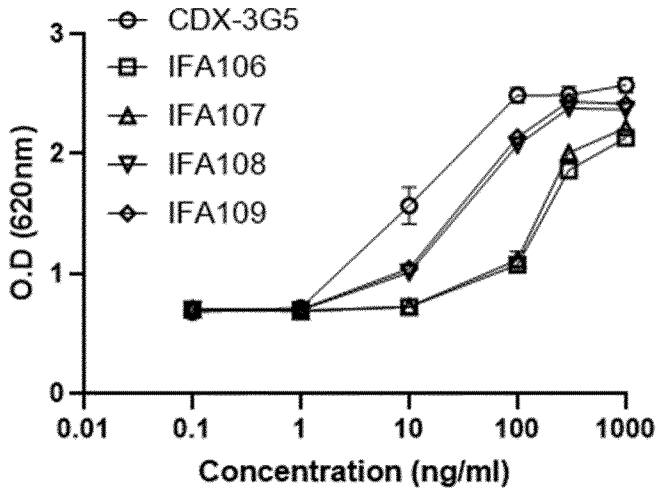


Fig. 15B

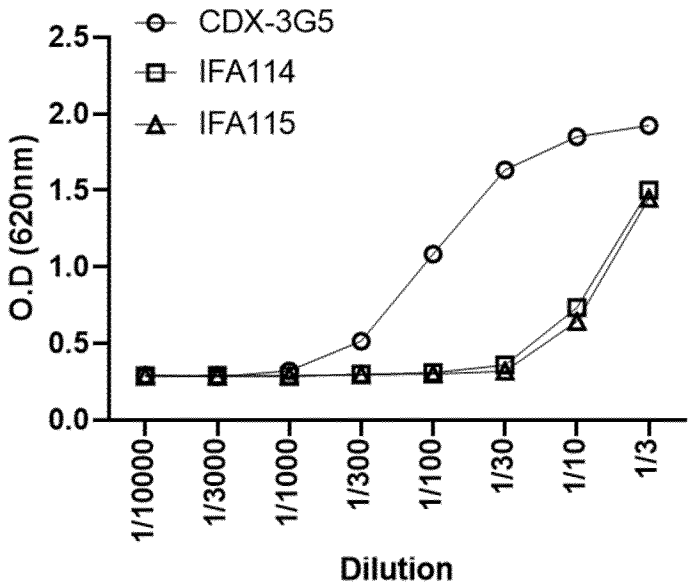


Fig. 15C

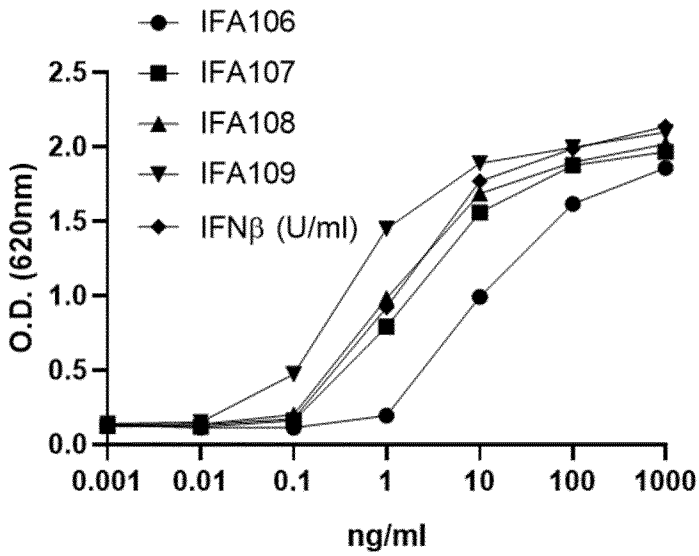


Fig. 15D

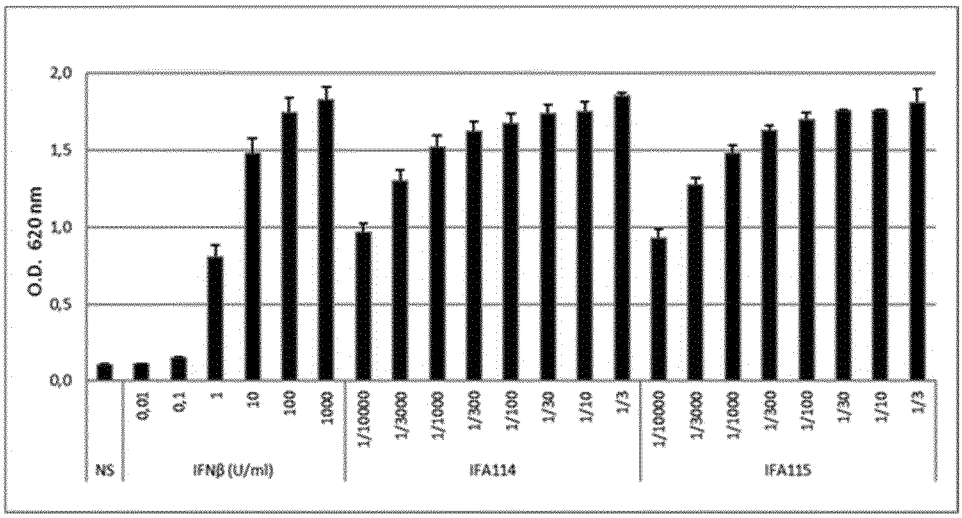


Fig. 16A

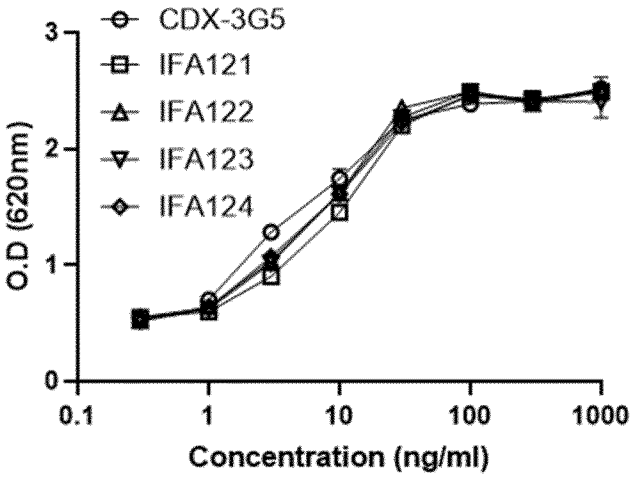


Fig. 16B

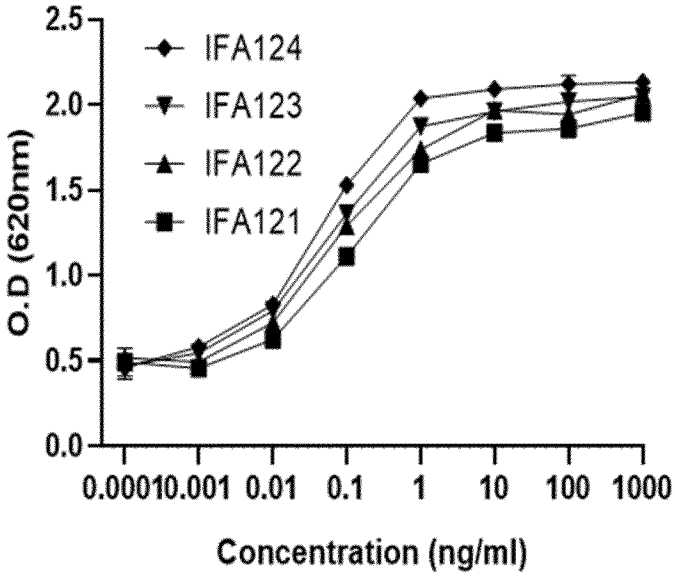


Fig. 17A

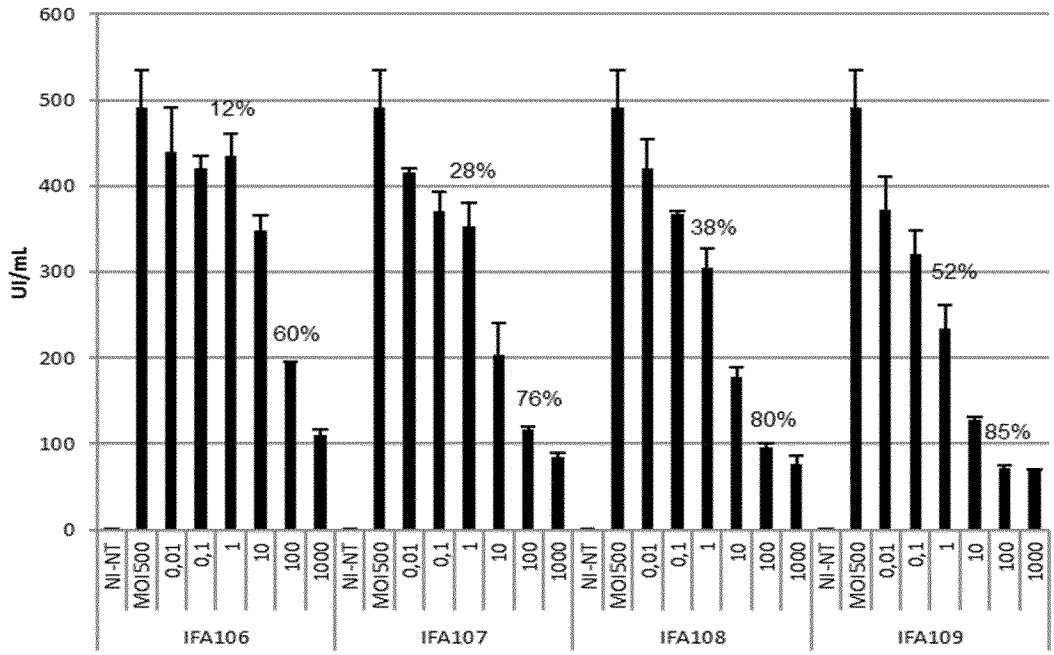


Fig. 17B

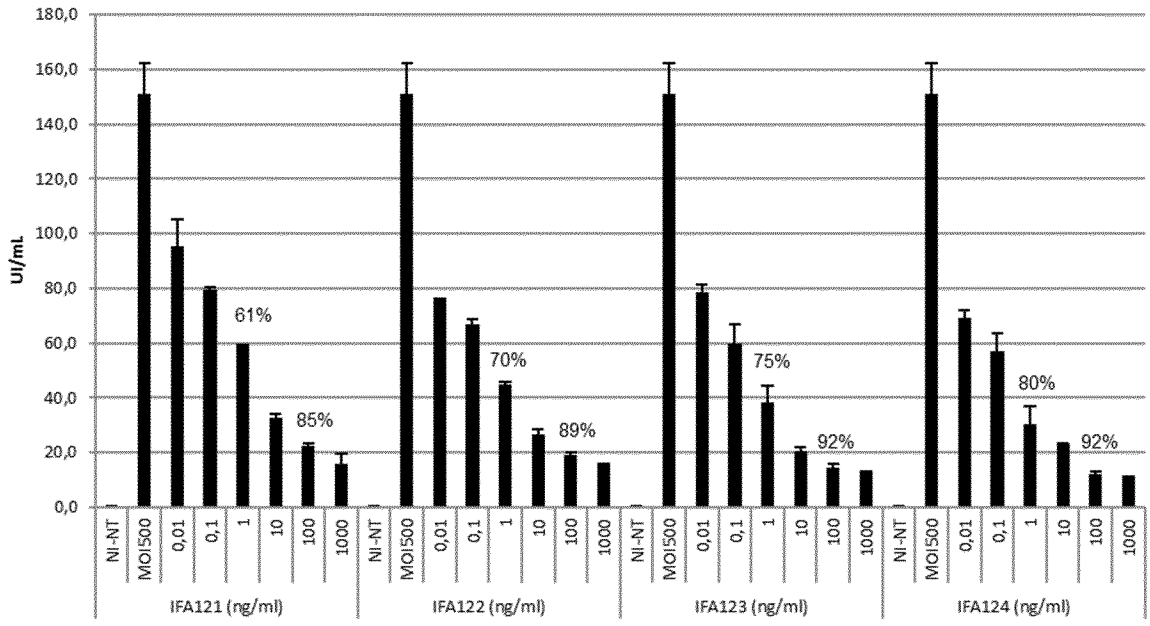
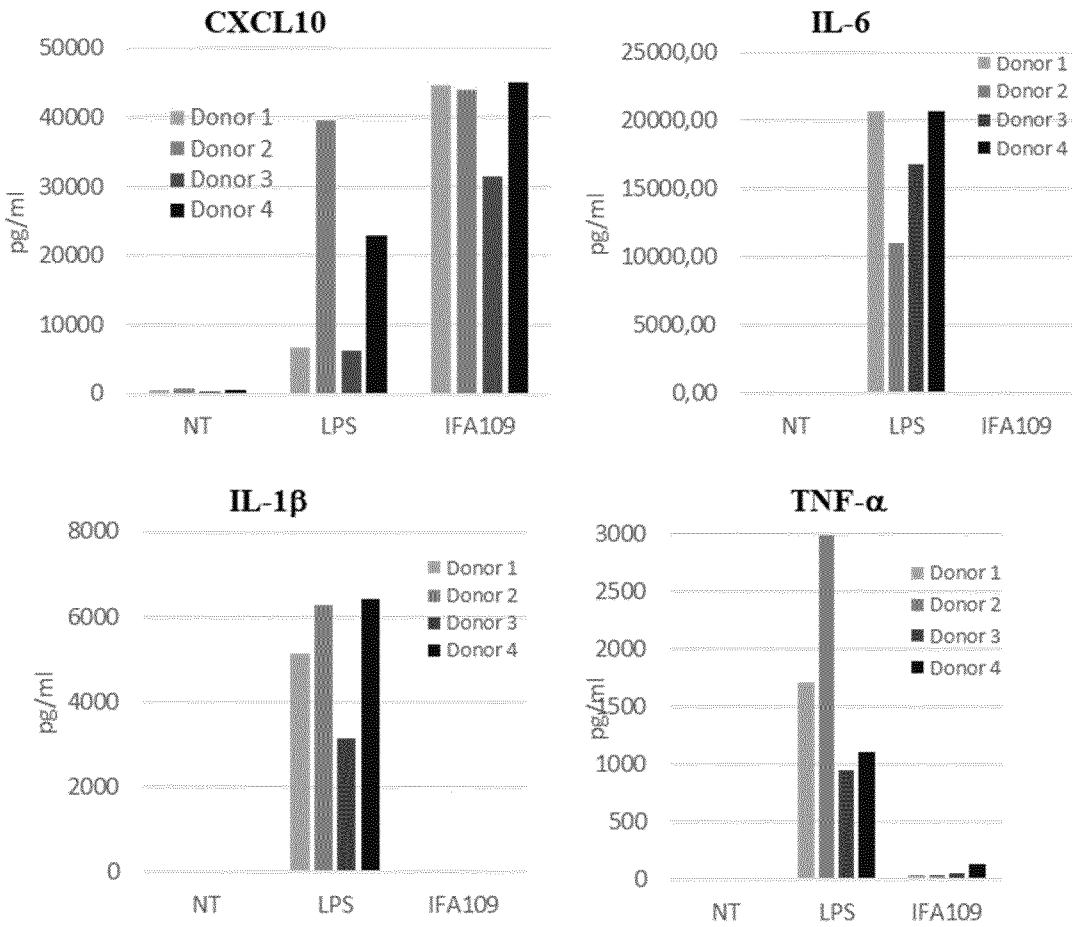


Fig. 18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30000
20000
10000
0
pg/ml
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Donor 2
Donor 3
Donor 4
NT
LPS
IFA109
IL-6
25000,00
20000,00
15000,00
10000,00
5000,00
0,00
pg/ml
Donor 1
Donor 2
Donor 3
Donor 4
NT
LPS
IFA109
IL-1β
8000
6000
4000
2000
0
pg/ml
Donor 1
Donor 2
Donor 3
Donor 4
NT
LPS
IFA109
TNF-α
3000
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pg/ml
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LPS
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SEQUENCE LISTING

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SANOFI

<120> Interferon-associated antigen binding proteins for use in treating hepatitis B infection.

<130> EVO22745PCT-A

<150> EP19 306 572.9
<151> 2019-12-04
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Val His Ser

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Leu Arg Gly Ala Arg Cys
20

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20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Asn Leu Leu Ile
35 40 45
Tyr Thr Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Asn Ile Phe Pro Leu
                85   90   95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100   105   110
Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115   120   125
Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130   135   140
Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145   150   155   160
Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                165   170   175
Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180   185   190
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Phe Asn Arg Gly Glu Cys
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<210> 4
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            20   25   30
Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile
        35   40   45
Tyr Ser Trp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Asn
    50   55   60
Leu Leu Ile Tyr Thr Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg
65   70   75   80
Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser
                85   90   95
Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Asn Ile
            100   105   110
Phe Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr
        115   120   125
Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu
    130   135   140
Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro
145   150   155   160
Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly
                165   170   175
Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr
            180   185   190
Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His
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Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val
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Thr Lys Ser Phe Asn Arg Gly Glu Cys
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<223> antiCD40 antibody light chain with signal peptide 2

<400> 5
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1   5   10   15
Leu Arg Gly Ala Arg Cys Asp Ile Gln Met Thr Gln Ser Pro Ser Ser
            20   25   30
Val Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser
        35   40   45
Gln Gly Ile Tyr Ser Trp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys
    50   55   60
Ala Pro Asn Leu Leu Ile Tyr Thr Ala Ser Thr Leu Gln Ser Gly Val
65   70   75   80
Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
                85   90   95
Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln
            100   105   110
Ala Asn Ile Phe Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
        115   120   125
Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp
    130   135   140
Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn
145   150   155   160
Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu
                165   170   175
Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp
            180   185   190
Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr
        195   200   205
Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser
    210   215   220
Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
225   230   235

<210> 6
<211> 451
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40 antibody heavy chain hIgG2 dK

<400> 6
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1   5   10   15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
            20   25   30
Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35   40   45
Gly Trp Ile Asn Pro Asp Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
    50   55   60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65   70   75   80
Met Glu Leu Asn Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85   90   95
Ala Arg Asp Gln Pro Leu Gly Tyr Cys Thr Asn Gly Val Cys Ser Tyr
            100   105   110
Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser
        115   120   125
Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr
    130   135   140
Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro
145   150   155   160
Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val
                165   170   175
His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser
            180   185   190
Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr
        195   200   205
Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val

```
    210                 215                 220
Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val
225                 230                 235                 240
Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
                245                 250                 255
Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
            260                 265                 270
His Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu
        275                 280                 285
Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr
    290                 295                 300
Phe Arg Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn
305                 310                 315                 320
Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro
                325                 330                 335
Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln
            340                 345                 350
Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val
        355                 360                 365
Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
    370                 375                 380
Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
385                 390                 395                 400
Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
                405                 410                 415
Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
            420                 425                 430
Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
        435                 440                 445
Ser Pro Gly
    450
```

<210> 7
<211> 470
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40 antibody heavy chain hIgG2 dK with signal peptide 1

<400> 7

```
Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1               5                   10                  15
Val His Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
            20                  25                  30
Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe
        35                  40                  45
Thr Gly Tyr Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu
    50                  55                  60
Glu Trp Met Gly Trp Ile Asn Pro Asp Ser Gly Gly Thr Asn Tyr Ala
65                  70                  75                  80
Gln Lys Phe Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser
                85                  90                  95
Thr Ala Tyr Met Glu Leu Asn Arg Leu Arg Ser Asp Asp Thr Ala Val
            100                 105                 110
Tyr Tyr Cys Ala Arg Asp Gln Pro Leu Gly Tyr Cys Thr Asn Gly Val
        115                 120                 125
Cys Ser Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
    130                 135                 140
Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser
145                 150                 155                 160
Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
                165                 170                 175
Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
            180                 185                 190
Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
        195                 200                 205
Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln
```

```
    210                 215                 220
Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp
225                 230                 235                 240
Lys Thr Val Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala
                245                 250                 255
Pro Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
            260                 265                 270
Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
        275                 280                 285
Asp Val Ser His Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp
    290                 295                 300
Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe
305                 310                 315                 320
Asn Ser Thr Phe Arg Val Val Ser Val Leu Thr Val Val His Gln Asp
                325                 330                 335
Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu
            340                 345                 350
Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg
        355                 360                 365
Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
    370                 375                 380
Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
385                 390                 395                 400
Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
                405                 410                 415
Thr Thr Pro Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
            420                 425                 430
Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
        435                 440                 445
Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
    450                 455                 460
Leu Ser Leu Ser Pro Gly
465                 470

<210> 8
<211> 473
<212> PRT
<213> Artificial Sequence


<220>
<223> antiCD40 antibody heavy chain hIgG2 dK with signal peptide 2

<400> 8
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1                 5                  10                  15
Leu Arg Gly Ala Arg Cys Gln Val Gln Leu Val Gln Ser Gly Ala Glu
            20                  25                  30
Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly
        35                  40                  45
Tyr Thr Phe Thr Gly Tyr Tyr Met His Trp Val Arg Gln Ala Pro Gly
    50                  55                  60
Gln Gly Leu Glu Trp Met Gly Trp Ile Asn Pro Asp Ser Gly Gly Thr
65                  70                  75                  80
Asn Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Met Thr Arg Asp Thr
                85                  90                  95
Ser Ile Ser Thr Ala Tyr Met Glu Leu Asn Arg Leu Arg Ser Asp Asp
            100                 105                 110
Thr Ala Val Tyr Tyr Cys Ala Arg Asp Gln Pro Leu Gly Tyr Cys Thr
        115                 120                 125
Asn Gly Val Cys Ser Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
    130                 135                 140
Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
145                 150                 155                 160
Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu
                165                 170                 175
Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
            180                 185                 190
Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
```

```
        195                 200                 205
Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Asn Phe
    210                 215                 220
Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr
225                 230                 235                 240
Lys Val Asp Lys Thr Val Glu Arg Lys Cys Cys Val Glu Cys Pro Pro
                245                 250                 255
Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro
            260                 265                 270
Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
        275                 280                 285
Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Gln Phe Asn Trp
    290                 295                 300
Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
305                 310                 315                 320
Glu Gln Phe Asn Ser Thr Phe Arg Val Val Ser Val Leu Thr Val Val
                325                 330                 335
His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
            340                 345                 350
Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly
        355                 360                 365
Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
    370                 375                 380
Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
385                 390                 395                 400
Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
                405                 410                 415
Asn Tyr Lys Thr Thr Pro Pro Met Leu Asp Ser Asp Gly Ser Phe Phe
            420                 425                 430
Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
        435                 440                 445
Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
    450                 455                 460
Gln Lys Ser Leu Ser Leu Ser Pro Gly
465                 470

<210> 9
<211> 452
<212> PRT
<213> Artificial Sequence


<220>
<223> antiCD40 antibody heavy chain hIgG2

<400> 9
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
            20                  25                  30
Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
Gly Trp Ile Asn Pro Asp Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
    50                  55                  60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Met Glu Leu Asn Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Asp Gln Pro Leu Gly Tyr Cys Thr Asn Gly Val Cys Ser Tyr
            100                 105                 110
Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser
        115                 120                 125
Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr
    130                 135                 140
Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro
145                 150                 155                 160
Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val
                165                 170                 175
His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser
```

```
            180                 185                 190
Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr
        195                 200                 205
Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val
    210                 215                 220
Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val
225                 230                 235                 240
Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
                245                 250                 255
Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
            260                 265                 270
His Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu
        275                 280                 285
Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr
    290                 295                 300
Phe Arg Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn
305                 310                 315                 320
Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro
                325                 330                 335
Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln
            340                 345                 350
Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val
        355                 360                 365
Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
    370                 375                 380
Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
385                 390                 395                 400
Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
                405                 410                 415
Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
            420                 425                 430
Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
        435                 440                 445
Ser Pro Gly Lys
    450

<210> 10
<211> 471
<212> PRT
<213> Artificial Sequence


<220>
<223> antiCD40 antibody heavy chain hIgG2 with signal peptide 1

<400> 10
Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1               5                   10                  15
Val His Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
            20                  25                  30
Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe
        35                  40                  45
Thr Gly Tyr Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu
    50                  55                  60
Glu Trp Met Gly Trp Ile Asn Pro Asp Ser Gly Gly Thr Asn Tyr Ala
65                  70                  75                  80
Gln Lys Phe Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser
                85                  90                  95
Thr Ala Tyr Met Glu Leu Asn Arg Leu Arg Ser Asp Asp Thr Ala Val
            100                 105                 110
Tyr Tyr Cys Ala Arg Asp Gln Pro Leu Gly Tyr Cys Thr Asn Gly Val
        115                 120                 125
Cys Ser Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
    130                 135                 140
Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser
145                 150                 155                 160
Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
                165                 170                 175
Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
```

```
            180                 185                 190
Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
        195                 200                 205
Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln
    210                 215                 220
Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp
225                 230                 235                 240
Lys Thr Val Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala
                245                 250                 255
Pro Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
            260                 265                 270
Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
        275                 280                 285
Asp Val Ser His Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp
    290                 295                 300
Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe
305                 310                 315                 320
Asn Ser Thr Phe Arg Val Val Ser Val Leu Thr Val Val His Gln Asp
                325                 330                 335
Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu
            340                 345                 350
Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg
        355                 360                 365
Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys
    370                 375                 380
Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
385                 390                 395                 400
Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
                405                 410                 415
Thr Thr Pro Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
            420                 425                 430
Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
        435                 440                 445
Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
    450                 455                 460
Leu Ser Leu Ser Pro Gly Lys
465                 470

<210> 11
<211> 474
<212> PRT
<213> Artificial Sequence


<220>
<223> antiCD40 antibody heavy chain hIgG2 with signal peptide 2

<400> 11
Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp
1               5                   10                  15
Leu Arg Gly Ala Arg Cys Gln Val Gln Leu Val Gln Ser Gly Ala Glu
            20                  25                  30
Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly
        35                  40                  45
Tyr Thr Phe Thr Gly Tyr Tyr Met His Trp Val Arg Gln Ala Pro Gly
    50                  55                  60
Gln Gly Leu Glu Trp Met Gly Trp Ile Asn Pro Asp Ser Gly Gly Thr
65                  70                  75                  80
Asn Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Met Thr Arg Asp Thr
                85                  90                  95
Ser Ile Ser Thr Ala Tyr Met Glu Leu Asn Arg Leu Arg Ser Asp Asp
            100                 105                 110
Thr Ala Val Tyr Tyr Cys Ala Arg Asp Gln Pro Leu Gly Tyr Cys Thr
        115                 120                 125
Asn Gly Val Cys Ser Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val
    130                 135                 140
Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala
145                 150                 155                 160
Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu
```

```
                165                 170                 175
Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly
            180                 185                 190
Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser
        195                 200                 205
Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Asn Phe
    210                 215                 220
Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr
225                 230                 235                 240
Lys Val Asp Lys Thr Val Glu Arg Lys Cys Cys Val Glu Cys Pro Pro
                245                 250                 255
Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro
            260                 265                 270
Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
        275                 280                 285
Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Gln Phe Asn Trp
    290                 295                 300
Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
305                 310                 315                 320
Glu Gln Phe Asn Ser Thr Phe Arg Val Val Ser Val Leu Thr Val Val
                325                 330                 335
His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
            340                 345                 350
Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly
        355                 360                 365
Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu
    370                 375                 380
Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr
385                 390                 395                 400
Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
                405                 410                 415
Asn Tyr Lys Thr Thr Pro Pro Met Leu Asp Ser Asp Gly Ser Phe Phe
            420                 425                 430
Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
        435                 440                 445
Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
    450                 455                 460
Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
465                 470

<210> 12
<211> 231
<212> PRT
<213> Artificial Sequence


<220>
<223> antiCD40 antibody hIgG2 Fab region heavy chain

<400> 12
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
            20                  25                  30
Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
Gly Trp Ile Asn Pro Asp Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
    50                  55                  60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Met Glu Leu Asn Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Asp Gln Pro Leu Gly Tyr Cys Thr Asn Gly Val Cys Ser Tyr
            100                 105                 110
Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser
        115                 120                 125
Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr
    130                 135                 140
Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro
```

145 150 155 160
Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val
165 170 175
His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser
180 185 190
Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr
195 200 205
Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val
210 215 220
Glu Arg Lys Cys Cys Val Glu
225 230

<210> 13
<211> 250
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40 antibody hIgG2 Fab region heavy chain with signal peptide 1

<400> 13
Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1 5 10 15
Val His Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys
20 25 30
Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe
35 40 45
Thr Gly Tyr Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu
50 55 60
Glu Trp Met Gly Trp Ile Asn Pro Asp Ser Gly Gly Thr Asn Tyr Ala
65 70 75 80
Gln Lys Phe Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser
85 90 95
Thr Ala Tyr Met Glu Leu Asn Arg Leu Arg Ser Asp Asp Thr Ala Val
100 105 110
Tyr Tyr Cys Ala Arg Asp Gln Pro Leu Gly Tyr Cys Thr Asn Gly Val
115 120 125
Cys Ser Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
130 135 140
Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser
145 150 155 160
Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
165 170 175
Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
180 185 190
Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
195 200 205
Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln
210 215 220
Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp
225 230 235 240
Lys Thr Val Glu Arg Lys Cys Cys Val Glu
245 250

<210> 14
<211> 166
<212> PRT
<213> Homo sapiens

<220>
<223> IFNÎ²

<400> 14
Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln
1 5 10 15
Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu

```
            20                  25                  30
Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln
        35                  40                  45
Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln
    50                  55                  60
Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn
65                  70                  75                  80
Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn
                85                  90                  95
His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr
            100                 105                 110
Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg
        115                 120                 125
Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr
    130                 135                 140
Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu
145                 150                 155                 160
Thr Gly Tyr Leu Arg Asn
                165
```

<210> 15
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> IFNÎ² C17S

<400> 15

```
Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln
1               5                   10                  15
Ser Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu
            20                  25                  30
Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln
        35                  40                  45
Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln
    50                  55                  60
Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn
65                  70                  75                  80
Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn
                85                  90                  95
His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr
            100                 105                 110
Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg
        115                 120                 125
Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr
    130                 135                 140
Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu
145                 150                 155                 160
Thr Gly Tyr Leu Arg Asn
                165
```

<210> 16
<211> 166
<212> PRT
<213> Artificial Sequence

<220>
<223> IFNÎ² C17S,N80Q

<400> 16

```
Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln
1               5                   10                  15
Ser Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu
            20                  25                  30
Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln
        35                  40                  45
```

Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln
    50   55   60
Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Gln
65   70   75   80
Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn
                85   90   95
His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr
            100   105   110
Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg
        115   120   125
Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr
    130   135   140
Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu
145   150   155   160
Thr Gly Tyr Leu Arg Asn
                165

<210> 17
<211> 165
<212> PRT
<213> Homo sapiens

<220>
<223> IFNÎ±2a

<400> 17
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
1   5   10   15
Leu Leu Ala Gln Met Arg Lys Ile Ser Leu Phe Ser Cys Leu Lys Asp
            20   25   30
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
        35   40   45
Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
    50   55   60
Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
65   70   75   80
Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
                85   90   95
Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
            100   105   110
Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
        115   120   125
Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
    130   135   140
Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
145   150   155   160
Leu Arg Ser Lys Glu
                165

<210> 18
<211> 175
<212> PRT
<213> Homo sapiens

<220>
<223> IFNÎ»2

<400> 18
Val Pro Val Ala Arg Leu His Gly Ala Leu Pro Asp Ala Arg Gly Cys
1   5   10   15
His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala Phe
            20   25   30
Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp Cys
        35   40   45
Arg Cys His Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln Leu
    50   55   60
Gln Val Arg Glu Arg Pro Met Ala Leu Glu Ala Glu Leu Ala Leu Thr

65 70 75 80
Leu Lys Val Leu Glu Ala Thr Ala Asp Thr Asp Pro Ala Leu Val Asp
85 90 95
Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Phe
100 105 110
Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg Gly
115 120 125
Arg Leu His His Trp Leu Tyr Arg Leu Gln Glu Ala Pro Lys Lys Glu
130 135 140
Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu
145 150 155 160
Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val
165 170 175

<210> 19
<211> 143
<212> PRT
<213> Homo sapiens

<220>
<223> IFNÎ³

<400> 19
Gln Asp Pro Tyr Val Lys Glu Ala Glu Asn Leu Lys Lys Tyr Phe Asn
1 5 10 15
Ala Gly His Ser Asp Val Ala Asp Asn Gly Thr Leu Phe Leu Gly Ile
20 25 30
Leu Lys Asn Trp Lys Glu Glu Ser Asp Arg Lys Ile Met Gln Ser Gln
35 40 45
Ile Val Ser Phe Tyr Phe Lys Leu Phe Lys Asn Phe Lys Asp Asp Gln
50 55 60
Ser Ile Gln Lys Ser Val Glu Thr Ile Lys Glu Asp Met Asn Val Lys
65 70 75 80
Phe Phe Asn Ser Asn Lys Lys Lys Arg Asp Asp Phe Glu Lys Leu Thr
85 90 95
Asn Tyr Ser Val Thr Asp Leu Asn Val Gln Arg Lys Ala Ile His Glu
100 105 110
Leu Ile Gln Val Met Ala Glu Leu Ser Pro Ala Ala Lys Thr Gly Lys
115 120 125
Arg Lys Arg Ser Gln Met Leu Phe Arg Gly Arg Arg Ala Ser Gln
130 135 140

<210> 20
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> RL linker

<400> 20
Pro Ala Pro Ala
1

<210> 21
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> GST linker

<400> 21
Ser Gly Gly Thr Ser Gly Ser Thr Ser Gly Thr Gly Ser
1 5 10

<210> 22
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> HL linker

<400> 22
Ala Glu Ala Ala Ala Lys Glu Ala Ala Ala Lys Ala
1   5   10

<210> 23
<211> 24
<212> PRT
<213> Artificial Sequence

<220>
<223> HL2 linker

<400> 23
Ala Glu Ala Ala Ala Lys Glu Ala Ala Ala Lys Ala Ala Glu Ala Ala
1   5   10   15
Ala Lys Glu Ala Ala Ala Lys Ala
            20

<210> 24
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> G4S2 linker

<400> 24
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1   5   10

<210> 25
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> G4S3 linker

<400> 25
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1   5   10   15

<210> 26
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> G4S4 linker

<400> 26
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1   5   10   15
Gly Gly Gly Ser
            20

<210> 27
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> TEV-6His tag

<400> 27
Glu Asn Leu Tyr Phe Gln Ser His His His His His His
1   5   10

<210> 28
<211> 392
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40_LC--HL--IFNÎ²

<400> 28
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
1   5   10   15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Tyr Ser Trp
            20   25   30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Asn Leu Leu Ile
        35   40   45
Tyr Thr Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Asn Ile Phe Pro Leu
                85   90   95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100   105   110
Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115   120   125
Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130   135   140
Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145   150   155   160
Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                165   170   175
Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180   185   190
Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195   200   205
Phe Asn Arg Gly Glu Cys Ala Glu Ala Ala Ala Lys Glu Ala Ala Ala
    210   215   220
Lys Ala Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn
225   230   235   240
Phe Gln Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr
                245   250   255
Cys Leu Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln
            260   265   270
Leu Gln Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met
        275   280   285
Leu Gln Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly
    290   295   300
Trp Asn Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln
305   310   315   320
Ile Asn His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp
                325   330   335
Phe Thr Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr
            340   345   350
Gly Arg Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala
        355   360   365

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Trp Thr Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn
    370                 375                 380
Arg Leu Thr Gly Tyr Leu Arg Asn
385                 390

<210> 29
<211> 392
<212> PRT
<213> Artificial Sequence


<220>
<223> antiCD40_LC--HL--IFNÎ²_C17S

<400> 29
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
1               5                   10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Tyr Ser Trp
            20                  25                  30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Asn Leu Leu Ile
        35                  40                  45
Tyr Thr Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Asn Ile Phe Pro Leu
                85                  90                  95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110
Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115                 120                 125
Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130                 135                 140
Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145                 150                 155                 160
Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                165                 170                 175
Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190
Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205
Phe Asn Arg Gly Glu Cys Ala Glu Ala Ala Ala Lys Glu Ala Ala Ala
    210                 215                 220
Lys Ala Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn
225                 230                 235                 240
Phe Gln Ser Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr
                245                 250                 255
Cys Leu Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln
            260                 265                 270
Leu Gln Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met
        275                 280                 285
Leu Gln Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly
    290                 295                 300
Trp Asn Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln
305                 310                 315                 320
Ile Asn His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp
                325                 330                 335
Phe Thr Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr
            340                 345                 350
Gly Arg Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala
        355                 360                 365
Trp Thr Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn
    370                 375                 380
Arg Leu Thr Gly Tyr Leu Arg Asn
385                 390

<210> 30
<211> 621
<212> PRT
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<213> Artificial Sequence

<220>
<223> antiCD40_hIgG2_dK_HC--RL--IFNÎ²

<400> 30
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1   5   10   15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
            20   25   30
Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35   40   45
Gly Trp Ile Asn Pro Asp Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
    50   55   60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65   70   75   80
Met Glu Leu Asn Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85   90   95
Ala Arg Asp Gln Pro Leu Gly Tyr Cys Thr Asn Gly Val Cys Ser Tyr
            100   105   110
Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser
        115   120   125
Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr
    130   135   140
Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro
145   150   155   160
Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val
                165   170   175
His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser
            180   185   190
Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr
        195   200   205
Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val
    210   215   220
Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val
225   230   235   240
Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
                245   250   255
Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
            260   265   270
His Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu
        275   280   285
Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr
    290   295   300
Phe Arg Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn
305   310   315   320
Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro
                325   330   335
Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln
            340   345   350
Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val
        355   360   365
Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
    370   375   380
Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
385   390   395   400
Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
                405   410   415
Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
            420   425   430
Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
        435   440   445
Ser Pro Gly Pro Ala Pro Ala Met Ser Tyr Asn Leu Leu Gly Phe Leu
    450   455   460
Gln Arg Ser Ser Asn Phe Gln Cys Gln Lys Leu Leu Trp Gln Leu Asn
465   470   475   480
Gly Arg Leu Glu Tyr Cys Leu Lys Asp Arg Met Asn Phe Asp Ile Pro
                485   490   495

Glu Glu Ile Lys Gln Leu Gln Gln Phe Gln Lys Glu Asp Ala Ala Leu
            500   505   510
Thr Ile Tyr Glu Met Leu Gln Asn Ile Phe Ala Ile Phe Arg Gln Asp
        515   520   525
Ser Ser Ser Thr Gly Trp Asn Glu Thr Ile Val Glu Asn Leu Leu Ala
    530   535   540
Asn Val Tyr His Gln Ile Asn His Leu Lys Thr Val Leu Glu Glu Lys
545   550   555   560
Leu Glu Lys Glu Asp Phe Thr Arg Gly Lys Leu Met Ser Ser Leu His
                565   570   575
Leu Lys Arg Tyr Tyr Gly Arg Ile Leu His Tyr Leu Lys Ala Lys Glu
            580   585   590
Tyr Ser His Cys Ala Trp Thr Ile Val Arg Val Glu Ile Leu Arg Asn
        595   600   605
Phe Tyr Phe Ile Asn Arg Leu Thr Gly Tyr Leu Arg Asn
    610   615   620

<210> 31
<211> 621
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40_hIgG2_dK_HC--RL--IFNÎ²_C17S

<400> 31
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1   5   10   15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
            20   25   30
Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35   40   45
Gly Trp Ile Asn Pro Asp Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
    50   55   60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65   70   75   80
Met Glu Leu Asn Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85   90   95
Ala Arg Asp Gln Pro Leu Gly Tyr Cys Thr Asn Gly Val Cys Ser Tyr
            100   105   110
Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser
        115   120   125
Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr
    130   135   140
Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro
145   150   155   160
Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val
                165   170   175
His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser
            180   185   190
Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr
        195   200   205
Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val
    210   215   220
Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val
225   230   235   240
Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
                245   250   255
Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
            260   265   270
His Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu
        275   280   285
Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr
    290   295   300
Phe Arg Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn
305   310   315   320
Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro
                325   330   335

Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln
            340   345   350
Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val
        355   360   365
Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
    370   375   380
Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
385   390   395   400
Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
                405   410   415
Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
            420   425   430
Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
        435   440   445
Ser Pro Gly Pro Ala Pro Ala Met Ser Tyr Asn Leu Leu Gly Phe Leu
    450   455   460
Gln Arg Ser Ser Asn Phe Gln Ser Gln Lys Leu Leu Trp Gln Leu Asn
465   470   475   480
Gly Arg Leu Glu Tyr Cys Leu Lys Asp Arg Met Asn Phe Asp Ile Pro
                485   490   495
Glu Glu Ile Lys Gln Leu Gln Gln Phe Gln Lys Glu Asp Ala Ala Leu
            500   505   510
Thr Ile Tyr Glu Met Leu Gln Asn Ile Phe Ala Ile Phe Arg Gln Asp
        515   520   525
Ser Ser Ser Thr Gly Trp Asn Glu Thr Ile Val Glu Asn Leu Leu Ala
    530   535   540
Asn Val Tyr His Gln Ile Asn His Leu Lys Thr Val Leu Glu Glu Lys
545   550   555   560
Leu Glu Lys Glu Asp Phe Thr Arg Gly Lys Leu Met Ser Ser Leu His
                565   570   575
Leu Lys Arg Tyr Tyr Gly Arg Ile Leu His Tyr Leu Lys Ala Lys Glu
            580   585   590
Tyr Ser His Cys Ala Trp Thr Ile Val Arg Val Glu Ile Leu Arg Asn
        595   600   605
Phe Tyr Phe Ile Asn Arg Leu Thr Gly Tyr Leu Arg Asn
    610   615   620

<210> 32
<211> 629
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40_hIgG2_dK_HC--HL--IFNÎ²

<400> 32
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1   5   10   15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
            20   25   30
Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35   40   45
Gly Trp Ile Asn Pro Asp Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
    50   55   60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65   70   75   80
Met Glu Leu Asn Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85   90   95
Ala Arg Asp Gln Pro Leu Gly Tyr Cys Thr Asn Gly Val Cys Ser Tyr
            100   105   110
Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser
        115   120   125
Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr
    130   135   140
Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro
145   150   155   160
Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val
                165   170   175

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His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser
            180                 185                 190
Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr
        195                 200                 205
Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val
    210                 215                 220
Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val
225                 230                 235                 240
Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
                245                 250                 255
Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
            260                 265                 270
His Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu
        275                 280                 285
Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr
    290                 295                 300
Phe Arg Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn
305                 310                 315                 320
Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro
                325                 330                 335
Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln
            340                 345                 350
Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val
        355                 360                 365
Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
    370                 375                 380
Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
385                 390                 395                 400
Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
                405                 410                 415
Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
            420                 425                 430
Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
        435                 440                 445
Ser Pro Gly Ala Glu Ala Ala Ala Lys Glu Ala Ala Ala Lys Ala Met
    450                 455                 460
Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln Cys
465                 470                 475                 480
Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu Lys
                485                 490                 495
Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln Gln
            500                 505                 510
Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln Asn
        515                 520                 525
Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn Glu
    530                 535                 540
Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn His
545                 550                 555                 560
Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr Arg
                565                 570                 575
Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg Ile
            580                 585                 590
Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr Ile
        595                 600                 605
Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu Thr
    610                 615                 620
Gly Tyr Leu Arg Asn
625
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<210> 33
<211> 629
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40_hIgG2_dK_HC--HL--IFNÎ²_C17S

<400> 33

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                  10                  15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
            20                  25                  30
Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
Gly Trp Ile Asn Pro Asp Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
    50                  55                  60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Met Glu Leu Asn Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Asp Gln Pro Leu Gly Tyr Cys Thr Asn Gly Val Cys Ser Tyr
            100                 105                 110
Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser
        115                 120                 125
Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr
    130                 135                 140
Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro
145                 150                 155                 160
Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val
                165                 170                 175
His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser
            180                 185                 190
Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr
        195                 200                 205
Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val
    210                 215                 220
Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val
225                 230                 235                 240
Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
                245                 250                 255
Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
            260                 265                 270
His Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu
        275                 280                 285
Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr
    290                 295                 300
Phe Arg Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn
305                 310                 315                 320
Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro
                325                 330                 335
Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln
            340                 345                 350
Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val
        355                 360                 365
Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
    370                 375                 380
Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
385                 390                 395                 400
Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
                405                 410                 415
Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
            420                 425                 430
Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
        435                 440                 445
Ser Pro Gly Ala Glu Ala Ala Ala Lys Glu Ala Ala Ala Lys Ala Met
    450                 455                 460
Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln Ser
465                 470                 475                 480
Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu Lys
                485                 490                 495
Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln Gln
            500                 505                 510
Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln Asn
        515                 520                 525
Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn Glu
    530                 535                 540
Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn His
```

545 550 555 560
Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr Arg
565 570 575
Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg Ile
580 585 590
Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr Ile
595 600 605
Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu Thr
610 615 620
Gly Tyr Leu Arg Asn
625

<210> 34
<211> 384
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40_LC-- RL--IFNÎ²

<400> 34
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Tyr Ser Trp
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Asn Leu Leu Ile
35 40 45
Tyr Thr Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Asn Ile Phe Pro Leu
85 90 95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110
Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125
Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140
Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160
Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175
Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190
Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205
Phe Asn Arg Gly Glu Cys Pro Ala Pro Ala Met Ser Tyr Asn Leu Leu
210 215 220
Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln Cys Gln Lys Leu Leu Trp
225 230 235 240
Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu Lys Asp Arg Met Asn Phe
245 250 255
Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln Gln Phe Gln Lys Glu Asp
260 265 270
Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln Asn Ile Phe Ala Ile Phe
275 280 285
Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn Glu Thr Ile Val Glu Asn
290 295 300
Leu Leu Ala Asn Val Tyr His Gln Ile Asn His Leu Lys Thr Val Leu
305 310 315 320
Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr Arg Gly Lys Leu Met Ser
325 330 335
Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg Ile Leu His Tyr Leu Lys
340 345 350
Ala Lys Glu Tyr Ser His Cys Ala Trp Thr Ile Val Arg Val Glu Ile
355 360 365
Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu Thr Gly Tyr Leu Arg Asn

370 375 380

<210> 35
<211> 384
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40_LC--RL--IFNÎ²_C17S

<400> 35
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Tyr Ser Trp
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Asn Leu Leu Ile
35 40 45
Tyr Thr Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Asn Ile Phe Pro Leu
85 90 95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110
Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125
Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140
Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160
Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175
Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190
Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205
Phe Asn Arg Gly Glu Cys Pro Ala Pro Ala Met Ser Tyr Asn Leu Leu
210 215 220
Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln Ser Gln Lys Leu Leu Trp
225 230 235 240
Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu Lys Asp Arg Met Asn Phe
245 250 255
Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln Gln Phe Gln Lys Glu Asp
260 265 270
Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln Asn Ile Phe Ala Ile Phe
275 280 285
Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn Glu Thr Ile Val Glu Asn
290 295 300
Leu Leu Ala Asn Val Tyr His Gln Ile Asn His Leu Lys Thr Val Leu
305 310 315 320
Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr Arg Gly Lys Leu Met Ser
325 330 335
Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg Ile Leu His Tyr Leu Lys
340 345 350
Ala Lys Glu Tyr Ser His Cys Ala Trp Thr Ile Val Arg Val Glu Ile
355 360 365
Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu Thr Gly Tyr Leu Arg Asn
370 375 380

<210> 36
<211> 393
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40_LC--GST--IFNÎ²_C17S

<400> 36
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
1   5   10   15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Tyr Ser Trp
            20   25   30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Asn Leu Leu Ile
        35   40   45
Tyr Thr Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Asn Ile Phe Pro Leu
                85   90   95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100   105   110
Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115   120   125
Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130   135   140
Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145   150   155   160
Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                165   170   175
Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180   185   190
Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195   200   205
Phe Asn Arg Gly Glu Cys Ser Gly Gly Thr Ser Gly Ser Thr Ser Gly
    210   215   220
Thr Gly Ser Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser
225   230   235   240
Asn Phe Gln Ser Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu
                245   250   255
Tyr Cys Leu Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys
            260   265   270
Gln Leu Gln Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu
        275   280   285
Met Leu Gln Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr
    290   295   300
Gly Trp Asn Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His
305   310   315   320
Gln Ile Asn His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu
                325   330   335
Asp Phe Thr Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr
            340   345   350
Tyr Gly Arg Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys
        355   360   365
Ala Trp Thr Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile
    370   375   380
Asn Arg Leu Thr Gly Tyr Leu Arg Asn
385   390

<210> 37
<211> 404
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40_LC--HL2--IFNÎ²_C17S

<400> 37
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Tyr Ser Trp
            20   25   30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Asn Leu Leu Ile
        35   40   45
Tyr Thr Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Asn Ile Phe Pro Leu
                85   90   95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100   105   110
Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115   120   125
Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130   135   140
Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145   150   155   160
Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                165   170   175
Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180   185   190
Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195   200   205
Phe Asn Arg Gly Glu Cys Ala Glu Ala Ala Ala Lys Glu Ala Ala Ala
    210   215   220
Lys Ala Ala Glu Ala Ala Ala Lys Glu Ala Ala Ala Lys Ala Met Ser
225   230   235   240
Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln Ser Gln
                245   250   255
Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu Lys Asp
            260   265   270
Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln Gln Phe
        275   280   285
Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln Asn Ile
    290   295   300
Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn Glu Thr
305   310   315   320
Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn His Leu
                325   330   335
Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr Arg Gly
            340   345   350
Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg Ile Leu
        355   360   365
His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr Ile Val
    370   375   380
Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu Thr Gly
385   390   395   400
Tyr Leu Arg Asn

<210> 38
<211> 626
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40_hIgG2_dK_HC--(G4S)2--IFNÎ±2a

<400> 38
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1   5   10   15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
            20   25   30
Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35   40   45
Gly Trp Ile Asn Pro Asp Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
    50   55   60

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Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Met Glu Leu Asn Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Asp Gln Pro Leu Gly Tyr Cys Thr Asn Gly Val Cys Ser Tyr
            100                 105                 110
Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser
        115                 120                 125
Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr
    130                 135                 140
Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro
145                 150                 155                 160
Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val
                165                 170                 175
His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser
            180                 185                 190
Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr
        195                 200                 205
Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val
    210                 215                 220
Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val
225                 230                 235                 240
Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
                245                 250                 255
Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
            260                 265                 270
His Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu
        275                 280                 285
Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr
    290                 295                 300
Phe Arg Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn
305                 310                 315                 320
Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro
                325                 330                 335
Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln
            340                 345                 350
Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val
        355                 360                 365
Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
    370                 375                 380
Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
385                 390                 395                 400
Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
                405                 410                 415
Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
            420                 425                 430
Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
        435                 440                 445
Ser Pro Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Cys Asp Leu
    450                 455                 460
Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met Leu Leu Ala
465                 470                 475                 480
Gln Met Arg Lys Ile Ser Leu Phe Ser Cys Leu Lys Asp Arg His Asp
                485                 490                 495
Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln Lys Ala Glu
            500                 505                 510
Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe Asn Leu Phe
        515                 520                 525
Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu Leu Asp Lys
    530                 535                 540
Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu Ala Cys Val
545                 550                 555                 560
Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys Glu Asp Ser
                565                 570                 575
Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu Tyr Leu Lys
            580                 585                 590
Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg Ala Glu Ile
        595                 600                 605
Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser Leu Arg Ser
```

610 615 620
Lys Glu
625

<210> 39
<211> 631
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40_hIgG2_dK_HC--(G4S)3--IFNÎ±2a

<400> 39
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20 25 30
Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Ile Asn Pro Asp Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Asn Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp Gln Pro Leu Gly Tyr Cys Thr Asn Gly Val Cys Ser Tyr
100 105 110
Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser
115 120 125
Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr
130 135 140
Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro
145 150 155 160
Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val
165 170 175
His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser
180 185 190
Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr
195 200 205
Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val
210 215 220
Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val
225 230 235 240
Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
245 250 255
Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
260 265 270
His Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu
275 280 285
Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr
290 295 300
Phe Arg Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn
305 310 315 320
Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro
325 330 335
Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln
340 345 350
Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val
355 360 365
Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
370 375 380
Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
385 390 395 400
Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
405 410 415
Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
420 425 430
Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu

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        435                 440                 445
Ser Pro Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
    450                 455                 460
Gly Ser Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr
465                 470                 475                 480
Leu Met Leu Leu Ala Gln Met Arg Lys Ile Ser Leu Phe Ser Cys Leu
                485                 490                 495
Lys Asp Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln
            500                 505                 510
Phe Gln Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln
        515                 520                 525
Ile Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu
    530                 535                 540
Thr Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp
545                 550                 555                 560
Leu Glu Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu
                565                 570                 575
Met Lys Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile
            580                 585                 590
Thr Leu Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val
        595                 600                 605
Val Arg Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln
    610                 615                 620
Glu Ser Leu Arg Ser Lys Glu
625                 630

<210> 40
<211> 636
<212> PRT
<213> Artificial Sequence


<220>
<223> antiCD40_hIgG2_dK_HC--(G4S)4--IFNÎ±2a

<400> 40
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
            20                  25                  30
Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
Gly Trp Ile Asn Pro Asp Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
    50                  55                  60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Met Glu Leu Asn Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Asp Gln Pro Leu Gly Tyr Cys Thr Asn Gly Val Cys Ser Tyr
            100                 105                 110
Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser
        115                 120                 125
Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr
    130                 135                 140
Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro
145                 150                 155                 160
Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val
                165                 170                 175
His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser
            180                 185                 190
Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr
        195                 200                 205
Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val
    210                 215                 220
Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val
225                 230                 235                 240
Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
                245                 250                 255
Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
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            260                 265                 270
His Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu
        275                 280                 285
Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr
    290                 295                 300
Phe Arg Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn
305                 310                 315                 320
Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro
                325                 330                 335
Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln
            340                 345                 350
Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val
        355                 360                 365
Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
    370                 375                 380
Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
385                 390                 395                 400
Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
                405                 410                 415
Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
            420                 425                 430
Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
        435                 440                 445
Ser Pro Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
    450                 455                 460
Gly Ser Gly Gly Gly Gly Ser Cys Asp Leu Pro Gln Thr His Ser Leu
465                 470                 475                 480
Gly Ser Arg Arg Thr Leu Met Leu Leu Ala Gln Met Arg Lys Ile Ser
                485                 490                 495
Leu Phe Ser Cys Leu Lys Asp Arg His Asp Phe Gly Phe Pro Gln Glu
            500                 505                 510
Glu Phe Gly Asn Gln Phe Gln Lys Ala Glu Thr Ile Pro Val Leu His
        515                 520                 525
Glu Met Ile Gln Gln Ile Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser
    530                 535                 540
Ala Ala Trp Asp Glu Thr Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr
545                 550                 555                 560
Gln Gln Leu Asn Asp Leu Glu Ala Cys Val Ile Gln Gly Val Gly Val
                565                 570                 575
Thr Glu Thr Pro Leu Met Lys Glu Asp Ser Ile Leu Ala Val Arg Lys
            580                 585                 590
Tyr Phe Gln Arg Ile Thr Leu Tyr Leu Lys Glu Lys Lys Tyr Ser Pro
        595                 600                 605
Cys Ala Trp Glu Val Val Arg Ala Glu Ile Met Arg Ser Phe Ser Leu
    610                 615                 620
Ser Thr Asn Leu Gln Glu Ser Leu Arg Ser Lys Glu
625                 630                 635

<210> 41
<211> 389
<212> PRT
<213> Artificial Sequence


<220>
<223> antiCD40_LC--G4S2--IFNÎ±2a

<400> 41
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
1               5                   10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Tyr Ser Trp
            20                  25                  30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Asn Leu Leu Ile
        35                  40                  45
Tyr Thr Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Asn Ile Phe Pro Leu
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                85                  90                  95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110
Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115                 120                 125
Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130                 135                 140
Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145                 150                 155                 160
Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                165                 170                 175
Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190
Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205
Phe Asn Arg Gly Glu Cys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
    210                 215                 220
Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met
225                 230                 235                 240
Leu Leu Ala Gln Met Arg Lys Ile Ser Leu Phe Ser Cys Leu Lys Asp
                245                 250                 255
Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln
            260                 265                 270
Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe
        275                 280                 285
Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu
    290                 295                 300
Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu
305                 310                 315                 320
Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys
                325                 330                 335
Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu
            340                 345                 350
Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg
        355                 360                 365
Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser
    370                 375                 380
Leu Arg Ser Lys Glu
385
```

<210> 42
<211> 394
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40_LC--G4S3--IFNÎ±2a

<400> 42

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
1               5                   10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Tyr Ser Trp
            20                  25                  30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Asn Leu Leu Ile
        35                  40                  45
Tyr Thr Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Asn Ile Phe Pro Leu
                85                  90                  95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110
Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115                 120                 125
Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130                 135                 140
Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
```

145 150 155 160
Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175
Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190
Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205
Phe Asn Arg Gly Glu Cys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
210 215 220
Gly Gly Gly Gly Ser Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser
225 230 235 240
Arg Arg Thr Leu Met Leu Leu Ala Gln Met Arg Lys Ile Ser Leu Phe
245 250 255
Ser Cys Leu Lys Asp Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe
260 265 270
Gly Asn Gln Phe Gln Lys Ala Glu Thr Ile Pro Val Leu His Glu Met
275 280 285
Ile Gln Gln Ile Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala
290 295 300
Trp Asp Glu Thr Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln
305 310 315 320
Leu Asn Asp Leu Glu Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu
325 330 335
Thr Pro Leu Met Lys Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe
340 345 350
Gln Arg Ile Thr Leu Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala
355 360 365
Trp Glu Val Val Arg Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr
370 375 380
Asn Leu Gln Glu Ser Leu Arg Ser Lys Glu
385 390

<210> 43
<211> 399
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40_LC--G4S4--IFNÎ±2a

<400> 43
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Tyr Ser Trp
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Asn Leu Leu Ile
35 40 45
Tyr Thr Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Asn Ile Phe Pro Leu
85 90 95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110
Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125
Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140
Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160
Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175
Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190
Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205
Phe Asn Arg Gly Glu Cys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser

```
    210                 215                 220
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Cys Asp Leu Pro Gln Thr
225                 230                 235                 240
His Ser Leu Gly Ser Arg Arg Thr Leu Met Leu Leu Ala Gln Met Arg
                245                 250                 255
Lys Ile Ser Leu Phe Ser Cys Leu Lys Asp Arg His Asp Phe Gly Phe
            260                 265                 270
Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln Lys Ala Glu Thr Ile Pro
        275                 280                 285
Val Leu His Glu Met Ile Gln Gln Ile Phe Asn Leu Phe Ser Thr Lys
    290                 295                 300
Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu Leu Asp Lys Phe Tyr Thr
305                 310                 315                 320
Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu Ala Cys Val Ile Gln Gly
                325                 330                 335
Val Gly Val Thr Glu Thr Pro Leu Met Lys Glu Asp Ser Ile Leu Ala
            340                 345                 350
Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu Tyr Leu Lys Glu Lys Lys
        355                 360                 365
Tyr Ser Pro Cys Ala Trp Glu Val Val Arg Ala Glu Ile Met Arg Ser
    370                 375                 380
Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser Leu Arg Ser Lys Glu
385                 390                 395

<210> 44
<211> 395
<212> PRT
<213> Artificial Sequence


<220>
<223> IFNÎ²--G4S3--antiCD40_LC

<400> 44
Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln
1               5                   10                  15
Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu
            20                  25                  30
Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln
        35                  40                  45
Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln
    50                  55                  60
Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn
65                  70                  75                  80
Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn
                85                  90                  95
His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr
            100                 105                 110
Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg
        115                 120                 125
Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr
    130                 135                 140
Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu
145                 150                 155                 160
Thr Gly Tyr Leu Arg Asn Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
                165                 170                 175
Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val
            180                 185                 190
Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln
        195                 200                 205
Gly Ile Tyr Ser Trp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala
    210                 215                 220
Pro Asn Leu Leu Ile Tyr Thr Ala Ser Thr Leu Gln Ser Gly Val Pro
225                 230                 235                 240
Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
                245                 250                 255
Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala
            260                 265                 270
Asn Ile Phe Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
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        275                 280                 285
Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
    290                 295                 300
Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
305                 310                 315                 320
Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
                325                 330                 335
Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
            340                 345                 350
Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
        355                 360                 365
Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
    370                 375                 380
Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
385                 390                 395

<210> 45
<211> 400
<212> PRT
<213> Artificial Sequence


<220>
<223> antiCD40_LC--G4S4--IFNÎ²

<400> 45
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
1               5                   10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Tyr Ser Trp
            20                  25                  30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Asn Leu Leu Ile
        35                  40                  45
Tyr Thr Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Asn Ile Phe Pro Leu
                85                  90                  95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110
Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115                 120                 125
Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130                 135                 140
Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145                 150                 155                 160
Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                165                 170                 175
Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190
Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205
Phe Asn Arg Gly Glu Cys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
    210                 215                 220
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Met Ser Tyr Asn Leu Leu
225                 230                 235                 240
Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln Cys Gln Lys Leu Leu Trp
                245                 250                 255
Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu Lys Asp Arg Met Asn Phe
            260                 265                 270
Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln Gln Phe Gln Lys Glu Asp
        275                 280                 285
Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln Asn Ile Phe Ala Ile Phe
    290                 295                 300
Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn Glu Thr Ile Val Glu Asn
305                 310                 315                 320
Leu Leu Ala Asn Val Tyr His Gln Ile Asn His Leu Lys Thr Val Leu
                325                 330                 335
Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr Arg Gly Lys Leu Met Ser
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            340                 345                 350
Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg Ile Leu His Tyr Leu Lys
        355                 360                 365
Ala Lys Glu Tyr Ser His Cys Ala Trp Thr Ile Val Arg Val Glu Ile
    370                 375                 380
Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu Thr Gly Tyr Leu Arg Asn
385                 390                 395                 400



<210> 46
<211> 636
<212> PRT
<213> Artificial Sequence


<220>
<223> IFNÎ²--(G4S)3--antiCD40_HC_IgG1_NNAS_dK

<400> 46
Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln
1               5                   10                  15
Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu
            20                  25                  30
Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln
        35                  40                  45
Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln
    50                  55                  60
Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn
65                  70                  75                  80
Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn
                85                  90                  95
His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr
            100                 105                 110
Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg
        115                 120                 125
Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr
    130                 135                 140
Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu
145                 150                 155                 160
Thr Gly Tyr Leu Arg Asn Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
                165                 170                 175
Gly Gly Gly Gly Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
            180                 185                 190
Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
        195                 200                 205
Thr Phe Thr Gly Tyr Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln
    210                 215                 220
Gly Leu Glu Trp Met Gly Trp Ile Asn Pro Asp Ser Gly Gly Thr Asn
225                 230                 235                 240
Tyr Ala Gln Lys Phe Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser
                245                 250                 255
Ile Ser Thr Ala Tyr Met Glu Leu Asn Arg Leu Arg Ser Asp Asp Thr
            260                 265                 270
Ala Val Tyr Tyr Cys Ala Arg Asp Gln Pro Leu Gly Tyr Cys Thr Asn
        275                 280                 285
Gly Val Cys Ser Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
    290                 295                 300
Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
305                 310                 315                 320
Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
                325                 330                 335
Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
            340                 345                 350
Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
        355                 360                 365
Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
    370                 375                 380
Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
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385 390 395 400
Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
405 410 415
Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu
420 425 430
Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
435 440 445
Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
450 455 460
Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
465 470 475 480
Pro Arg Glu Glu Gln Tyr Asn Asn Ala Ser Arg Val Val Ser Val Leu
485 490 495
Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
500 505 510
Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
515 520 525
Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
530 535 540
Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
545 550 555 560
Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
565 570 575
Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
580 585 590
Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
595 600 605
Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
610 615 620
His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
625 630 635

<210> 47
<211> 641
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40_HC_IgG1_NNAS_dK--(G4S)4--IFNÎ²

<400> 47
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20 25 30
Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Ile Asn Pro Asp Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Asn Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp Gln Pro Leu Gly Tyr Cys Thr Asn Gly Val Cys Ser Tyr
100 105 110
Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser
115 120 125
Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr
130 135 140
Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro
145 150 155 160
Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val
165 170 175
His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser
180 185 190
Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile
195 200 205
Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val

```
    210                 215                 220
Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
225                 230                 235                 240
Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
                245                 250                 255
Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
            260                 265                 270
Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
        275                 280                 285
Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
    290                 295                 300
Tyr Asn Asn Ala Ser Arg Val Val Ser Val Leu Thr Val Leu His Gln
305                 310                 315                 320
Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
                325                 330                 335
Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
            340                 345                 350
Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr
        355                 360                 365
Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
    370                 375                 380
Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
385                 390                 395                 400
Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
                405                 410                 415
Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
            420                 425                 430
Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
        435                 440                 445
Ser Leu Ser Leu Ser Pro Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly
    450                 455                 460
Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Met Ser Tyr Asn Leu
465                 470                 475                 480
Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln Cys Gln Lys Leu Leu
                485                 490                 495
Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu Lys Asp Arg Met Asn
            500                 505                 510
Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln Gln Phe Gln Lys Glu
        515                 520                 525
Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln Asn Ile Phe Ala Ile
    530                 535                 540
Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn Glu Thr Ile Val Glu
545                 550                 555                 560
Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn His Leu Lys Thr Val
                565                 570                 575
Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr Arg Gly Lys Leu Met
            580                 585                 590
Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg Ile Leu His Tyr Leu
        595                 600                 605
Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr Ile Val Arg Val Glu
    610                 615                 620
Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu Thr Gly Tyr Leu Arg
625                 630                 635                 640
Asn
```

<210> 48
<211> 456
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40 antibody hIgG1 heavy chain NNAS

<400> 48

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
```

```
            20                  25                  30
Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
Gly Trp Ile Asn Pro Asp Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
    50                  55                  60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Met Glu Leu Asn Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Asp Gln Pro Leu Gly Tyr Cys Thr Asn Gly Val Cys Ser Tyr
            100                 105                 110
Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser
        115                 120                 125
Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr
    130                 135                 140
Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro
145                 150                 155                 160
Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val
                165                 170                 175
His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser
            180                 185                 190
Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile
        195                 200                 205
Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val
    210                 215                 220
Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
225                 230                 235                 240
Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
                245                 250                 255
Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
            260                 265                 270
Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
        275                 280                 285
Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
    290                 295                 300
Tyr Asn Asn Ala Ser Arg Val Val Ser Val Leu Thr Val Leu His Gln
305                 310                 315                 320
Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
                325                 330                 335
Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
            340                 345                 350
Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr
        355                 360                 365
Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
    370                 375                 380
Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
385                 390                 395                 400
Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
                405                 410                 415
Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
            420                 425                 430
Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
        435                 440                 445
Ser Leu Ser Leu Ser Pro Gly Lys
    450                 455

<210> 49
<211> 455
<212> PRT
<213> Artificial Sequence


<220>
<223> antiCD40 antibody hIgG1 heavy chain -NNAS-dK

<400> 49
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
```

```
            20                  25                  30
Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
Gly Trp Ile Asn Pro Asp Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
    50                  55                  60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Met Glu Leu Asn Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Asp Gln Pro Leu Gly Tyr Cys Thr Asn Gly Val Cys Ser Tyr
            100                 105                 110
Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser
        115                 120                 125
Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr
    130                 135                 140
Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro
145                 150                 155                 160
Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val
                165                 170                 175
His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser
            180                 185                 190
Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile
        195                 200                 205
Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val
    210                 215                 220
Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
225                 230                 235                 240
Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
                245                 250                 255
Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
            260                 265                 270
Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
        275                 280                 285
Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
    290                 295                 300
Tyr Asn Asn Ala Ser Arg Val Val Ser Val Leu Thr Val Leu His Gln
305                 310                 315                 320
Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
                325                 330                 335
Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
            340                 345                 350
Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr
        355                 360                 365
Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
    370                 375                 380
Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
385                 390                 395                 400
Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
                405                 410                 415
Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
            420                 425                 430
Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
        435                 440                 445
Ser Leu Ser Leu Ser Pro Gly
    450                 455

<210> 50
<211> 244
<212> PRT
<213> Artificial Sequence


<220>
<223> antiCD40 antibody hIgG2 Fab region heavy chain--TEV--6His tag

<400> 50
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
```

```
            20                  25                  30
Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45
Gly Trp Ile Asn Pro Asp Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
    50                  55                  60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Met Glu Leu Asn Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Asp Gln Pro Leu Gly Tyr Cys Thr Asn Gly Val Cys Ser Tyr
            100                 105                 110
Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser
        115                 120                 125
Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr
    130                 135                 140
Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro
145                 150                 155                 160
Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val
                165                 170                 175
His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser
            180                 185                 190
Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr
        195                 200                 205
Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val
    210                 215                 220
Glu Arg Lys Cys Cys Val Glu Glu Asn Leu Tyr Phe Gln Ser His His
225                 230                 235                 240
His His His His
```

<210> 51
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40 antibody VL domain

<400> 51

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
1               5                   10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Tyr Ser Trp
            20                  25                  30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Asn Leu Leu Ile
        35                  40                  45
Tyr Thr Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Asn Ile Phe Pro Leu
                85                  90                  95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105
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<210> 52
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40 antibody CDRL1

<400> 52

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Arg Ala Ser Gln Gly Ile Tyr Ser Trp Leu Ala
1               5                   10
```

<210> 53

<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40 antibody CDRL2

<400> 53
Thr Ala Ser Thr Leu Gln Ser
1 5

<210> 54
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40 antibody CDRL3

<400> 54
Gln Gln Ala Asn Ile Phe Pro Leu Thr
1 5

<210> 55
<211> 126
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40 antibody VH domain

<400> 55
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20 25 30
Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Ile Asn Pro Asp Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Asn Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp Gln Pro Leu Gly Tyr Cys Thr Asn Gly Val Cys Ser Tyr
100 105 110
Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 56
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40 antibody CDRH1

<400> 56
Thr Gly Tyr Tyr Met His
1 5

<210> 57
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40 antibody CDRH2

<400> 57
Trp Ile Asn Pro Asp Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe Gln
1   5   10   15
Gly

<210> 58
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40 antibody CDRH3

<400> 58
Asp Gln Pro Leu Gly Tyr Cys Thr Asn Gly Val Cys Ser Tyr Phe Asp
1   5   10   15
Tyr

<210> 59
<211> 213
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40 antibody_light chain

<400> 59
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1   5   10   15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Arg Ser Asn
            20   25   30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35   40   45
Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
    50   55   60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Asn Ser Leu Gln Ser
65   70   75   80
Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln His Asn Lys Trp Ile Thr
                85   90   95
Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Arg Thr Val Ala Ala Pro
            100   105   110
Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
        115   120   125
Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
    130   135   140
Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
145   150   155   160
Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
                165   170   175
Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
            180   185   190
Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
        195   200   205
Asn Arg Gly Glu Cys
    210

<210> 60
<211> 232
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40 antibody_light chain with signal peptide 1

<400> 60
Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1   5   10   15
Val His Ser Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val
            20   25   30
Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val
        35   40   45
Arg Ser Asn Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg
    50   55   60
Leu Leu Ile Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg
65   70   75   80
Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Asn Ser
                85   90   95
Leu Gln Ser Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln His Asn Lys
            100   105   110
Trp Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Arg Thr Val
        115   120   125
Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys
    130   135   140
Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg
145   150   155   160
Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn
                165   170   175
Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser
            180   185   190
Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys
        195   200   205
Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr
    210   215   220
Lys Ser Phe Asn Arg Gly Glu Cys
225   230

<210> 61
<211> 447
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40 antibody_heavy chain hIgG2 dK

<400> 61
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Lys
1   5   10   15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Asn
            20   25   30
Gly Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45
Ala Val Ile Trp Ser Asp Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val
    50   55   60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95
Ala Arg Ala Ser Gly Ser Gly Ser Tyr Tyr Asn Phe Phe Asp Tyr Trp
            100   105   110
Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
        115   120   125
Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr
    130   135   140
Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145   150   155   160
Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
                165   170   175

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Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
            180                 185                 190
Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp
        195                 200                 205
His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys Cys
    210                 215                 220
Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser
225                 230                 235                 240
Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
                245                 250                 255
Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
            260                 265                 270
Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
        275                 280                 285
Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Val Val
    290                 295                 300
Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305                 310                 315                 320
Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr
                325                 330                 335
Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
            340                 345                 350
Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
        355                 360                 365
Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
    370                 375                 380
Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu Asp
385                 390                 395                 400
Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
                405                 410                 415
Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
            420                 425                 430
Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
        435                 440                 445

<210> 62
<211> 466
<212> PRT
<213> Artificial Sequence


<220>
<223> antiCD40 antibody_heavy chain hIgG2 dK with Signal peptide 1

<400> 62
Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1               5                   10                  15
Val His Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln
            20                  25                  30
Pro Gly Lys Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
        35                  40                  45
Ser Ser Asn Gly Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
    50                  55                  60
Glu Trp Val Ala Val Ile Trp Ser Asp Gly Ser Asn Lys Phe Tyr Ala
65                  70                  75                  80
Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
                85                  90                  95
Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
            100                 105                 110
Tyr Tyr Cys Ala Arg Ala Ser Gly Ser Gly Ser Tyr Tyr Asn Phe Phe
        115                 120                 125
Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr
    130                 135                 140
Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser
145                 150                 155                 160
Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu
                165                 170                 175
Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His
            180                 185                 190
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Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
        195                 200                 205
Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys
    210                 215                 220
Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu
225                 230                 235                 240
Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala
                245                 250                 255
Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
            260                 265                 270
Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
        275                 280                 285
Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val
    290                 295                 300
His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe
305                 310                 315                 320
Arg Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly
                325                 330                 335
Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile
            340                 345                 350
Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val
        355                 360                 365
Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
    370                 375                 380
Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
385                 390                 395                 400
Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
                405                 410                 415
Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
            420                 425                 430
Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
        435                 440                 445
His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
    450                 455                 460
Pro Gly
465

<210> 63
<211> 227
<212> PRT
<213> Artificial Sequence


<220>
<223> antiCD40 antibody Fab region heavy chain hIgG2

<400> 63
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Lys
1               5                   10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Asn
            20                  25                  30
Gly Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ala Val Ile Trp Ser Asp Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Ala Ser Gly Ser Gly Ser Tyr Tyr Asn Phe Phe Asp Tyr Trp
            100                 105                 110
Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
        115                 120                 125
Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr
    130                 135                 140
Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145                 150                 155                 160
Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
                165                 170                 175
```

```
Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
            180                 185                 190
Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp
        195                 200                 205
His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys Cys
    210                 215                 220
Cys Val Glu
225
```

<210> 64
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40 antibody Fab region heavy chain hIgG2 with signal peptide 1

<400> 64

```
Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
1               5                   10                  15
Val His Ser Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln
            20                  25                  30
Pro Gly Lys Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
        35                  40                  45
Ser Ser Asn Gly Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu
    50                  55                  60
Glu Trp Val Ala Val Ile Trp Ser Asp Gly Ser Asn Lys Phe Tyr Ala
65                  70                  75                  80
Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn
                85                  90                  95
Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val
            100                 105                 110
Tyr Tyr Cys Ala Arg Ala Ser Gly Ser Gly Ser Tyr Tyr Asn Phe Phe
        115                 120                 125
Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr
    130                 135                 140
Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser
145                 150                 155                 160
Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu
                165                 170                 175
Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His
            180                 185                 190
Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
        195                 200                 205
Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys
    210                 215                 220
Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu
225                 230                 235                 240
Arg Lys Cys Cys Val Glu
                245
```

<210> 65
<211> 240
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40 antibody Fab region region heavy chain hIgG2--TEV--6His tag

<400> 65

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Lys
1               5                   10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Asn
            20                  25                  30
Gly Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
```

```
        35                  40                  45
Ala Val Ile Trp Ser Asp Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Ala Ser Gly Ser Gly Ser Tyr Tyr Asn Phe Phe Asp Tyr Trp
            100                 105                 110
Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
        115                 120                 125
Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr
    130                 135                 140
Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145                 150                 155                 160
Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
                165                 170                 175
Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
            180                 185                 190
Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp
        195                 200                 205
His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys Cys
    210                 215                 220
Cys Val Glu Glu Asn Leu Tyr Phe Gln Ser His His His His His His
225                 230                 235                 240



<210> 66
<211> 616
<212> PRT
<213> Artificial Sequence


<220>
<223> antiCD40_hIgG2_dK_HC--RL--IFNÎ²dM

<400> 66
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Lys
1               5                   10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Asn
            20                  25                  30
Gly Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ala Val Ile Trp Ser Asp Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Ala Ser Gly Ser Gly Ser Tyr Tyr Asn Phe Phe Asp Tyr Trp
            100                 105                 110
Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
        115                 120                 125
Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr
    130                 135                 140
Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145                 150                 155                 160
Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
                165                 170                 175
Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
            180                 185                 190
Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp
        195                 200                 205
His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys Cys
    210                 215                 220
Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser
225                 230                 235                 240
Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
```

```
                245                 250                 255
Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
            260                 265                 270
Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
        275                 280                 285
Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Val Val
    290                 295                 300
Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305                 310                 315                 320
Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr
                325                 330                 335
Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
            340                 345                 350
Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
        355                 360                 365
Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
    370                 375                 380
Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu Asp
385                 390                 395                 400
Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
                405                 410                 415
Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
            420                 425                 430
Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Pro
        435                 440                 445
Ala Pro Ala Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn
    450                 455                 460
Phe Gln Cys Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr
465                 470                 475                 480
Cys Leu Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln
                485                 490                 495
Leu Gln Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met
            500                 505                 510
Leu Gln Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly
        515                 520                 525
Trp Asn Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln
    530                 535                 540
Ile Asn His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp
545                 550                 555                 560
Phe Thr Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr
                565                 570                 575
Gly Arg Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala
            580                 585                 590
Trp Thr Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn
        595                 600                 605
Arg Leu Thr Gly Tyr Leu Arg Asn
    610                 615

<210> 67
<211> 616
<212> PRT
<213> Artificial Sequence


<220>
<223> antiCD40_hIgG2_dK_HC--RL--IFNÎ²dM_C17S

<400> 67
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Lys
1               5                   10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Asn
            20                  25                  30
Gly Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ala Val Ile Trp Ser Asp Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
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```
                85                  90                  95
Ala Arg Ala Ser Gly Ser Gly Ser Tyr Tyr Asn Phe Phe Asp Tyr Trp
            100                 105                 110
Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
        115                 120                 125
Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr
    130                 135                 140
Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145                 150                 155                 160
Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
                165                 170                 175
Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
            180                 185                 190
Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp
        195                 200                 205
His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys Cys
    210                 215                 220
Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser
225                 230                 235                 240
Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
                245                 250                 255
Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
            260                 265                 270
Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
        275                 280                 285
Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Val Val
    290                 295                 300
Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305                 310                 315                 320
Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr
                325                 330                 335
Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
            340                 345                 350
Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
        355                 360                 365
Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
    370                 375                 380
Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu Asp
385                 390                 395                 400
Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
                405                 410                 415
Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
            420                 425                 430
Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Pro
        435                 440                 445
Ala Pro Ala Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn
    450                 455                 460
Phe Gln Ser Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr
465                 470                 475                 480
Cys Leu Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln
                485                 490                 495
Leu Gln Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met
            500                 505                 510
Leu Gln Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly
        515                 520                 525
Trp Asn Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln
    530                 535                 540
Ile Asn His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp
545                 550                 555                 560
Phe Thr Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr
                565                 570                 575
Gly Arg Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala
            580                 585                 590
Trp Thr Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn
        595                 600                 605
Arg Leu Thr Gly Tyr Leu Arg Asn
    610                 615
```

<210> 68

<211> 624
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40_hIgG2_dK_HC--HL--IFNÎ²dM

<400> 68
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Lys
1   5   10   15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Asn
            20   25   30
Gly Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45
Ala Val Ile Trp Ser Asp Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val
    50   55   60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95
Ala Arg Ala Ser Gly Ser Gly Ser Tyr Tyr Asn Phe Phe Asp Tyr Trp
            100   105   110
Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
        115   120   125
Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr
    130   135   140
Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145   150   155   160
Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
                165   170   175
Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
            180   185   190
Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp
        195   200   205
His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys Cys
    210   215   220
Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser
225   230   235   240
Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
                245   250   255
Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
            260   265   270
Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
        275   280   285
Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Val Val
    290   295   300
Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305   310   315   320
Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr
                325   330   335
Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
            340   345   350
Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
        355   360   365
Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
    370   375   380
Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu Asp
385   390   395   400
Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
                405   410   415
Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
            420   425   430
Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Ala
        435   440   445
Glu Ala Ala Ala Lys Glu Ala Ala Ala Lys Ala Ser Tyr Asn Leu Leu
    450   455   460
Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln Cys Gln Lys Leu Leu Trp
465   470   475   480

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Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu Lys Asp Arg Met Asn Phe
                485                 490                 495
Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln Gln Phe Gln Lys Glu Asp
            500                 505                 510
Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln Asn Ile Phe Ala Ile Phe
        515                 520                 525
Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn Glu Thr Ile Val Glu Asn
    530                 535                 540
Leu Leu Ala Asn Val Tyr His Gln Ile Asn His Leu Lys Thr Val Leu
545                 550                 555                 560
Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr Arg Gly Lys Leu Met Ser
                565                 570                 575
Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg Ile Leu His Tyr Leu Lys
            580                 585                 590
Ala Lys Glu Tyr Ser His Cys Ala Trp Thr Ile Val Arg Val Glu Ile
        595                 600                 605
Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu Thr Gly Tyr Leu Arg Asn
    610                 615                 620



<210> 69
<211> 624
<212> PRT
<213> Artificial Sequence


<220>
<223> antiCD40_hIgG2_dK_HC--HL--IFNÎ²dM_C17S

<400> 69
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Lys
1               5                   10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Asn
            20                  25                  30
Gly Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ala Val Ile Trp Ser Asp Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Ala Ser Gly Ser Gly Ser Tyr Tyr Asn Phe Phe Asp Tyr Trp
            100                 105                 110
Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
        115                 120                 125
Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr
    130                 135                 140
Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145                 150                 155                 160
Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
                165                 170                 175
Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
            180                 185                 190
Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp
        195                 200                 205
His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys Cys
    210                 215                 220
Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser
225                 230                 235                 240
Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
                245                 250                 255
Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
            260                 265                 270
Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
        275                 280                 285
Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Val Val
    290                 295                 300
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Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305 310 315 320
Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr
325 330 335
Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
340 345 350
Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
355 360 365
Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
370 375 380
Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu Asp
385 390 395 400
Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
405 410 415
Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
420 425 430
Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Ala
435 440 445
Glu Ala Ala Ala Lys Glu Ala Ala Ala Lys Ala Ser Tyr Asn Leu Leu
450 455 460
Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln Ser Gln Lys Leu Leu Trp
465 470 475 480
Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu Lys Asp Arg Met Asn Phe
485 490 495
Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln Gln Phe Gln Lys Glu Asp
500 505 510
Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln Asn Ile Phe Ala Ile Phe
515 520 525
Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn Glu Thr Ile Val Glu Asn
530 535 540
Leu Leu Ala Asn Val Tyr His Gln Ile Asn His Leu Lys Thr Val Leu
545 550 555 560
Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr Arg Gly Lys Leu Met Ser
565 570 575
Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg Ile Leu His Tyr Leu Lys
580 585 590
Ala Lys Glu Tyr Ser His Cys Ala Trp Thr Ile Val Arg Val Glu Ile
595 600 605
Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu Thr Gly Tyr Leu Arg Asn
610 615 620

<210> 70
<211> 403
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40_LC--HL2--IFNÎ²_C17S

<400> 70
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1 5 10 15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Arg Ser Asn
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45
Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Asn Ser Leu Gln Ser
65 70 75 80
Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln His Asn Lys Trp Ile Thr
85 90 95
Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Arg Thr Val Ala Ala Pro
100 105 110
Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
115 120 125

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
    130   135   140
Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
145   150   155   160
Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
                165   170   175
Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
            180   185   190
Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
        195   200   205
Asn Arg Gly Glu Cys Ala Glu Ala Ala Ala Lys Glu Ala Ala Ala Lys
    210   215   220
Ala Ala Glu Ala Ala Ala Lys Glu Ala Ala Ala Lys Ala Met Ser Tyr
225   230   235   240
Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln Ser Gln Lys
                245   250   255
Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu Lys Asp Arg
            260   265   270
Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln Gln Phe Gln
        275   280   285
Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln Asn Ile Phe
    290   295   300
Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn Glu Thr Ile
305   310   315   320
Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn His Leu Lys
                325   330   335
Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr Arg Gly Lys
            340   345   350
Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg Ile Leu His
        355   360   365
Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr Ile Val Arg
    370   375   380
Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu Thr Gly Tyr
385   390   395   400
Leu Arg Asn

<210> 71
<211> 394
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40_LC--G4S3--IFNÎ²_C17S

<400> 71
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1   5   10   15
Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Arg Ser Asn
            20   25   30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35   40   45
Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
    50   55   60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Asn Ser Leu Gln Ser
65   70   75   80
Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln His Asn Lys Trp Ile Thr
                85   90   95
Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Arg Thr Val Ala Ala Pro
            100   105   110
Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
        115   120   125
Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
    130   135   140
Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
145   150   155   160
Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
                165   170   175

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Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
            180                 185                 190
Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
        195                 200                 205
Asn Arg Gly Glu Cys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    210                 215                 220
Gly Gly Gly Ser Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser
225                 230                 235                 240
Ser Asn Phe Gln Ser Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu
                245                 250                 255
Glu Tyr Cys Leu Lys Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile
            260                 265                 270
Lys Gln Leu Gln Gln Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr
        275                 280                 285
Glu Met Leu Gln Asn Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser
    290                 295                 300
Thr Gly Trp Asn Glu Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr
305                 310                 315                 320
His Gln Ile Asn His Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys
                325                 330                 335
Glu Asp Phe Thr Arg Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg
            340                 345                 350
Tyr Tyr Gly Arg Ile Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His
        355                 360                 365
Cys Ala Trp Thr Ile Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe
    370                 375                 380
Ile Asn Arg Leu Thr Gly Tyr Leu Arg Asn
385                 390

<210> 72
<211> 622
<212> PRT
<213> Artificial Sequence


<220>
<223> antiCD40_hIgG2_dK_HC--G4S2--IFNÎ±2a

<400> 72
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Lys
1               5                   10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Asn
            20                  25                  30
Gly Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ala Val Ile Trp Ser Asp Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Ala Ser Gly Ser Gly Ser Tyr Tyr Asn Phe Phe Asp Tyr Trp
            100                 105                 110
Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
        115                 120                 125
Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr
    130                 135                 140
Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145                 150                 155                 160
Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
                165                 170                 175
Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
            180                 185                 190
Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp
        195                 200                 205
His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys Cys
    210                 215                 220
Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser
225                 230                 235                 240
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Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
245 250 255
Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
260 265 270
Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
275 280 285
Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Val Val
290 295 300
Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305 310 315 320
Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr
325 330 335
Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
340 345 350
Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
355 360 365
Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
370 375 380
Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu Asp
385 390 395 400
Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
405 410 415
Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
420 425 430
Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Gly
435 440 445
Gly Gly Gly Ser Gly Gly Gly Gly Ser Cys Asp Leu Pro Gln Thr His
450 455 460
Ser Leu Gly Ser Arg Arg Thr Leu Met Leu Leu Ala Gln Met Arg Lys
465 470 475 480
Ile Ser Leu Phe Ser Cys Leu Lys Asp Arg His Asp Phe Gly Phe Pro
485 490 495
Gln Glu Glu Phe Gly Asn Gln Phe Gln Lys Ala Glu Thr Ile Pro Val
500 505 510
Leu His Glu Met Ile Gln Gln Ile Phe Asn Leu Phe Ser Thr Lys Asp
515 520 525
Ser Ser Ala Ala Trp Asp Glu Thr Leu Leu Asp Lys Phe Tyr Thr Glu
530 535 540
Leu Tyr Gln Gln Leu Asn Asp Leu Glu Ala Cys Val Ile Gln Gly Val
545 550 555 560
Gly Val Thr Glu Thr Pro Leu Met Lys Glu Asp Ser Ile Leu Ala Val
565 570 575
Arg Lys Tyr Phe Gln Arg Ile Thr Leu Tyr Leu Lys Glu Lys Lys Tyr
580 585 590
Ser Pro Cys Ala Trp Glu Val Val Arg Ala Glu Ile Met Arg Ser Phe
595 600 605
Ser Leu Ser Thr Asn Leu Gln Glu Ser Leu Arg Ser Lys Glu
610 615 620

<210> 73
<211> 627
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40_hIgG2_dK_HC--G4S3--IFNÎ±2a

<400> 73
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Lys
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Asn
20 25 30
Gly Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ala Val Ile Trp Ser Asp Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

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Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Ala Ser Gly Ser Gly Ser Tyr Tyr Asn Phe Phe Asp Tyr Trp
            100                 105                 110
Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
        115                 120                 125
Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr
    130                 135                 140
Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145                 150                 155                 160
Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
                165                 170                 175
Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
            180                 185                 190
Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp
        195                 200                 205
His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys Cys
    210                 215                 220
Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser
225                 230                 235                 240
Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
                245                 250                 255
Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
            260                 265                 270
Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
        275                 280                 285
Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Val Val
    290                 295                 300
Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305                 310                 315                 320
Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr
                325                 330                 335
Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
            340                 345                 350
Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
        355                 360                 365
Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
    370                 375                 380
Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu Asp
385                 390                 395                 400
Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
                405                 410                 415
Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
            420                 425                 430
Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Gly
        435                 440                 445
Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Cys Asp
    450                 455                 460
Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met Leu Leu
465                 470                 475                 480
Ala Gln Met Arg Lys Ile Ser Leu Phe Ser Cys Leu Lys Asp Arg His
                485                 490                 495
Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln Lys Ala
            500                 505                 510
Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe Asn Leu
        515                 520                 525
Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu Leu Asp
    530                 535                 540
Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu Ala Cys
545                 550                 555                 560
Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys Glu Asp
                565                 570                 575
Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu Tyr Leu
            580                 585                 590
Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg Ala Glu
        595                 600                 605
Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser Leu Arg
    610                 615                 620
Ser Lys Glu
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625

<210> 74
<211> 632
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40_hIgG2_dK_HC--G4S4--IFNÎ±2a

<400> 74
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Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Lys
1               5                  10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Asn
            20                  25                  30
Gly Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ala Val Ile Trp Ser Asp Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Ala Ser Gly Ser Gly Ser Tyr Tyr Asn Phe Phe Asp Tyr Trp
            100                 105                 110
Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
        115                 120                 125
Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr
    130                 135                 140
Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145                 150                 155                 160
Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
                165                 170                 175
Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
            180                 185                 190
Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp
        195                 200                 205
His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys Cys
    210                 215                 220
Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser
225                 230                 235                 240
Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
                245                 250                 255
Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
            260                 265                 270
Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
        275                 280                 285
Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Val Val
    290                 295                 300
Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305                 310                 315                 320
Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr
                325                 330                 335
Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
            340                 345                 350
Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
        355                 360                 365
Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
    370                 375                 380
Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu Asp
385                 390                 395                 400
Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
                405                 410                 415
Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
            420                 425                 430
Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Gly
        435                 440                 445
Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
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    450                 455                 460
Gly Gly Ser Cys Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg
465                 470                 475                 480
Thr Leu Met Leu Leu Ala Gln Met Arg Lys Ile Ser Leu Phe Ser Cys
                485                 490                 495
Leu Lys Asp Arg His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn
            500                 505                 510
Gln Phe Gln Lys Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln
        515                 520                 525
Gln Ile Phe Asn Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp
    530                 535                 540
Glu Thr Leu Leu Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn
545                 550                 555                 560
Asp Leu Glu Ala Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro
                565                 570                 575
Leu Met Lys Glu Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg
            580                 585                 590
Ile Thr Leu Tyr Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu
        595                 600                 605
Val Val Arg Ala Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu
    610                 615                 620
Gln Glu Ser Leu Arg Ser Lys Glu
625                 630

<210> 75
<211> 624
<212> PRT
<213> Artificial Sequence


<220>
<223> antiCD40_hIgG2_dK_HC--HL--IFNÎ±2a

<400> 75
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Lys
1               5                   10                  15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Asn
            20                  25                  30
Gly Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
Ala Val Ile Trp Ser Asp Gly Ser Asn Lys Phe Tyr Ala Asp Ser Val
    50                  55                  60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Ala Ser Gly Ser Gly Ser Tyr Tyr Asn Phe Phe Asp Tyr Trp
            100                 105                 110
Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
        115                 120                 125
Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr Ser Glu Ser Thr
    130                 135                 140
Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145                 150                 155                 160
Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
                165                 170                 175
Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
            180                 185                 190
Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr Cys Asn Val Asp
        195                 200                 205
His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val Glu Arg Lys Cys
    210                 215                 220
Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser
225                 230                 235                 240
Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
                245                 250                 255
Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
            260                 265                 270
Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
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        275                 280                 285
Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Val Val
    290                 295                 300
Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305                 310                 315                 320
Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr
                325                 330                 335
Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
            340                 345                 350
Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
        355                 360                 365
Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
    370                 375                 380
Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu Asp
385                 390                 395                 400
Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
                405                 410                 415
Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
            420                 425                 430
Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Ala
        435                 440                 445
Glu Ala Ala Ala Lys Glu Ala Ala Ala Lys Ala Cys Asp Leu Pro Gln
    450                 455                 460
Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met Leu Leu Ala Gln Met
465                 470                 475                 480
Arg Lys Ile Ser Leu Phe Ser Cys Leu Lys Asp Arg His Asp Phe Gly
                485                 490                 495
Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln Lys Ala Glu Thr Ile
            500                 505                 510
Pro Val Leu His Glu Met Ile Gln Gln Ile Phe Asn Leu Phe Ser Thr
        515                 520                 525
Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu Leu Asp Lys Phe Tyr
    530                 535                 540
Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu Ala Cys Val Ile Gln
545                 550                 555                 560
Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys Glu Asp Ser Ile Leu
                565                 570                 575
Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu Tyr Leu Lys Glu Lys
            580                 585                 590
Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg Ala Glu Ile Met Arg
        595                 600                 605
Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser Leu Arg Ser Lys Glu
    610                 615                 620



<210> 76
<211> 165
<212> PRT
<213> Artificial Sequence


<220>
<223> IFNÎ² dM

<400> 76
Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln Cys
1               5                   10                  15
Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu Lys
            20                  25                  30
Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln Gln
        35                  40                  45
Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln Asn
    50                  55                  60
Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn Glu
65                  70                  75                  80
Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn His
                85                  90                  95
Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr Arg
```

```
            100                 105                 110
Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg Ile
        115                 120                 125
Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr Ile
    130                 135                 140
Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu Thr
145                 150                 155                 160
Gly Tyr Leu Arg Asn
                165
```

<210> 77
<211> 165
<212> PRT
<213> Artificial Sequence

<220>
<223> IFNÎ² dM C17S

<400> 77

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Ser Tyr Asn Leu Leu Gly Phe Leu Gln Arg Ser Ser Asn Phe Gln Ser
1               5                   10                  15
Gln Lys Leu Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr Cys Leu Lys
            20                  25                  30
Asp Arg Met Asn Phe Asp Ile Pro Glu Glu Ile Lys Gln Leu Gln Gln
        35                  40                  45
Phe Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr Glu Met Leu Gln Asn
    50                  55                  60
Ile Phe Ala Ile Phe Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn Glu
65                  70                  75                  80
Thr Ile Val Glu Asn Leu Leu Ala Asn Val Tyr His Gln Ile Asn His
                85                  90                  95
Leu Lys Thr Val Leu Glu Glu Lys Leu Glu Lys Glu Asp Phe Thr Arg
            100                 105                 110
Gly Lys Leu Met Ser Ser Leu His Leu Lys Arg Tyr Tyr Gly Arg Ile
        115                 120                 125
Leu His Tyr Leu Lys Ala Lys Glu Tyr Ser His Cys Ala Trp Thr Ile
    130                 135                 140
Val Arg Val Glu Ile Leu Arg Asn Phe Tyr Phe Ile Asn Arg Leu Thr
145                 150                 155                 160
Gly Tyr Leu Arg Asn
                165
```

<210> 78
<211> 1947
<212> DNA
<213> Artificial Sequence

<220>
<223> Nucleic acid encoding SEQ ID NO 32

<400> 78

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atgggctggt cctgcatcat tctgtttctg gtggccacag ccacaggcgt gcactctcag      60

gttcaactgg ttcagtctgg cgccgaagtg aagaaaccag gcgccagcgt gaaggtgtcc     120

tgtaaagcca gcggctacac ctttaccggc tactacatgc actgggtccg acaggctcca     180

ggacagggac ttgagtggat gggctggatc aatcctgaca gcggcggcac caactacgcc     240

cagaaattcc agggcagagt gaccatgacc agagacacca gcatcagcac cgcctacatg     300

gaactgaacc ggctgagatc cgacgacacc gccgtgtact attgcgccag agatcagcct     360

ctgggctact gcacaaatgg cgtgtgcagc tacttcgact actggggcca gggcacactg     420

gttacagtgt ctagcgcctc tacaaagggc ccctccgttt ttcctctggc tccttgttct     480
```

agaagcacca gcgagtctac agccgctctg ggctgtctgg tcaaggacta ctttcctgag 540

cctgtgaccg tgtcctggaa tagcggagca ctgacatccg gcgtgcacac atttccagct 600

gtgctgcaga gcagcggcct gtactctctg tctagcgtgg tcaccgtgcc tagcagcaat 660

ttcggcaccc agacctacac ctgtaacgtg gaccacaagc ctagcaacac caaggtggac 720

aagaccgtgg aacggaagtg ctgcgtggaa tgccctcctt gtcctgctcc tccagtggcc 780

ggaccttccg tgtttctgtt ccctccaaag cctaaggaca ccctgatgat cagcagaacc 840

cctgaagtga cctgcgtggt ggtggatgtg tctcacgagg atcccgaggt gcagttcaat 900

tggtacgtgg acggcgtgga agtgcacaac gccaagacca agcctagaga ggaacagttc 960

aacagcacct tcagagtggt gtccgtgctg accgtggtgc atcaggactg gctgaacggc 1020

aaagagtaca agtgcaaggt gtccaacaag ggcctgcctg ctcctatcga gaaaaccatc 1080

agcaagacca aaggccagcc tcgcgagcct caggtttaca cactgcctcc aagccgggaa 1140

gagatgacca agaatcaggt gtccctgacc tgcctcgtga agggcttcta cccttccgat 1200

atcgccgtgg aatgggagag caatggccag cctgagaaca actacaagac cacacctcct 1260

atgctggaca gcgacggctc attcttcctg tacagcaagc tgacagtgga caagtccaga 1320

tggcagcagg gcaacgtgtt cagctgttct gtgatgcacg aggccctgca caaccactac 1380

acccagaagt ctctgtctct gagccctggc gctgaagccg ctgctaaaga agctgccgcc 1440

aaggccatga gctacaacct gctgggcttt ctgcagcgga gcagcaactt ccagtgccag 1500

aaactgctgt ggcagctgaa tggccggctg gaatactgcc tgaaggaccg gatgaacttc 1560

gacatccccg aggaaatcaa gcagctgcag cagttccaga aagaggacgc cgctctgacc 1620

atctacgaga tgctgcagaa catcttcgcc atcttccggc aggatagcag cagcaccgga 1680

tggaacgaga caatcgtgga aaatctgctg gccaacgtgt accaccagat caaccacctg 1740

aaaaccgtgc tggaagagaa gctggaaaaa gaggacttca cccggggcaa gctgatgagc 1800

agcctgcacc tgaagcggta ctacggcaga atcctgcact acctcaaggc caaagagtat 1860

agccactgcg cctggaccat cgtgcgcgtg gaaatcctgc ggaacttcta cttcatcaac 1920

agactgaccg gctacctgcg caactga 1947

<210> 79
<211> 174
<212> PRT
<213> Artificial Sequence

<220>
<223> IFNω

<400> 79
Leu Gly Cys Asp Leu Pro Gln Asn His Gly Leu Leu Ser Arg Asn Thr
1 5 10 15
Leu Val Leu Leu His Gln Met Arg Arg Ile Ser Pro Phe Leu Cys Leu
20 25 30
Lys Asp Arg Arg Asp Phe Arg Phe Pro Gln Glu Met Val Lys Gly Ser
35 40 45
Gln Leu Gln Lys Ala His Val Met Ser Val Leu His Glu Met Leu Gln
50 55 60

Gln Ile Phe Ser Leu Phe His Thr Glu Arg Ser Ser Ala Ala Trp Asn
65 70 75 80
Met Thr Leu Leu Asp Gln Leu His Thr Gly Leu His Gln Gln Leu Gln
85 90 95
His Leu Glu Thr Cys Leu Leu Gln Val Val Gly Glu Gly Glu Ser Ala
100 105 110
Gly Ala Ile Ser Ser Pro Ala Leu Thr Leu Arg Arg Tyr Phe Gln Gly
115 120 125
Ile Arg Val Tyr Leu Lys Glu Lys Lys Tyr Ser Asp Cys Ala Trp Glu
130 135 140
Val Val Arg Met Glu Ile Met Lys Ser Leu Phe Leu Ser Thr Asn Met
145 150 155 160
Gln Glu Arg Leu Arg Ser Lys Asp Arg Asp Leu Gly Ser Ser
165 170

<210> 80
<211> 187
<212> PRT
<213> Artificial Sequence

<220>
<223> IFNε

<400> 80
Leu Asp Leu Lys Leu Ile Ile Phe Gln Gln Arg Gln Val Asn Gln Glu
1 5 10 15
Ser Leu Lys Leu Leu Asn Lys Leu Gln Thr Leu Ser Ile Gln Gln Cys
20 25 30
Leu Pro His Arg Lys Asn Phe Leu Leu Pro Gln Lys Ser Leu Ser Pro
35 40 45
Gln Gln Tyr Gln Lys Gly His Thr Leu Ala Ile Leu His Glu Met Leu
50 55 60
Gln Gln Ile Phe Ser Leu Phe Arg Ala Asn Ile Ser Leu Asp Gly Trp
65 70 75 80
Glu Glu Asn His Thr Glu Lys Phe Leu Ile Gln Leu His Gln Gln Leu
85 90 95
Glu Tyr Leu Glu Ala Leu Met Gly Leu Glu Ala Glu Lys Leu Ser Gly
100 105 110
Thr Leu Gly Ser Asp Asn Leu Arg Leu Gln Val Lys Met Tyr Phe Arg
115 120 125
Arg Ile His Asp Tyr Leu Glu Asn Gln Asp Tyr Ser Thr Cys Ala Trp
130 135 140
Ala Ile Val Gln Val Glu Ile Ser Arg Cys Leu Phe Phe Val Phe Ser
145 150 155 160
Leu Thr Glu Lys Leu Ser Lys Gln Gly Arg Pro Leu Asn Asp Met Lys
165 170 175
Gln Glu Leu Thr Thr Glu Phe Arg Ser Pro Arg
180 185

<210> 81
<211> 628
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40_hIgG2 dK_HC--HL--IFNα2A

<400> 81
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20 25 30
Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Ile Asn Pro Asp Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr

```
65                  70                  75                  80
Met Glu Leu Asn Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Asp Gln Pro Leu Gly Tyr Cys Thr Asn Gly Val Cys Ser Tyr
            100                 105                 110
Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser
        115                 120                 125
Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr
    130                 135                 140
Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro
145                 150                 155                 160
Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val
                165                 170                 175
His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser
            180                 185                 190
Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr
        195                 200                 205
Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val
    210                 215                 220
Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val
225                 230                 235                 240
Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
                245                 250                 255
Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
            260                 265                 270
His Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu
        275                 280                 285
Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr
    290                 295                 300
Phe Arg Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn
305                 310                 315                 320
Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro
                325                 330                 335
Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln
            340                 345                 350
Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val
        355                 360                 365
Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
    370                 375                 380
Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
385                 390                 395                 400
Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
                405                 410                 415
Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
            420                 425                 430
Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
        435                 440                 445
Ser Pro Gly Ala Glu Ala Ala Ala Lys Glu Ala Ala Ala Lys Ala Cys
    450                 455                 460
Asp Leu Pro Gln Thr His Ser Leu Gly Ser Arg Arg Thr Leu Met Leu
465                 470                 475                 480
Leu Ala Gln Met Arg Lys Ile Ser Leu Phe Ser Cys Leu Lys Asp Arg
                485                 490                 495
His Asp Phe Gly Phe Pro Gln Glu Glu Phe Gly Asn Gln Phe Gln Lys
            500                 505                 510
Ala Glu Thr Ile Pro Val Leu His Glu Met Ile Gln Gln Ile Phe Asn
        515                 520                 525
Leu Phe Ser Thr Lys Asp Ser Ser Ala Ala Trp Asp Glu Thr Leu Leu
    530                 535                 540
Asp Lys Phe Tyr Thr Glu Leu Tyr Gln Gln Leu Asn Asp Leu Glu Ala
545                 550                 555                 560
Cys Val Ile Gln Gly Val Gly Val Thr Glu Thr Pro Leu Met Lys Glu
                565                 570                 575
Asp Ser Ile Leu Ala Val Arg Lys Tyr Phe Gln Arg Ile Thr Leu Tyr
            580                 585                 590
Leu Lys Glu Lys Lys Tyr Ser Pro Cys Ala Trp Glu Val Val Arg Ala
        595                 600                 605
Glu Ile Met Arg Ser Phe Ser Leu Ser Thr Asn Leu Gln Glu Ser Leu
    610                 615                 620
```

Arg Ser Lys Glu
625

<210> 82
<211> 398
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40_LC-derivative--HL--IFNα2A

<400> 82
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Tyr Ser Trp
20 25 30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Asn Leu Leu Ile
35 40 45
Tyr Thr Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Asn Ile Phe Pro Leu
85 90 95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
100 105 110
Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
115 120 125
Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
130 135 140
Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145 150 155 160
Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
165 170 175
Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
180 185 190
Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
195 200 205
Phe Asn Arg Gly Glu Lys Ser Leu Ser Leu Ser Pro Gly Ala Glu Ala
210 215 220
Ala Ala Lys Glu Ala Ala Ala Lys Ala Cys Asp Leu Pro Gln Thr His
225 230 235 240
Ser Leu Gly Ser Arg Arg Thr Leu Met Leu Leu Ala Gln Met Arg Lys
245 250 255
Ile Ser Leu Phe Ser Cys Leu Lys Asp Arg His Asp Phe Gly Phe Pro
260 265 270
Gln Glu Glu Phe Gly Asn Gln Phe Gln Lys Ala Glu Thr Ile Pro Val
275 280 285
Leu His Glu Met Ile Gln Gln Ile Phe Asn Leu Phe Ser Thr Lys Asp
290 295 300
Ser Ser Ala Ala Trp Asp Glu Thr Leu Leu Asp Lys Phe Tyr Thr Glu
305 310 315 320
Leu Tyr Gln Gln Leu Asn Asp Leu Glu Ala Cys Val Ile Gln Gly Val
325 330 335
Gly Val Thr Glu Thr Pro Leu Met Lys Glu Asp Ser Ile Leu Ala Val
340 345 350
Arg Lys Tyr Phe Gln Arg Ile Thr Leu Tyr Leu Lys Glu Lys Lys Tyr
355 360 365
Ser Pro Cys Ala Trp Glu Val Val Arg Ala Glu Ile Met Arg Ser Phe
370 375 380
Ser Leu Ser Thr Asn Leu Gln Glu Ser Leu Arg Ser Lys Glu
385 390 395

<210> 83
<211> 377
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40_LC--(G4S)4--IFNγ

<400> 83
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
1   5   10   15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Tyr Ser Trp
            20   25   30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Asn Leu Leu Ile
        35   40   45
Tyr Thr Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Asn Ile Phe Pro Leu
                85   90   95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100   105   110
Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115   120   125
Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130   135   140
Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145   150   155   160
Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                165   170   175
Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180   185   190
Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195   200   205
Phe Asn Arg Gly Glu Cys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
    210   215   220
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Asp Pro Tyr Val Lys
225   230   235   240
Glu Ala Glu Asn Leu Lys Lys Tyr Phe Asn Ala Gly His Ser Asp Val
                245   250   255
Ala Asp Asn Gly Thr Leu Phe Leu Gly Ile Leu Lys Asn Trp Lys Glu
            260   265   270
Glu Ser Asp Arg Lys Ile Met Gln Ser Gln Ile Val Ser Phe Tyr Phe
        275   280   285
Lys Leu Phe Lys Asn Phe Lys Asp Asp Gln Ser Ile Gln Lys Ser Val
    290   295   300
Glu Thr Ile Lys Glu Asp Met Asn Val Lys Phe Phe Asn Ser Asn Lys
305   310   315   320
Lys Lys Arg Asp Asp Phe Glu Lys Leu Thr Asn Tyr Ser Val Thr Asp
                325   330   335
Leu Asn Val Gln Arg Lys Ala Ile His Glu Leu Ile Gln Val Met Ala
            340   345   350
Glu Leu Ser Pro Ala Ala Lys Thr Gly Lys Arg Lys Arg Ser Gln Met
        355   360   365
Leu Phe Arg Gly Arg Arg Ala Ser Gln
    370   375

<210> 84
<211> 614
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40_hIgG2 dK_HC--(G4S)4--IFNγ

<400> 84
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1   5   10   15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
            20   25   30
Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met

```
        35                  40                  45
Gly Trp Ile Asn Pro Asp Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
    50                  55                  60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80
Met Glu Leu Asn Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
Ala Arg Asp Gln Pro Leu Gly Tyr Cys Thr Asn Gly Val Cys Ser Tyr
            100                 105                 110
Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser
        115                 120                 125
Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr
    130                 135                 140
Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro
145                 150                 155                 160
Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val
                165                 170                 175
His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser
            180                 185                 190
Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr
        195                 200                 205
Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val
    210                 215                 220
Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val
225                 230                 235                 240
Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
                245                 250                 255
Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
            260                 265                 270
His Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu
        275                 280                 285
Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr
    290                 295                 300
Phe Arg Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn
305                 310                 315                 320
Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro
                325                 330                 335
Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln
            340                 345                 350
Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val
        355                 360                 365
Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
    370                 375                 380
Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
385                 390                 395                 400
Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
                405                 410                 415
Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
            420                 425                 430
Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
        435                 440                 445
Ser Pro Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
    450                 455                 460
Gly Ser Gly Gly Gly Gly Ser Gln Asp Pro Tyr Val Lys Glu Ala Glu
465                 470                 475                 480
Asn Leu Lys Lys Tyr Phe Asn Ala Gly His Ser Asp Val Ala Asp Asn
                485                 490                 495
Gly Thr Leu Phe Leu Gly Ile Leu Lys Asn Trp Lys Glu Glu Ser Asp
            500                 505                 510
Arg Lys Ile Met Gln Ser Gln Ile Val Ser Phe Tyr Phe Lys Leu Phe
        515                 520                 525
Lys Asn Phe Lys Asp Asp Gln Ser Ile Gln Lys Ser Val Glu Thr Ile
    530                 535                 540
Lys Glu Asp Met Asn Val Lys Phe Phe Asn Ser Asn Lys Lys Lys Arg
545                 550                 555                 560
Asp Asp Phe Glu Lys Leu Thr Asn Tyr Ser Val Thr Asp Leu Asn Val
                565                 570                 575
Gln Arg Lys Ala Ile His Glu Leu Ile Gln Val Met Ala Glu Leu Ser
            580                 585                 590
```

```
Pro Ala Ala Lys Thr Gly Lys Arg Lys Arg Ser Gln Met Leu Phe Arg
        595                 600                 605
Gly Arg Arg Ala Ser Gln
    610
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<210> 85
<211> 409
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40_LC--(G4S)4--IFNλ2

<400> 85

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
1               5                   10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Tyr Ser Trp
            20                  25                  30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Asn Leu Leu Ile
        35                  40                  45
Tyr Thr Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Asn Ile Phe Pro Leu
                85                  90                  95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110
Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115                 120                 125
Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130                 135                 140
Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145                 150                 155                 160
Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                165                 170                 175
Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190
Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205
Phe Asn Arg Gly Glu Cys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
    210                 215                 220
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Val Pro Val Ala Arg Leu
225                 230                 235                 240
His Gly Ala Leu Pro Asp Ala Arg Gly Cys His Ile Ala Gln Phe Lys
                245                 250                 255
Ser Leu Ser Pro Gln Glu Leu Gln Ala Phe Lys Arg Ala Lys Asp Ala
            260                 265                 270
Leu Glu Glu Ser Leu Leu Leu Lys Asp Cys Arg Cys His Ser Arg Leu
        275                 280                 285
Phe Pro Arg Thr Trp Asp Leu Arg Gln Leu Gln Val Arg Glu Arg Pro
    290                 295                 300
Met Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu Lys Val Leu Glu Ala
305                 310                 315                 320
Thr Ala Asp Thr Asp Pro Ala Leu Val Asp Val Leu Asp Gln Pro Leu
                325                 330                 335
His Thr Leu His His Ile Leu Ser Gln Phe Arg Ala Cys Ile Gln Pro
            340                 345                 350
Gln Pro Thr Ala Gly Pro Arg Thr Arg Gly Arg Leu His His Trp Leu
        355                 360                 365
Tyr Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Pro Gly Cys Leu Glu
    370                 375                 380
Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg Asp Leu Asn
385                 390                 395                 400
Cys Val Ala Ser Gly Asp Leu Cys Val
                405
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<210> 86

<211> 646
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40_hIgG2 dK_HC--(G4S)4--IFNλ2

<400> 86
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1   5   10   15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
            20   25   30
Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35   40   45
Gly Trp Ile Asn Pro Asp Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
    50   55   60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65   70   75   80
Met Glu Leu Asn Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85   90   95
Ala Arg Asp Gln Pro Leu Gly Tyr Cys Thr Asn Gly Val Cys Ser Tyr
            100   105   110
Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser
        115   120   125
Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr
    130   135   140
Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro
145   150   155   160
Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val
                165   170   175
His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser
            180   185   190
Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr
        195   200   205
Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val
    210   215   220
Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val
225   230   235   240
Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
                245   250   255
Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
            260   265   270
His Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu
        275   280   285
Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr
    290   295   300
Phe Arg Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn
305   310   315   320
Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro
                325   330   335
Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln
            340   345   350
Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val
        355   360   365
Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
    370   375   380
Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
385   390   395   400
Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
                405   410   415
Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
            420   425   430
Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
        435   440   445
Ser Pro Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
    450   455   460
Gly Ser Gly Gly Gly Gly Ser Val Pro Val Ala Arg Leu His Gly Ala
465   470   475   480

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Leu Pro Asp Ala Arg Gly Cys His Ile Ala Gln Phe Lys Ser Leu Ser
                485                 490                 495
Pro Gln Glu Leu Gln Ala Phe Lys Arg Ala Lys Asp Ala Leu Glu Glu
            500                 505                 510
Ser Leu Leu Leu Lys Asp Cys Arg Cys His Ser Arg Leu Phe Pro Arg
        515                 520                 525
Thr Trp Asp Leu Arg Gln Leu Gln Val Arg Glu Arg Pro Met Ala Leu
    530                 535                 540
Glu Ala Glu Leu Ala Leu Thr Leu Lys Val Leu Glu Ala Thr Ala Asp
545                 550                 555                 560
Thr Asp Pro Ala Leu Val Asp Val Leu Asp Gln Pro Leu His Thr Leu
                565                 570                 575
His His Ile Leu Ser Gln Phe Arg Ala Cys Ile Gln Pro Gln Pro Thr
            580                 585                 590
Ala Gly Pro Arg Thr Arg Gly Arg Leu His His Trp Leu Tyr Arg Leu
        595                 600                 605
Gln Glu Ala Pro Lys Lys Glu Ser Pro Gly Cys Leu Glu Ala Ser Val
    610                 615                 620
Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg Asp Leu Asn Cys Val Ala
625                 630                 635                 640
Ser Gly Asp Leu Cys Val
                645
```

<210> 87
<211> 408
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40_LC--(G4S)4--IFNω

<400> 87

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Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
1               5                   10                  15
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Tyr Ser Trp
            20                  25                  30
Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Asn Leu Leu Ile
        35                  40                  45
Tyr Thr Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60
Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80
Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Asn Ile Phe Pro Leu
                85                  90                  95
Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110
Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115                 120                 125
Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130                 135                 140
Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145                 150                 155                 160
Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                165                 170                 175
Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190
Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205
Phe Asn Arg Gly Glu Cys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
    210                 215                 220
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Leu Gly Cys Asp Leu Pro
225                 230                 235                 240
Gln Asn His Gly Leu Leu Ser Arg Asn Thr Leu Val Leu Leu His Gln
                245                 250                 255
Met Arg Arg Ile Ser Pro Phe Leu Cys Leu Lys Asp Arg Arg Asp Phe
            260                 265                 270
Arg Phe Pro Gln Glu Met Val Lys Gly Ser Gln Leu Gln Lys Ala His
        275                 280                 285
```

Val Met Ser Val Leu His Glu Met Leu Gln Gln Ile Phe Ser Leu Phe
290 295 300
His Thr Glu Arg Ser Ser Ala Ala Trp Asn Met Thr Leu Leu Asp Gln
305 310 315 320
Leu His Thr Gly Leu His Gln Gln Leu Gln His Leu Glu Thr Cys Leu
325 330 335
Leu Gln Val Val Gly Glu Gly Glu Ser Ala Gly Ala Ile Ser Ser Pro
340 345 350
Ala Leu Thr Leu Arg Arg Tyr Phe Gln Gly Ile Arg Val Tyr Leu Lys
355 360 365
Glu Lys Lys Tyr Ser Asp Cys Ala Trp Glu Val Val Arg Met Glu Ile
370 375 380
Met Lys Ser Leu Phe Leu Ser Thr Asn Met Gln Glu Arg Leu Arg Ser
385 390 395 400
Lys Asp Arg Asp Leu Gly Ser Ser
405

<210> 88
<211> 658
<212> PRT
<213> Artificial Sequence

<220>
<223> antiCD40_hIgG2 dK_HC--(G4S)4--IFNε

<400> 88
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20 25 30
Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45
Gly Trp Ile Asn Pro Asp Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
50 55 60
Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Asn Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp Gln Pro Leu Gly Tyr Cys Thr Asn Gly Val Cys Ser Tyr
100 105 110
Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser
115 120 125
Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys Ser Arg Ser Thr
130 135 140
Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro
145 150 155 160
Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val
165 170 175
His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser
180 185 190
Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr Gln Thr Tyr Thr
195 200 205
Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val Asp Lys Thr Val
210 215 220
Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro Ala Pro Pro Val
225 230 235 240
Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
245 250 255
Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
260 265 270
His Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu
275 280 285
Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr
290 295 300
Phe Arg Val Val Ser Val Leu Thr Val Val His Gln Asp Trp Leu Asn
305 310 315 320
Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ala Pro
325 330 335

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Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln
            340                 345                 350
Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val
        355                 360                 365
Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
    370                 375                 380
Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
385                 390                 395                 400
Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
                405                 410                 415
Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
            420                 425                 430
Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
        435                 440                 445
Ser Pro Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
    450                 455                 460
Gly Ser Gly Gly Gly Gly Ser Leu Asp Leu Lys Leu Ile Ile Phe Gln
465                 470                 475                 480
Gln Arg Gln Val Asn Gln Glu Ser Leu Lys Leu Leu Asn Lys Leu Gln
                485                 490                 495
Thr Leu Ser Ile Gln Gln Cys Leu Pro His Arg Lys Asn Phe Leu Leu
            500                 505                 510
Pro Gln Lys Ser Leu Ser Pro Gln Gln Tyr Gln Lys Gly His Thr Leu
        515                 520                 525
Ala Ile Leu His Glu Met Leu Gln Gln Ile Phe Ser Leu Phe Arg Ala
    530                 535                 540
Asn Ile Ser Leu Asp Gly Trp Glu Glu Asn His Thr Glu Lys Phe Leu
545                 550                 555                 560
Ile Gln Leu His Gln Gln Leu Glu Tyr Leu Glu Ala Leu Met Gly Leu
                565                 570                 575
Glu Ala Glu Lys Leu Ser Gly Thr Leu Gly Ser Asp Asn Leu Arg Leu
            580                 585                 590
Gln Val Lys Met Tyr Phe Arg Arg Ile His Asp Tyr Leu Glu Asn Gln
        595                 600                 605
Asp Tyr Ser Thr Cys Ala Trp Ala Ile Val Gln Val Glu Ile Ser Arg
    610                 615                 620
Cys Leu Phe Phe Val Phe Ser Leu Thr Glu Lys Leu Ser Lys Gln Gly
625                 630                 635                 640
Arg Pro Leu Asn Asp Met Lys Gln Glu Leu Thr Thr Glu Phe Arg Ser
                645                 650                 655
Pro Arg
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