[000129] An exemplary AAT-Fc fusion protein is the AAT-hFc1 (human IgG1 Fc) described herein. As shown below, AAT polypeptide portion of the fusion protein is underlined (SEQ ID NO: 2) and the IgG-Fc polypeptide portion of the fusion protein is italicized (SEQ ID NO: 3).

AAT-hFc1 (human IgG1 Fc)

EDPQGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVSIATAF
AMLSLGTKADTHDEILEGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFLSE
GLKLVDKFLEDVKKLYHSEAFTVNFGDTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFA
LVNYIFFKGKWERPFEVKDTEEEDFHVDQVTTVKVPMMKRLGMFNIQHCKKLSSWVLLMKY
LGNATAIFFLPDEGKLQHLENELTHDIITKFLENEDRRSASLHLPKLSITGTYDLKSVLGQ
LGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDEKGTEAAGAMFLEAIPMSIPPEVKF
NKPFVFLMIEQNTKSPLFMGKVVNPTQKEPKSCDKTHTCPPCP*APELLGGPSVFLFPPKPK*
DTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVK
GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEA
LHNHYTQKSLSLSPGK (SEQ ID NO:16)

[000130] An exemplary AAT-Fc fusion protein is the AAT-hFc2 (human IgG2 Fc), described herein. As shown below, AAT polypeptide portion of the fusion protein is underlined (SEQ ID NO: 2) and the IgG-Fc polypeptide portion of the fusion protein is italicized (SEQ ID NO: 4).

AAT-hFc2 (human IgG2 Fc)

EDPQGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVSIATAF
AMLSLGTKADTHDEILEGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFLSE
GLKLVDKFLEDVKKLYHSEAFTVNFGDTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFA
LVNYIFFKGKWERPFEVKDTEEEDFHVDQVTTVKVPMMKRLGMFNIQHCKKLSSWVLLMKY
LGNATAIFFLPDEGKLQHLENELTHDIITKFLENEDRRSASLHLPKLSITGTYDLKSVLGQ
LGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDEKGTEAAGAMFLEAIPMSIPPEVKF
NKPFVFLMIEQNTKSPLFMGKVVNPTQK*ERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLM*
ISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTFRVVSVLTVVHQDW
LNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYP

SDIAVEWESNGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNH YTQKSLSLSPGK (SEQ ID NO: 17)

[000131] An exemplary AAT-Fc fusion protein is the AAT-MM-EL-hFc1 (human IgG1 Fc, Met351Glu/Met358Leu), described herein. As shown below, AAT polypeptide portion of the fusion protein is underlined (SEQ ID NO: 34), the IgG-Fc polypeptide portion of the fusion protein is italicized (SEQ ID NO: 3), and the Met351Glu mutation is boxed, and the Met358Leu mutation is shaded in grey.

AAT-MM-EL-hFc1 (human IgG1 Fc, Met351Glu/Met358Leu)

EDPQGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVSIATAF AMLSLGTKADTHDEILEGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFLSE GLKLVDKFLEDVKKLYHSEAFTVNFGDTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFA LVNYIFFKGKWERPFEVKDTEEEDFHVDQVTTVKVPMMKRLGMFNIQHCKKLSSWVLLMKY LGNATAIFFLPDEGKLQHLENELTHDIITKFLENEDRRSASLHLPKLSITGTYDLKSVLGQ LGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDEKGTEAAGAEFLEAIPLSIPPEVKF NKPFVFLMIEQNTKSPLFMGKVVNPTQK*EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPK DTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEA LHNHYTQKSLSLSPGK* (SEQ ID NO: 18)

[000132] An exemplary AAT-Fc fusion protein is the AAT-MM-EL-hFc2 (human IgG2 Fc, Met351Glu/Met358Leu), described herein. As shown below, AAT polypeptide portion of the fusion protein is underlined (SEQ ID NO: 34), the IgG-Fc polypeptide portion of the fusion protein is italicized (SEQ ID NO: 4), the Met351Glu mutation is boxed, and the Met358Leu mutation is shaded in grey.

AAT-MM-EL-hFc2 (human IgG2 Fc, Met351Glu/Met358Leu)

EDPQGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVSIATAF AMLSLGTKADTHDEILEGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFLSE GLKLVDKFLEDVKKLYHSEAFTVNFGDTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFA LVNYIFFKGKWERPFEVKDTEEEDFHVDQVTTVKVPMMKRLGMFNIQHCKKLSSWVLLMKY

LGNATAIFFLPDEGKLQHLENELTHDIITKFLENEDRRSASLHLPKLSITGTYDLKSVLGQ
LGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDEKGTEAAGAEFLEAIPESIPPEVKF
NKPFVFLMIEQNTKSPLFMGKVVNPTQK*ERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLM*
ISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTFRVVSVLTVVHQDW
LNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYP
SDIAVEWESNGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNH
YTQKSLSLSPGK (SEQ ID NO: 19)

[000133] An exemplary AAT-Fc fusion protein is the AAT-MM-LL-hFc1(human IgG1 Fc, Met351Leu/Met358Leu), described herein. As shown below, AAT polypeptide portion of the fusion protein is underlined (SEQ ID NO: 35), the IgG-Fc polypeptide portion of the fusion protein is italicized (SEQ ID NO: 3), the Met351Leu mutation is shaded in black, and the Met358Leu mutation is shaded in grey.

AAT-MM-LL-hFc1(human IgG1 Fc, Met351Leu/Met358Leu)

EDPQGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVSIATAF
AMLSLGTKADTHDEILEGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFLSE
GLKLVDKFLEDVKKLYHSEAFTVNFGDTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFA
LVNYIFFKGKWERPFEVKDTEEEDFHVDQVTTVKVPMMKRLGMFNIQHCKKLSSWVLLMKY
LGNATAIFFLPDEGKLQHLENELTHDIITKFLENEDRRSASLHLPKLSITGTYDLKSVLGQ
LGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDEKGTEAAGALFLEAIPESIPPEVKF
NKPFVFLMIEQNTKSPLFMGKVVNPTQK*EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPK*
DTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVK
GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEA
LHNHYTQKSLSLSPGK(SEQ ID NO:36)

[000134] An exemplary AAT-Fc fusion protein is the AAT-MM:LL-hFc2(human IgG2 Fc, Met351Leu/Met358Leu), described herein. As shown below, AAT polypeptide portion of the fusion protein is underlined (SEQ ID NO: 35), the IgG-Fc polypeptide portion of the fusion protein is italicized (SEQ ID NO: 4), the Met351Leu mutation is shaded in black, and the Met358Leu mutation is shaded in grey.

AAT-MM:LL-hFc2(human IgG2 Fc, Met351Leu/Met358Leu)

EDPQGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVSIATAF
AMLSLGTKADTHDEILEGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFLSE
GLKLVDKFLEDVKKLYHSEAFTVNFGDTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFA
LVNYIFFKGKWERPFEVKDTEEEDFHVDQVTTVKVPMMKRLGMFNIQHCKKLSSWVLLMKY
LGNATAIFFLPDEGKLQHLENELTHDIITKFLENEDRRSASLHLPKLSITGTYDLKSVLGQ
LGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDEKGTEAAGAMFLEAIPMSIPPEVKF
NKPFVFLMIEQNTKSPLFMGKVVNPTQKERKCCVECPPCP*APPVAGPSVFLFPPKPKDTLM*
ISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTFRVVSVLTVVHQDW
LNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYP
SDIAVEWESNGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNH
YTQKSLSLSPGK (SEQ ID NO:20)

[000135] An exemplary AAT-Fc fusion protein is the AAT-hFc1-AAT (human IgG1), described herein. As shown below, AAT polypeptide portion of the fusion protein is underlined (SEQ ID NO: 2), the IgG-Fc polypeptide portion of the fusion protein is italicized (SEQ ID NO: 3).

AAT-hFc1-AAT (human IgG1)

EDPQGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVSIATAF
AMLSLGTKADTHDEILEGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFLSE
GLKLVDKFLEDVKKLYHSEAFTVNFGDTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFA
LVNYIFFKGKWERPFEVKDTEEEDFHVDQVTTVKVPMMKRLGMFNIQHCKKLSSWVLLMKY
LGNATAIFFLPDEGKLQHLENELTHDIITKFLENEDRRSASLHLPKLSITGTYDLKSVLGQ
LGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDEKGTEAAGAMFLEAIPMSIPPEVKF
NKPFVFLMIEQNTKSPLFMGKVVNPTQKEPKSCDKTHTCPPCP*APELLGGPSVFLFPPKPK*
DTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL
HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVK
GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEA
*LHNHYTQKSLSLSPGK*ASTGSEDPQGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQ
LAHQSNSTNIFFSPVSIATAFAMLSLGTKADTHDEILEGLNFNLTEIPEAQIHEGFQELLR
TLNQPDSQLQLTTGNGLFLSEGLKLVDKFLEDVKKLYHSEAFTVNFGDTEEAKKQINDYVE

~~KGTQGKIVDLVKELDRDTVFALVNYIFFKGKWERPFEVKDTEEEDFHVDQVTTVKVPMMKR~~
~~LGMFNIQHCKKLSSWVLLMKYLGNATAIFFLPDEGKLQHLENELTHDIITKFLENEDRRSA~~
~~SLHLPKLSITGTYDLKSVLGQLGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDEKGT~~
~~EAAGAMFLEAIPMSIPPEVKFNKPFVFLMIEQNTKSPLFMGKVVNPTQK (SEQ ID~~
~~NO:21)~~

[000136] These exemplary AAT-Fc fusion proteins were made using the following techniques.

[000137] The gene encoding human AAT was PCR amplified from human liver cDNA (Zyagen). Specific point mutations within the gene encoding AAT or the Fc region were generated by overlapping PCR. The AAT encoding gene was cloned in frame with a gene encoding the hinge region, followed by a CH2 domain, and a CH3 domain of human IgG1, IgG2, IgG3, IgG4, or IgM into a mammalian expression vector, containing a mammalian secretion signal sequence up stream of the AAT gene insertion site. These expression vectors were transfected into mammalian cells (specifically HEK293 or CHO cells) and grown for several days in 8% CO_2 at 37° C. The recombinant AAT-Fc fusion proteins were purified from the expression cell supernatant by protein A chromatography. Importantly, a near neutral pH buffer was used (Gentle Ag/Ab Elution Buffer, Thermo Scientific) to elute the AAT-Fc fusion protein from the protein A resin. The AAT-Fc fusion protein can not be eluted from protein A resin using a standard low pH elution, as the ability of AAT to inhibit NE is compromised following low pH treatment, likely due to a low pH mediated oligomerization of AAT. Figure 1F shows the effects of low pH elution on the ability of AAT to inhibit neutrophil elastase. AAT-Fc fusion protein can be purified either by protein A and a near neutral pH elution buffer, by CaptureSelect® Alpha-1 Antitrypsin affinity matrix (BAC BV).

[000138] The purified AAT-Fc fusion proteins were tested for activity by determining their ability to inhibit neutrophil elastase (NE). Figure 1B and 1D show a reducing SDS-PAGE gel of purified serum derived AAT (sdAAT) and AAT-Fc fusion proteins (Fig 1B-lane 1: sdAAT, lane 2: AAT-Fc (SEQ ID NO: 16), lane 3: AAT-EL-Fc (SEQ ID NO: 18), Fig 1D AAT-Fc-AAT (SEQ ID NO: 20). The proteins were visualized by staining with coomassie blue.

Example 2: AAT-TNFα Targeting Molecule Fusion Proteins

[000142] The studies presented herein describe several, non-limiting examples of recombinant AAT derivatives comprising human AAT fused to an anti-TNFα antibody or a derivative of a TNFα receptor. These examples are provided below to further illustrate different features of the present invention. The examples also illustrate useful methodology for practicing the invention. These examples do not and are not intended to limit the claimed invention.

[000143] The fusion proteins below include cytokine targeting polypeptide sequences that are from or are derived from (i) the anti-TNFα antibody D2E7 (also known as Adalimumab or Humira®), or (ii) the extracellular domain of Type 2 TNFα Receptor (TNFR2-ECD). The AAT polypeptide portion of the fusion protein is underlined, the antibody constant regions (CH1-hinge-CH2-CH3, or CL) are italicized, and D2E7-VH, D2E7-VK, and TNFR2-ECD are denoted in bold text. While these examples include a hinge sequence and/or a linker sequence, fusion proteins of the invention can be made using any hinge sequence and/or a linker sequence suitable in length and/or flexibility. Alternatively fusion proteins can be made without using a hinge and/or a linker sequence.

~~**[000144]** An exemplary AAT-TNFα fusion protein is D2E7-Light Chain-AAT $(G_3S)_2$ Linker, described herein. As shown below, the AAT polypeptide portion of the fusion protein is underlined (SEQ ID NO: 2), D2E7-VK is denoted in bold text (SEQ ID NO: 37), and the antibody constant regions are italicized (SEQ ID NO: 38)~~

~~**D2E7-Light Chain-AAT $(G_3S)_2$ Linker**~~

~~**DIQMTQSPSSLSASVGDRVTITCRASQGIRNYLAWYQQKPGKAPKLLIYAASTLQSGVPSR FSGSGSGTDFTLTISSLQPEDVATYYCQRYNRAPYTFGQGTKVEIK***RTVAAPSVFIFPPSD EQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSK ADYEKHKVYACEVTHQGLSSPVTKSFNRGEC*~~GGGSGGGS~~EDPQGDAAQKTDTSHHDQDHPT FNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVSIATAFAMLSLGTKADTHDEILEGLNFN LTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFLSEGLKLVDKFLEDVKKLYHSEAFT VNFGDTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFALVNYIFFKGKWERPFEVKDTEE EDFHVDQVTTVKVPMMKRLGMFNIQHCKKLSSWVLLMKYLGNATAIFFLPDEGKLQHLENE LTHDIITKFLENEDRRSASLHLPKLSITGTYDLKSVLGQLGITKVFSNGADLSGVTEEAPL~~

KLSKAVHKAVLTIDEKGTEAAGAMFLEAIPMSIPPEVKFNKPFVFLMIEQNTKSPLFMGKV
VNPTQK (SEQ ID NO:22)

[000145] An exemplary AAT-TNFα fusion protein is D2E7-Light Chain-AAT ASTGS Linker, described herein. As shown below, the AAT polypeptide portion of the fusion protein is underlined (SEQ ID NO: 2), D2E7-VK is denoted in bold text (SEQ ID NO: 37), and the antibody constant regions is italicized (SEQ ID NO: 38)

D2E7-Light Chain-AAT ASTGS Linker

DIQMTQSPSSLSASVGDRVTITCRASQGIRNYLAWYQQKPGKAPKLLIYAASTLQSGVPSR
FSGSGSGTDFTLTISSLQPEDVATYYCQRYNRAPYTFGQGTKVEIK*RTVAAPSVFIFPPSD*
EQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSK
*ADYEKHKVYACEVTHQGLSSPVTKSFNRGEC*ASTGSEDPQGDAAQKTDTSHHDQDHPTFNK
ITPNLAEFAFSLYRQLAHQSNSTNIFFSPVSIATAFAMLSLGTKADTHDEILEGLNFNLTE
IPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFLSEGLKLVDKFLEDVKKLYHSEAFTVNF
GDTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFALVNYIFFKGKWERPFEVKDTEEEDF
HVDQVTTVKVPMMKRLGMFNIQHCKKLSSWVLLMKYLGNATAIFFLPDEGKLQHLENELTH
DIITKFLENEDRRSASLHLPKLSITGTYDLKSVLGQLGITKVFSNGADLSGVTEEAPLKLS
KAVHKAVLTIDEKGTEAAGAMFLEAIPMSIPPEVKFNKPFVFLMIEQNTKSPLFMGKVVNP
TQK (SEQ ID NO:23)

[000146] An exemplary AAT-TNFα fusion protein is D2E7-Heavy Chain-AAT $(G_3S)_2$ Linker, described herein. As shown below, the AAT polypeptide portion of the fusion protein is underlined (SEQ ID NO: 2), D2E7-VH is denoted in bold text (SEQ ID NO: 39), and the antibody constant regions is italicized (SEQ ID NO: 40)

D2E7-Heavy Chain-AAT $(G_3S)_2$ Linker

EVQLVESGGGLVQPGRSLRLSCAASGFTFDDYAMHWVRQAPGKGLEWVSAITWNSGHIDYA
DSVEGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAKVSYLSTASSLDYWGQGTL*VTVSSA*
STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL
YSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSV
FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYR
VVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQ

VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVF
*SCSVMHEALHNHYTQKSLSLSPGK*GGGSGGGSEDPQGDAAQKTDTSHHDQDHPTFNKITPN
LAEFAFSLYRQLAHQSNSTNIFFSPVSIATAFAMLSLGTKADTHDEILEGLNFNLTEIPEA
QIHEGFQELLRTLNQPDSQLQLTTGNGLFLSEGLKLVDKFLEDVKKLYHSEAFTVNFGDTE
EAKKQINDYVEKGTQGKIVDLVKELDRDTVFALVNYIFFKGKWERPFEVKDTEEEDFHVDQ
VTTVKVPMMKRLGMFNIQHCKKLSSWVLLMKYLGNATAIFFLPDEGKLQHLENELTHDIIT
KFLENEDRRSASLHLPKLSITGTYDLKSVLGQLGITKVFSNGADLSGVTEEAPLKLSKAVH
KAVLTIDEKGTEAAGAMFLEAIPMSIPPEVKFNKPFVFLMIEQNTKSPLFMGKVVNPTQK
(SEQ ID NO:24)

[000147] An exemplary AAT-TNFα fusion protein is D2E7-Heavy Chain-AAT ASTGS Linker, described herein. As shown below, the AAT polypeptide portion of the fusion protein is underlined (SEQ ID NO: 2), D2E7-VH is denoted in bold text (SEQ ID NO: 39), and the antibody constant regions is italicized (SEQ ID NO: 40)

D2E7-Heavy Chain-AAT ASTGS Linker

EVQLVESGGGLVQPGRSLRLSCAASGFTFDDYAMHWVRQAPGKGLEWVSAITWNSGHIDYA
DSVEGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAKVSYLSTASSLDYWGQGTL*VTVSSA*
STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL
YSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSV
FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYR
VVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQ
VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVF
*SCSVMHEALHNHYTQKSLSLSPGK*ASTGSEDPQGDAAQKTDTSHHDQDHPTFNKITPNLAE
FAFSLYRQLAHQSNSTNIFFSPVSIATAFAMLSLGTKADTHDEILEGLNFNLTEIPEAQIH
EGFQELLRTLNQPDSQLQLTTGNGLFLSEGLKLVDKFLEDVKKLYHSEAFTVNFGDTEEAK
KQINDYVEKGTQGKIVDLVKELDRDTVFALVNYIFFKGKWERPFEVKDTEEEDFHVDQVTT
VKVPMMKRLGMFNIQHCKKLSSWVLLMKYLGNATAIFFLPDEGKLQHLENELTHDIITKFL
ENEDRRSASLHLPKLSITGTYDLKSVLGQLGITKVFSNGADLSGVTEEAPLKLSKAVHKAV
LTIDEKGTEAAGAMFLEAIPMSIPPEVKFNKPFVFLMIEQNTKSPLFMGKVVNPTQK
(SEQ ID NO:25)

[00149] An exemplary AAT-TNFα fusion protein is TNFR2-ECD-Fc1-AAT$(G_3S)_2$ Linker, described herein. As shown below, the AAT polypeptide portion of the fusion protein is underlined (SEQ ID NO: 2), TNFR2-ECD is denoted in bold text (SEQ ID NO: 41), and the antibody constant regions is italicized (SEQ ID NO: 42)

TNFR2-ECD-Fc1-AAT$(G_3S)_2$ Linker

LPAQVAFTPYAPEPGSTCRLREYYDQTAQMCCSKCSPGQHAKVFCTKTSDTVCDSCEDSTY
TQLWNWVPECLSCGSRCSSDQVETQACTREQNRICTCRPGWYCALSKQEGCRLCAPLRKCR
PGFGVARPGTETSDVVCKPCAPGTFSNTTSSTDICRPHQICNVVAIPGNASMDAVCTSTSP
TRSMAPGAVHLPQPVSTRSQHTQPTPEPSTAPSTSFLLPMGPSPPAEGSTGD*EPKSCDKTH*
TCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPQVKFNWYVDGVQVH
NAKTKPREQQYNSTYRVVSVLTVLHQNWLDGKEYKCKVSNKALPAPIEKTISKAKGQPREP
QVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLY
*SKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*GGGSGGGSEDPQGDAAQKTDT
SHHDQDHPTFNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVSIATAFAMLSLGTKADTHD
EILEGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFLSEGLKLVDKFLEDVK
KLYHSEAFTVNFGDTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFALVNYIFFKGKWER
PFEVKDTEEEDFHVDQVTTVKVPMMKRLGMFNIQHCKKLSSWVLLMKYLGNATAIFFLPDE
GKLQHLENELTHDIITKFLENEDRRSASLHLPKLSITGTYDLKSVLGQLGITKVFSNGADL
SGVTEEAPLKLSKAVHKAVLTIDEKGTEAAGAMFLEAIPMSIPPEVKFNKPFVFLMIEQNT
KSPLFMGKVVNPTQK (SEQ ID NO:26)

[00150] An exemplary AAT-TNFα fusion protein is TNFR2-ECD-Fc1-AAT ASTGS Linker, described herein. As shown below, the AAT polypeptide portion of the fusion protein is underlined (SEQ ID NO: 2), TNFR2-ECD is denoted in bold text (SEQ ID NO: 41), and the antibody constant regions is italicized (SEQ ID NO: 42)

TNFR2-ECD-Fc1-AAT ASTGS Linker

LPAQVAFTPYAPEPGSTCRLREYYDQTAQMCCSKCSPGQHAKVFCTKTSDTVCDSCEDSTY
TQLWNWVPECLSCGSRCSSDQVETQACTREQNRICTCRPGWYCALSKQEGCRLCAPLRKCR
PGFGVARPGTETSDVVCKPCAPGTFSNTTSSTDICRPHQICNVVAIPGNASMDAVCTSTSP
TRSMAPGAVHLPQPVSTRSQHTQPTPEPSTAPSTSFLLPMGPSPPAEGSTGD*EPKSCDKTH*
TCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPQVKFNWYVDGVQVH

~~NAKTKPREQQYNSTYRVVSVLTVLHQNWLDGKEYKCKVSNKALPAPIEKTISKAKGQPREP~~
~~QVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLY~~
~~SKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK~~ASTGS~~EDPQGDAAQKTDTSHH~~
~~DQDHPTFNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVSIATAFAMLSLGTKADTHDEIL~~
~~EGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFLSEGLKLVDKFLEDVKKLY~~
~~HSEAFTVNFGDTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFALVNYIFFKGKWERPFE~~
~~VKDTEEEDFHVDQVTTVKVPMMKRLGMFNIQHCKKLSSWVLLMKYLGNATAIFFLPDEGKL~~
~~QHLENELTHDIITKFLENEDRRSASLHLPKLSITGTYDLKSVLGQLGITKVFSNGADLSGV~~
~~TEEAPLKLSKAVHKAVLTIDEKGTEAAGAMFLEAIPMSIPPEVKFNKPFVFLMIEQNTKSP~~
~~LFMGKVVNPTQK (SEQ ID NO:27)~~

[000148] These exemplary AAT-TNFα targeting molecule fusion proteins were made using the following techniques.

[000149] The genes encoding the variable heavy (VH) and variable kappa (VK) regions of the anti-TNFα antibody, D2E7, were generated by gene synthesis. The D2E7-VH gene was cloned in frame with a gene encoding a human IgG1 antibody heavy chain constant region, consisting of a CH1 domain, a hinge domain, a CH2 domain, and a CH3 domain, into a mammalian expression vector, containing a mammalian secretion signal sequence up stream of the VH domain insertion site (D2E7-HC). The D2E7-VK gene was cloned in frame with a human antibody kappa light chain constant (CL) domain, into a mammalian expression vector, containing a mammalian secretion signal sequence up stream of the VK domain insertion site (D2E7-LC). The AAT encoding gene and the adjacent 5' linker sequence were cloned in frame into the 3' end of either, the CH3 domain of the D2E7 heavy chain gene (D2E7-HC-AAT), or the CL domain of the D2E7 light chain gene (D2E7-LC-AAT) coding sequences in the above described mammalian expression vectors. The extracellular domain of the TNFα Receptor 2 (TNFR2-ECD) was generated by gene synthesis and cloned in frame with a gene encoding the hinge region, followed by a CH2 domain and a CH3 domain of human IgG1 (hFc1) into a mammalian expression, containing a mammalian secretion signal sequence up stream of the TNFR2-ECD insertion site. The AAT encoding gene and the adjacent 5' linker sequence were cloned in frame into the 3' end of the gene encoding TNFR2-ECD-hFc1 into a mammalian expression vector (TNFR2-ECD-hFc1-AAT).

and/or flexibility. Alternatively fusion proteins can be made without using a hinge and/or a linker sequence. For example, the polypeptide components can be directly attached.

~~[000155] An exemplary AAT-Fc-SLPI fusion protein is AAT-hFc1-SLPI (human IgG1 Fc), described herein. As shown below, the AAT polypeptide portion of the fusion protein is underlined (SEQ ID NO: 2), the Fc portion is italicized (SEQ ID NO: 3), and the WAP domain containing polypeptide is in bold font (SEQ ID NO: 9)~~

~~**AAT-hFc1-SLPI (human IgG1 Fc)**~~

~~EDPQGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVSIATAF AMLSLGTKADTHDEILEGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFLSE GLKLVDKFLEDVKKLYHSEAFTVNFGDTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFA LVNYIFFKGKWERPFEVKDTEEEDFHVDQVTTVKVPMMKRLGMFNIQHCKKLSSWVLLMKY LGNATAIFFLPDEGKLQHLENELTHDIITKFLENEDRRSASLHLPKLSITGTYDLKSVLGQ LGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDEKGTEAAGAMFLEAIPMSIPPEVKF NKPFVFLMIEQNTKSPLFMGKVVNPTQK*EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPK DTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEA LHNHYTQKSLSLSPGKAST*~~**~~**GSGKSFKAGVCPPKKSAQCLRYKKPECQSDWQCPGKKRCCP DTCGIKCLDPVDTPNPTRRKPGKCPVTYGQCLMLNPPNFCEMDGQCKRDLKCCMGMCGKSC VSPVKA**~~ (SEQ ID NO:28)

~~[000156] An exemplary AAT-Fc-SLPI fusion protein is AAT-hFc1-SLPI (human IgG1 Fc), described herein. As shown below, the AAT polypeptide portion of the fusion protein is underlined (SEQ ID NO: 2), the Fc portion is italicized (SEQ ID NO: 3), and the WAP domain containing polypeptide is in bold font (SEQ ID NO: 12)~~

~~**AAT-hFc1-Elafin (human IgG1 Fc)**~~

~~EDPQGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVSIATAF AMLSLGTKADTHDEILEGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFLSE GLKLVDKFLEDVKKLYHSEAFTVNFGDTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFA LVNYIFFKGKWERPFEVKDTEEEDFHVDQVTTVKVPMMKRLGMFNIQHCKKLSSWVLLMKY LGNATAIFFLPDEGKLQHLENELTHDIITKFLENEDRRSASLHLPKLSITGTYDLKSVLGQ~~

~~LGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDEKGTEAAGAMFLEAIPMSIPPEVKF NKPFVFLMIEQNTKSPLFMGKVVNPTQKEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPK DTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEA LHNHYTQKSLSLSPGKASTGS~~**~~AVTGVPVKGQDTVKGRVPFNGQDPVKGQVSVKGQDKVKAQ EPVKGPVSTKPGSCPIILIRCAMLNPPNRCLKDTDCPGIKKCCEGSCGMACFVPQ~~ (~~SEQ ID NO.29~~)

[000157] The genes encoding the SLPI and Elafin were PCR amplified from human spleen cDNA (Zyagen). These genes were cloned into the mammalian expression vectors of example 1, wherein the SLPI or Elafin gene was inserted in frame with the AAT-Fc gene. These expression vectors were transfected into mammalian cells (specifically HEK293 or CHO cells) and grown for several days in 8% CO_2 at 37° C. The recombinant AAT-Fc-WAP domain fusion proteins were purified from the expression cell supernatant by protein A chromatography. A near neutral pH buffer was used (Gentle Ag/Ab Elution Buffer, Thermo Scientific) to elute the AAT-Fc-WAP domain fusion protein from the protein A resin.

[000158] Figure 3B shows an SDS-PAGE gel of the AAT-Fc-WAP fusion proteins (lane 1 AAT-Fc-Elafin, lane 2 AAT-Fc-SLPI). The proteins were visualized by staining with coomassie blue. The purified AAT-Fc-WAP domain fusion proteins were tested for activity by determining their ability to inhibit neutrophil elastase. NE inhibitory assays were conducted as described above. Human serum derived AAT (sdAAT) and the AAT-Fc fusion protein were used as a positive control in these assays. Relative to sdAAT, the AAT-Fc-WAP targeting molecule fusion proteins display enhanced potency of NE inhibition of neutrophil elastase (Figure 3C).

Example 4 AAT-Albumin

[000159] The studies presented herein describe several, non-limiting examples of recombinant AAT derivatives comprising human AAT fused an albumin polypeptide. These examples are provided below to further illustrate different features of the present invention. The examples also illustrate useful methodology for practicing the invention. These examples do not and are not intended to limit the claimed invention. The AAT portion is

underlined and the albumin portion is italicized. For example, the polypeptide components can be directly attached.

[000160] An exemplary AAT-Albumin fusion protein is AAT-HSA, described herein. As shown below, the AAT polypeptide portion of the fusion protein is underlined (SEQ ID NO: 2), and the albumin polypeptide is italicized (SEQ ID NO: 14)

AAT-HSA

EDPQGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVSIATAF
AMLSLGTKADTHDEILEGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFLSE
GLKLVDKFLEDVKKLYHSEAFTVNFGDTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFA
LVNYIFFKGKWERPFEVKDTEEEDFHVDQVTTVKVPMMKRLGMFNIQHCKKLSSWVLLMKY
LGNATAIFFLPDEGKLQHLENELTHDIITKFLENEDRRSASLHLPKLSITGTYDLKSVLGQ
LGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDEKGTEAAGAMFLEAIPMSIPPEVKF
NKPFVFLMIEQNTKSPLFMGKVVNPTQKASTGSDAHKSEVAHRFKDLGEENFKALVLIAFA
QYLQQCPFEDHVKLVNEVTEFAKTCVADESAENCDKSLHTLFGDKLCTVATLRETYGEMAD
CCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMCTAFHDNEETFLKKYLYEIARRHPYFY
APELLFFAKRYKAAFTECCQAADKAACLLPKLDELRDEGKASSAKQRLKCASLQKFGERAF
KAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGDLLECADDRADLAKYICENQDSIS
SKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESKDVCKNYAEAKDVFLGMFLYE
YARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVFDEFKPLVEEPQNLIKQNCEL
FEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKCCKHPEAKRMPCAEDYLSV
VLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPKEFNAETFTFHADICTL
SEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKADDKETCFAEEGKKLVA
ASQAALGL (SEQ ID NO:30)

[000161] An exemplary AAT-Albumin fusion protein is AAT-HSA Domain 3, described herein. As shown below, the AAT polypeptide portion of the fusion protein is underlined (SEQ ID NO: 2), and the albumin polypeptide is italicized (SEQ ID NO: 15)

AAT-HSA Domain 3

EDPQGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVSIATAF
AMLSLGTKADTHDEILEGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFLSE

~~GLKLVDKFLEDVKKLYHSEAFTVNFGDTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFA~~
~~LVNYIFFKGKWERPFEVKDTEEEDFHVDQVTTVKVPMMKRLGMFNIQHCKKLSSWVLLMKY~~
~~LGNATAIFFLPDEGKLQHLENELTHDIITKFLENEDRRSASLHLPKLSITGTYDLKSVLGQ~~
~~LGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDEKGTEAAGAMFLEAIPMSIPPEVKF~~
~~NKPFVFLMIEQNTKSPLFMGKVVNPTQKASTGSEEPQNLIKQNCELFEQLGEYKFQNALLV~~
~~RYTKKVPQVSTPTLVEVSRNLGKVGSKCCKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVS~~
~~DRVTKCCTESLVNRRPCFSALEVDETYVPKEFNAETFTFHADICTLSEKERQIKKQTALVE~~
~~LVKHKPKATKEQLKAVMDDFAAFVEKCCKADDKETCFAEEGKKLVA (SEQ ID NO:31)~~

[000162] The gene encoding human serum albumin (HSA) was PCR amplified from human liver cDNA (Zyagen). A mammalian expression vector was generated, wherein gene encoding HSA or the domain 3 of HSA, was cloned in frame to the 3' end of the AAT encoding gene, containing a mammalian secretion signal sequence up stream of AAT.

[000163] These expression vectors were transfected into mammalian cells (specifically HEK293 or CHO cells) and grown for several days in 8% CO_2 at 37° C. The recombinant AAT-HSA fusion proteins were purified from the expression cell supernatant using the CaptureSelect® Alpha-1 Antitrypsin affinity matrix (BAC BV), wherein the binding buffer consisted of 20mM Tris, 150mM NaCl, pH 7.4 and the elution buffer consisted of 20mM Tris, 2M $MgCl_2$ pH 7.4.

[000164] Figure 4B shows an SDS-PAGE gel of the AAT-HSA fusion protein The proteins were visualized by staining with coomassie blue. The purified AAT-HSA fusion proteins were tested for activity by determining their ability to inhibit neutrophil elastase. NE inhibitory assays were conducted as described above. Human serum derived AAT (sdAAT) was used as a positive control in these assays. Relative to sdAAT, the AAT-HS fusion protein displays similar potency of NE inhibition, demonstrating that the fusion to albumin does not dampen the capacity of AAT to inhibit NE (Figure 4C.)

Other Embodiments

[000165] While the invention has been described in conjunction with the detailed description thereof, the foregoing description is intended to illustrate and not limit the scope of the invention, which is defined by the scope of the appended claims. Other aspects, advantages, and modifications are within the scope of the following claims.

What is claimed is:

1. An isolated fusion protein comprising at least one human serpin polypeptide operably linked to a second polypeptide wherein the second polypeptide comprises at least one the following:

an immunoglobulin Fc polypeptide or an amino acid sequence that is derived from an immunoglobulin Fc polypeptide;

a cytokine targeting polypeptide or a sequence derived from a cytokine targeting polypeptide;

a WAP domain containing polypeptide or a sequence derived from a WAP domain containing polypeptide; or

an albumin polypeptide or an amino acid sequence that is derived from a serum albumin polypeptide.

2. An isolated fusion protein comprising at least one alpha-1 antitrypsin (AAT) polypeptide operably linked to a second polypeptide of at least one of the following:

an immunoglobulin Fc polypeptide;

a cytokine targeting peptide;

a human secretory leukocyte proteinase inhibitor (SLPI) polypeptide; and

an immunoglobulin Fc polypeptide and a human SLPI polypeptide, wherein the SLPI polypeptide comprises the WAP2 domain of human SLPI; or

a human serum albumin (HSA) polypeptide.

3. An isolated fusion protein comprising at least one alpha-1 antitrypsin (AAT) polypeptide operably linked to a second polypeptide of at least one of the following:

an immunoglobulin Fc polypeptide;

a cytokine targeting peptide;

a human Elafin polypeptide;

a human Elafin polypeptide and an immunoglobulin Fc polypeptide, wherein the Elafin polypeptide comprises the WAP domain of human Elafin; or

a human serum albumin (HSA) polypeptide.

4. The fusion protein of claim 1 wherein the human serpin polypeptide is a human alpha-1 antitrypsin (AAT) polypeptide or is derived from a human AAT polypeptide.

5. The isolated fusion protein of any one of claims 2-4, wherein AAT polypeptide comprises the amino acid sequence of SEQ ID NO: 2.

6. The isolated fusion protein of any one of claims 2-4, wherein the AAT polypeptide comprises the reactive site loop of AAT comprising the amino acid sequence of SEQ ID NO: 1 or a mutated reactive site loop of AAT comprising the amino acid sequence of SEQ ID NO: 32 or 33.

7. The isolated fusion protein of any one of claims 2-4, wherein the immunoglobulin Fc polypeptide is a human Fc polypeptide.

8. The isolated fusion protein of claim 7, wherein human Fc polypeptide is a human IgM polypeptide or a human IgG Fc polypeptide.

9. The isolated fusion protein of claim 8, wherein the human IgG Fc polypeptide is a human IgG1 polypeptide, a human IgG2 Fc polypeptide, human IgG3 Fc polypeptide, or human IgG4 Fc polypeptide.

10. The isolated fusion protein of any one of claims 1-3, wherein the immunoglobulin Fc polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 3, 4, 5, 6, and 7.

11. The isolated fusion protein of claim 1, wherein the serpin polypeptide and the immunoglobulin Fc polypeptide are operably linked via a hinge region, a linker region, or both a hinge region and linker region.

12. The isolated fusion protein of any one of claims 2-4, wherein the AAT polypeptide and the immunoglobulin Fc polypeptide are operably linked via a hinge region, a linker region, or both a hinge region and linker region.

13. The isolated fusion protein of claim 11 or claim 12, wherein the hinge region, the linker region or both the hinge region and the linker region comprise a peptide sequence.

14. The isolated fusion protein of any one of claims 1-3, wherein the fusion protein comprises an amino acid sequence selected from SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, and SEQ ID NO: 21.

15. The isolated fusion protein of any one of claims 1-6, wherein the cytokine targeting polypeptide is a human cytokine receptor polypeptide or a derivative of a human cytokine receptor polypeptide, a cytokine targeting polypeptide that binds a cytokine receptor or a cytokine targeting polypeptide binds a human cytokine.

16. The isolated fusion protein of claim 15, wherein the human cytokine receptor polypeptide comprises multiple subunits.

17. The isolated fusion protein of claim 15 or claim 16, wherein the human cytokine receptor is a receptor for TNFα, IgE, IL-12, IL-23, IL-6, IL-1α, IL-1β, IL-17, IL-13, the p40 subunit of IL-12 and IL-23, IL-4, IL-10, IL-2, IL-18, IL-27, or IL-32.

18. The isolated fusion protein of claim 17, wherein the cytokine receptor is a receptor for human TNFα.

19. The isolated fusion protein of claim 15, wherein the human cytokine is TNFα, IgE, IL-12, IL-23, IL-6, IL-1α, IL-1β, IL-17, IL-13, the p40 subunit of IL-12 and IL-23, IL-4, IL-10, IL-2, IL-18, IL-27, or IL-32.

20. The isolated fusion protein of claim 19, wherein the cytokine is human TNFα.

21. The isolated fusion protein of claim 15, wherein the cytokine targeting polypeptide is an antibody or an antibody fragment.

22. The isolated fusion protein of claim 21, wherein the antibody or antibody fragment is chimeric, humanized, or fully human.

23. The isolated fusion protein of claim 1-6, where the fusion protein comprises an amino acid sequence selected from SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 26, and SEQ ID NO: 27.

24. The isolated fusion protein of claim 1, wherein the WAP domain containing polypeptide sequence comprises a SLPI polypeptide sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 8, 9 and 10.

25. The isolated fusion protein of claims 1, wherein the WAP domain containing polypeptide sequence comprises an elafin polypeptide sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 11, 12 and 13.

26. The isolated fusion protein of claim 1, wherein the fusion protein comprises a serpin polypeptide, a WAP domain-containing polypeptide and an immunoglobulin Fc polypeptide such that at least two of the serpin polypeptide, the WAP domain-containing polypeptide and the immunoglobulin Fc polypeptide are operably linked via a hinge region, a linker region, or both a hinge region and linker region.

27. The isolated fusion protein of claim 2, wherein the fusion protein comprises an AAT polypeptide, a SLPI polypeptide and an immunoglobulin Fc polypeptide such that at least two of the AAT polypeptide, the SLPI polypeptide and the immunoglobulin Fc polypeptide are operably linked via a hinge region, a linker region, or both a hinge region and linker region.

28. The isolated fusion protein of claim 3, wherein the fusion protein comprises an AAT polypeptide, an Elafin polypeptide and an immunoglobulin Fc polypeptide such that at least two of the AAT polypeptide, the Elafin polypeptide and the immunoglobulin Fc polypeptide are operably linked via a hinge region, a linker region, or both a hinge region and linker region.

29. The isolated fusion protein of any one of claims 2-4, wherein the fusion protein comprises two AAT polypeptides and an immunoglobulin Fc polypeptide.

30. The isolated fusion protein of claim 29, wherein each of the two AAT polypeptides are operably linked to the immunoglobulin Fc polypeptide via a hinge region, a linker region, or both a hinge region and linker region such that the fusion protein has the structural arrangement from N-terminus to C-terminus as follows: AAT polypeptide-immunoglobulin Fc polypeptide-AAT polypeptide.

31. The isolated fusion protein of any one of claims 26-30, wherein the hinge region, the linker region or both the hinge region and the linker region comprise a peptide sequence.

32. The isolated fusion protein of claim 2, wherein the fusion protein comprises the amino acid sequence of SEQ ID NO: 28.

33. The isolated fusion protein of claim 2, where the fusion protein comprises the amino acid sequence of SEQ ID NO: 29.

34. The fusion protein of claim 1, wherein the albumin polypeptide is a human serum albumin (HSA) polypeptide or is derived from a HSA polypeptide.

35. The isolated fusion protein of any one of claims 2, 3 or 34, wherein HSA polypeptide comprises the amino acid sequence of SEQ ID NO: 14 or the amino acid sequence of SEQ ID NO: 15.

36. The isolated fusion protein of any one of claims 2, 3 or 34, wherein the HSA polypeptide comprises domain 3 of HSA.

37. The isolated fusion protein of claim 34, wherein the serpin is operably linked to HSA via an albumin binding polypeptide.

38. The isolated fusion protein of claim 2 or claim 3, wherein the AAT polypeptide is operably linked to HSA via an albumin binding polypeptide.

39. The isolated fusion protein of claim 37 or 38, wherein the albumin binding polypeptide is an antibody or antibody fragment or derived from an antibody or antibody fragment.

40. The isolated fusion protein of claim 39, wherein the antibody or antibody fragment or chimeric, humanized, or fully human.

41. The isolated fusion protein of claims 37 or 38, wherein the albumin binding polypeptide is a peptide.

42. The isolated fusion protein of claims 47, wherein the albumin binding polypeptide is Domain 3 of *Streptococcal* Protein G or a sequence derived from Domain 3 of *Streptococcal* Protein G.

43. The isolated fusion protein of claim 1, wherein the serpin is covalently linked to a HSA polypeptide.

44. The isolated fusion protein of claim 1, wherein the serpin is non-covalently linked to a HSA polypeptide.

45. The isolated fusion protein any one of claims 1-3, where the fusion protein comprises the amino acid sequence of SEQ ID NO: 30 or 31.

46. The isolated fusion protein of any one of claims 1-3, wherein the immunoglobulin Fc polypeptide is modified to enhance FcRn binding.

47. The isolated fusion protein of any one of claims 1-3, wherein the immunoglobulin Fc polypeptide comprising at least one of the following mutations: Met252Tyr, Ser254Thr, Thr256Glu, Met428Leu or Asn434Ser

48. A method of treating or alleviating a symptom of a disease or disorder associated with aberrant serine protease expression or activity in a subject in need thereof, the method comprising administering a fusion protein according to any one of the previous claims.

49. A method of treating or alleviating inflammation or a symptom of an inflammatory disease or disorder while reducing the risk of infection, in a subject in need thereof, the method comprising administering a fusion protein according to any one of the previous claims.

50. A method of reducing the risk of infection in a subject in need thereof, the method comprising administering a fusion protein according to any one of the previous claims.

51. The method of any one of claims 48-51, wherein the subject is a human.

52. The method of 49, wherein the inflammatory disease or disorder is selected from the following: emphysema, chronic obstructive pulmonary disease (COPD), acute respiratory distress syndrome (ARDS), allergic asthma, cystic fibrosis, cancers of the lung, ischemia-reperfusion injury, ischemia/reperfusion injury following cardiac transplantation, myocardial infarction, rheumatoid arthritis, septic arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, psoriasis, type I and/or type II diabetes, pneumonia, sepsis, graft versus host disease (GVHD), wound healing, Systemic lupus erythematosus, and Multiple sclerosis.

53. The method of 50, wherein the infection is selected from bacterial infections, fungal infections, or viral infections.

[000129] An exemplary AAT-Fc fusion protein is the AAT-hFc1 (human IgG1 Fc) described herein. As shown below, AAT polypeptide portion of the fusion protein is underlined (SEQ ID NO: 2), the hinge region is shown in normal text (SEQ ID NO: 43), and the IgG-Fc polypeptide portion of the fusion protein is italicized (SEQ ID NO: 3).

AAT-hFc1 (human IgG1 Fc)

EDPQGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVSIATAFAMLSLGTKA
DTHDEILEGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFLSEGLKLVDKFLEDVKKLYHS
EAFTVNFGDTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFALVNYIFFKGKWERPFEVKDTEEEDFHV
DQVTTVKVPMMKRLGMFNIQHCKKLSSWVLLMKYLGNATAIFFLPDEGKLQHLENELTHDIITKFLENED
RRSASLHLPKLSITGTYDLKSVLGQLGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDEKGTEAAGA
MFLEAIPMSIPPEVKFNKPFVFLMIEQNTKSPLFMGKVVNPTQKEPKSCDKTHTCPPCP*APELLGGPSVF*
LFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEW
ESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
(SEQ ID NO:16)

[000130] An exemplary AAT-Fc fusion protein is the AAT-hFc2 (human IgG2 Fc), described herein. As shown below, AAT polypeptide portion of the fusion protein is underlined (SEQ ID NO: 2), the hinge region is shown in normal text (SEQ ID NO: 44), and the IgG-Fc polypeptide portion of the fusion protein is italicized (SEQ ID NO: 4).

AAT-hFc2 (human IgG2 Fc)

EDPQGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVSIATAFAMLSLGTKA
DTHDEILEGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFLSEGLKLVDKFLEDVKKLYHS
EAFTVNFGDTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFALVNYIFFKGKWERPFEVKDTEEEDFHV
DQVTTVKVPMMKRLGMFNIQHCKKLSSWVLLMKYLGNATAIFFLPDEGKLQHLENELTHDIITKFLENED
RRSASLHLPKLSITGTYDLKSVLGQLGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDEKGTEAAGA
MFLEAIPMSIPPEVKFNKPFVFLMIEQNTKSPLFMGKVVNPTQKERKCCVECPPCP*APPVAGPSVFLFPP*
KPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTFRVVSVLTVVHQDWLN
GKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNG
QPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID
NO: 17)

[000131] An exemplary AAT-Fc fusion protein is the AAT-MM-EL-hFc1 (human IgG1 Fc, Met351Glu/Met358Leu), described herein. As shown below, AAT polypeptide portion of the fusion protein is underlined (SEQ ID NO: 34), the hinge region is shown in normal text (SEQ ID NO: 43), the IgG-Fc polypeptide portion of the fusion protein is italicized (SEQ ID NO: 3), and the Met351Glu mutation is boxed, and the Met358Leu mutation is shaded in grey.

AAT-MM-EL-hFc1 (human IgG1 Fc, Met351Glu/Met358Leu)

EDPQGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVSIATAFAMLSLGTKA
DTHDEILEGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFLSEGLKLVDKFLEDVKKLYHS
EAFTVNFGDTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFALVNYIFFKGKWERPFEVKDTEEEDFHV
DQVTTVKVPMMKRLGMFNIQHCKKLSSWVLLMKYLGNATAIFFLPDEGKLQHLENELTHDIITKFLENED
RRSASLHLPKLSITGTYDLKSVLGQLGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDEKGTEAAGA
EFLEAIPLSIPPEVKFNKPFVFLMIEQNTKSPLFMGKVVNPTQKEPKSCDKTHTCPPCP*APELLGGPSVF*
LFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEW
ESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
(SEQ ID NO: 18)

[000132] An exemplary AAT-Fc fusion protein is the AAT-MM-EL-hFc2 (human IgG2 Fc, Met351Glu/Met358Leu), described herein. As shown below, AAT polypeptide portion of the fusion protein is underlined (SEQ ID NO: 34), the hinge region is shown in normal text (SEQ ID NO: 44), the IgG-Fc polypeptide portion of the fusion protein is italicized (SEQ ID NO: 4), the Met351Glu mutation is boxed, and the Met358Leu mutation is shaded in grey.

AAT-MM-EL-hFc2 (human IgG2 Fc, Met351Glu/Met358Leu)

EDPQGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVSIATAFAMLSLGTKA
DTHDEILEGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFLSEGLKLVDKFLEDVKKLYHS
EAFTVNFGDTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFALVNYIFFKGKWERPFEVKDTEEEDFHV
DQVTTVKVPMMKRLGMFNIQHCKKLSSWVLLMKYLGNATAIFFLPDEGKLQHLENELTHDIITKFLENED
RRSASLHLPKLSITGTYDLKSVLGQLGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDEKGTEAAGA
EFLEAIPLSIPPEVKFNKPFVFLMIEQNTKSPLFMGKVVNPTQKERKCCVECPPCP*APPVAGPSVFLFPP*

KPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTFRVVSVLTVVHQDWLN
GKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNG
QPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 19)

[000133] An exemplary AAT-Fc fusion protein is the AAT-MM-LL-hFc1(human IgG1 Fc, Met351Leu/Met358Leu), described herein. As shown below, AAT polypeptide portion of the fusion protein is underlined (SEQ ID NO: 35), the hinge region is shown in normal text (SEQ ID NO: 43), the IgG-Fc polypeptide portion of the fusion protein is italicized (SEQ ID NO: 3), the Met351Leu mutation is shaded in black, and the Met358Leu mutation is shaded in grey.

AAT-MM-LL-hFc1(human IgG1 Fc, Met351Leu/Met358Leu)

EDPQGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVSIATAFAMLSLGTKA
DTHDEILEGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFLSEGLKLVDKFLEDVKKLYHS
EAFTVNFGDTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFALVNYIFFKGKWERPFEVKDTEEEDFHV
DQVTTVKVPMMKRLGMFNIQHCKKLSSWVLLMKYLGNATAIFFLPDEGKLQHLENELTHDIITKFLENED
RRSASLHLPKLSITGTYDLKSVLGQLGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDEKGTEAAGA
LFLEAIPLSIPPEVKFNKPFVFLMIEQNTKSPLFMGKVVNPTQKEPKSCDKTHTCPPCP*APELLGGPSVF*
LFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEW
ESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK(SEQ ID NO:36)

[000134] An exemplary AAT-Fc fusion protein is the AAT-MM:LL-hFc2(human IgG2 Fc, Met351Leu/Met358Leu), described herein. As shown below, AAT polypeptide portion of the fusion protein is underlined (SEQ ID NO: 35), the hinge region is shown in normal text (SEQ ID NO: 44), the IgG-Fc polypeptide portion of the fusion protein is italicized (SEQ ID NO: 4), the Met351Leu mutation is shaded in black, and the Met358Leu mutation is shaded in grey.

AAT-MM:LL-hFc2(human IgG2 Fc, Met351Leu/Met358Leu)

EDPQGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVSIATAFAMLSLGTKA
DTHDEILEGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFLSEGLKLVDKFLEDVKKLYHS

EAFTVNFGDTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFALVNYIFFKGKWERPFEVKDTEEEDFHV
DQVTTVKVPMMKRLGMFNIQHCKKLSSWVLLMKYLGNATAIFFLPDEGKLQHLENELTHDIITKFLENED
RRSASLHLPKLSITGTYDLKSVLGQLGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDEKGTEAAGA
LFLEAIPLSIPPEVKFNKPFVFLMIEQNTKSPLFMGKVVNPTQKERKCCVECPPCP*APPVAGPSVFLFPP*
KPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTFRVVSVLTVVHQDWLN
GKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNG
QPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID
NO:20)

[000135] An exemplary AAT-Fc fusion protein is the AAT-hFc1-AAT (human IgG1), described herein. As shown below, AAT polypeptide portion of the fusion protein is underlined (SEQ ID NO: 2), the hinge region is shown in normal text (SEQ ID NO: 43), the ASTGS linker is shown in normal text (SEQ ID NO: 45), and the IgG-Fc polypeptide portion of the fusion protein is italicized (SEQ ID NO: 3).

AAT-hFc1-AAT (human IgG1)

EDPQGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVSIATAFAMLSLGTKA
DTHDEILEGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFLSEGLKLVDKFLEDVKKLYHS
EAFTVNFGDTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFALVNYIFFKGKWERPFEVKDTEEEDFHV
DQVTTVKVPMMKRLGMFNIQHCKKLSSWVLLMKYLGNATAIFFLPDEGKLQHLENELTHDIITKFLENED
RRSASLHLPKLSITGTYDLKSVLGQLGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDEKGTEAAGA
MFLEAIPMSIPPEVKFNKPFVFLMIEQNTKSPLFMGKVVNPTQKEPKSCDKTHTCPPCP*APELLGGPSVF*
LFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQ
DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEW
*ESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*ASTG
SEDPQGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVSIATAFAMLSLGTK
ADTHDEILEGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFLSEGLKLVDKFLEDVKKLYH
SEAFTVNFGDTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFALVNYIFFKGKWERPFEVKDTEEEDFH
VDQVTTVKVPMMKRLGMFNIQHCKKLSSWVLLMKYLGNATAIFFLPDEGKLQHLENELTHDIITKFLENE
DRRSASLHLPKLSITGTYDLKSVLGQLGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDEKGTEAAG
AMFLEAIPMSIPPEVKFNKPFVFLMIEQNTKSPLFMGKVVNPTQK (SEQ ID NO:21)

[000144] An exemplary AAT-TNFα fusion protein is D2E7-Light Chain-AAT $(G_3S)_2$ Linker, described herein. As shown below, the AAT polypeptide portion of the fusion protein is underlined (SEQ ID NO: 2), D2E7-VK is denoted in bold text (SEQ ID NO: 37), the $(G_3S)_2$ linker is shown in normal text (SEQ ID NO: 46), and the antibody constant regions are italicized (SEQ ID NO: 38)

D2E7-Light Chain-AAT $(G_3S)_2$ Linker

DIQMTQSPSSLSASVGDRVTITCRASQGIRNYLAWYQQKPGKAPKLLIYAASTLQSGVPSRFSGSGSGTDFTLT ISSLQPEDVATYYCQRYNRAPYTFGQGTKVEIK*RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQW KVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC*GGGSGGGS EDPQGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVSIATAFAMLSLGTKADTHD EILEGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFLSEGLKLVDKFLEDVKKLYHSEAFTVNFG DTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFALVNYIFFKGKWERPFEVKDTEEEDFHVDQVTTVKVPMMK RLGMFNIQHCKKLSSWVLLMKYLGNATAIFFLPDEGKLQHLENELTHDIITKFLENEDRRSASLHLPKLSITGT YDLKSVLGQLGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDEKGTEAAGAMFLEAIPMSIPPEVKFNKPF VFLMIEQNTKSPLFMGKVVNPTQK (SEQ ID NO:22)

[000145] An exemplary AAT-TNFα fusion protein is D2E7-Light Chain-AAT ASTGS Linker, described herein. As shown below, the AAT polypeptide portion of the fusion protein is underlined (SEQ ID NO: 2), D2E7-VK is denoted in bold text (SEQ ID NO: 37), the ASTGS linker is shown in normal text (SEQ ID NO: 45), and the antibody constant regions is italicized (SEQ ID NO: 38)

D2E7-Light Chain-AAT ASTGS Linker

DIQMTQSPSSLSASVGDRVTITCRASQGIRNYLAWYQQKPGKAPKLLIYAASTLQSGVPSRFSGSGSGTDFTLT ISSLQPEDVATYYCQRYNRAPYTFGQGTKVEIK*RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQW KVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC*ASTGSEDP QGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVSIATAFAMLSLGTKADTHDEIL EGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFLSEGLKLVDKFLEDVKKLYHSEAFTVNFGDTE EAKKQINDYVEKGTQGKIVDLVKELDRDTVFALVNYIFFKGKWERPFEVKDTEEEDFHVDQVTTVKVPMMKRLG MFNIQHCKKLSSWVLLMKYLGNATAIFFLPDEGKLQHLENELTHDIITKFLENEDRRSASLHLPKLSITGTYDL KSVLGQLGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDEKGTEAAGAMFLEAIPMSIPPEVKFNKPFVFL MIEQNTKSPLFMGKVVNPTQK (SEQ ID NO:23)

[000146] An exemplary AAT-TNFα fusion protein is D2E7-Heavy Chain-AAT $(G_3S)_2$ Linker, described herein. As shown below, the AAT polypeptide portion of the fusion protein is underlined (SEQ ID NO: 2), D2E7-VH is denoted in bold text (SEQ ID NO: 39), the $(G_3S)_2$ linker is shown in normal text (SEQ ID NO: 46), and the antibody constant regions is italicized (SEQ ID NO: 40)

D2E7-Heavy Chain-AAT $(G_3S)_2$ Linker

EVQLVESGGGLVQPGRSLRLSCAASGFTFDDYAMHWVRQAPGKGLEWVSAITWNSGHIDYADSVEGRFTISRDN
AKNSLYLQMNSLRAEDTAVYYCAKVSYLSTASSLDYWGQGTL*VTVSSASTKGPSVFPLAPSSKSTSGGTAALGC*
LVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPK
SCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPR
EEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS
*LSLSPGK*GGGSGGGSEDPQGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVSIAT
AFAMLSLGTKADTHDEILEGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFLSEGLKLVDKFLED
VKKLYHSEAFTVNFGDTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFALVNYIFFKGKWERPFEVKDTEEED
FHVDQVTTVKVPMMKRLGMFNIQHCKKLSSWVLLMKYLGNATAIFFLPDEGKLQHLENELTHDIITKFLENEDR
RSASLHLPKLSITGTYDLKSVLGQLGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDEKGTEAAGAMFLEA
IPMSIPPEVKFNKPFVFLMIEQNTKSPLFMGKVVNPTQK (SEQ ID NO:24)

[000147] An exemplary AAT-TNFα fusion protein is D2E7-Heavy Chain-AAT ASTGS Linker, described herein. As shown below, the AAT polypeptide portion of the fusion protein is underlined (SEQ ID NO: 2), D2E7-VH is denoted in bold text (SEQ ID NO: 39), the ASTGS linker is shown in normal text (SEQ ID NO: 45), and the antibody constant regions is italicized (SEQ ID NO: 40)

D2E7-Heavy Chain-AAT ASTGS Linker

EVQLVESGGGLVQPGRSLRLSCAASGFTFDDYAMHWVRQAPGKGLEWVSAITWNSGHIDYADSVEGRFTISRDN
AKNSLYLQMNSLRAEDTAVYYCAKVSYLSTASSLDYWGQGTL*VTVSSASTKGPSVFPLAPSSKSTSGGTAALGC*
LVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPK
SCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPR
EEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS
*LSLSPGK*ASTGSEDPQGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVSIATAFA
MLSLGTKADTHDEILEGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFLSEGLKLVDKFLEDVKK
LYHSEAFTVNFGDTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFALVNYIFFKGKWERPFEVKDTEEEDFHV
DQVTTVKVPMMKRLGMFNIQHCKKLSSWVLLMKYLGNATAIFFLPDEGKLQHLENELTHDIITKFLENEDRRSA
SLHLPKLSITGTYDLKSVLGQLGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDEKGTEAAGAMFLEAIPM
SIPPEVKFNKPFVFLMIEQNTKSPLFMGKVVNPTQK (SEQ ID NO:25)

[00149] An exemplary AAT-TNFα fusion protein is TNFR2-ECD-Fc1-AAT$(G_3S)_2$ Linker, described herein. As shown below, the AAT polypeptide portion of the fusion protein is underlined (SEQ ID NO: 2), TNFR2-ECD is denoted in bold text (SEQ ID NO: 41), the hinge region is shown in normal text (SEQ ID NO:

43), the $(G_3S)_2$ linker is shown in normal text (SEQ ID NO: 46), and the antibody constant regions is italicized (SEQ ID NO: 42)

TNFR2-ECD-Fc1-AAT$(G_3S)_2$ Linker

LPAQVAFTPYAPEPGSTCRLREYYDQTAQMCCSKCSPGQHAKVFCTKTSDTVCDSCEDSTYTQLWNWVPECLSC
GSRCSSDQVETQACTREQNRICTCRPGWYCALSKQEGCRLCAPLRKCRPGFGVARPGTETSDVVCKPCAPGTFS
NTTSSTDICRPHQICNVVAIPGNASMDAVCTSTSPTRSMAPGAVHLPQPVSTRSQHTQPTPEPSTAPSTSFLLP
MGPSPPAEGSTGDEPKSCDKTHTCPPCP*APELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPQVKFN*
WYVDGVQVHNAKTKPREQQYNSTYRVVSVLTVLHQNWLDGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYT
LPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFS
*CSVMHEALHNHYTQKSLSLSPGK*GGGSGGGSEDPQGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQLAH
QSNSTNIFFSPVSIATAFAMLSLGTKADTHDEILEGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNG
LFLSEGLKLVDKFLEDVKKLYHSEAFTVNFGDTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFALVNYIFFK
GKWERPFEVKDTEEEDFHVDQVTTVKVPMMKRLGMFNIQHCKKLSSWVLLMKYLGNATAIFFLPDEGKLQHLEN
ELTHDIITKFLENEDRRSASLHLPKLSITGTYDLKSVLGQLGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLT
IDEKGTEAAGAMFLEAIPMSIPPEVKFNKPFVFLMIEQNTKSPLFMGKVVNPTQK (SEQ ID NO:26)

[00150] An exemplary AAT-TNFα fusion protein is TNFR2-ECD-Fc1-AAT ASTGS Linker, described herein. As shown below, the AAT polypeptide portion of the fusion protein is underlined (SEQ ID NO: 2), TNFR2-ECD is denoted in bold text (SEQ ID NO: 41), the hinge region is shown in normal text (SEQ ID NO: 43), the ASTGS linker is shown in normal text (SEQ ID NO: 45), and the antibody constant regions is italicized (SEQ ID NO: 42)

TNFR2-ECD-Fc1-AAT ASTGS Linker

LPAQVAFTPYAPEPGSTCRLREYYDQTAQMCCSKCSPGQHAKVFCTKTSDTVCDSCEDSTYTQLWNWVPECLSC
GSRCSSDQVETQACTREQNRICTCRPGWYCALSKQEGCRLCAPLRKCRPGFGVARPGTETSDVVCKPCAPGTFS
NTTSSTDICRPHQICNVVAIPGNASMDAVCTSTSPTRSMAPGAVHLPQPVSTRSQHTQPTPEPSTAPSTSFLLP
MGPSPPAEGSTGDEPKSCDKTHTCPPCP*APELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPQVKFN*
WYVDGVQVHNAKTKPREQQYNSTYRVVSVLTVLHQNWLDGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYT
LPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFS
*CSVMHEALHNHYTQKSLSLSPGK*ASTGSEDPQGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQLAHQSN
STNIFFSPVSIATAFAMLSLGTKADTHDEILEGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFL
SEGLKLVDKFLEDVKKLYHSEAFTVNFGDTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFALVNYIFFKGKW
ERPFEVKDTEEEDFHVDQVTTVKVPMMKRLGMFNIQHCKKLSSWVLLMKYLGNATAIFFLPDEGKLQHLENELT
HDIITKFLENEDRRSASLHLPKLSITGTYDLKSVLGQLGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDE
KGTEAAGAMFLEAIPMSIPPEVKFNKPFVFLMIEQNTKSPLFMGKVVNPTQK (SEQ ID NO:27)

and/or flexibility. Alternatively fusion proteins can be made without using a hinge and/or a linker sequence. For example, the polypeptide components can be directly attached.

[000155] An exemplary AAT-Fc-SLPI fusion protein is AAT-hFc1-SLPI (human IgG1 Fc), described herein. As shown below, the AAT polypeptide portion of the fusion protein is underlined (SEQ ID NO: 2), the hinge region is shown in normal text (SEQ ID NO: 43), the ASTGS linker is shown in normal text (SEQ ID NO: 45), the Fc portion is italicized (SEQ ID NO: 3), and the WAP domain containing polypeptide is in bold font (SEQ ID NO: 9)

AAT-hFc1-SLPI (human IgG1 Fc)

EDPQGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVSIATAFAMLSLGTKADTHD
EILEGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFLSEGLKLVDKFLEDVKKLYHSEAFTVNFG
DTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFALVNYIFFKGKWERPFEVKDTEEEDFHVDQVTTVKVPMMK
RLGMFNIQHCKKLSSWVLLMKYLGNATAIFFLPDEGKLQHLENELTHDIITKFLENEDRRSASLHLPKLSITGT
YDLKSVLGQLGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDEKGTEAAGAMFLEAIPMSIPPEVKFNKPF
VFLMIEQNTKSPLFMGKVVNPTQK*EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVD*
VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKA
KGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVD
*KSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*ASTGS**SGKSFKAGVCPPKKSAQCLRYKKPECQSDWQCPGK**
KRCCPDTCGIKCLDPVDTPNPTRRKPGKCPVTYGQCLMLNPPNFCEMDGQCKRDLKCCMGMCGKSCVSPVKA
(SEQ ID NO:28)

[000156] An exemplary AAT-Fc-Elafin fusion protein is AAT-hFc1-Elafin (human IgG1 Fc), described herein. As shown below, the AAT polypeptide portion of the fusion protein is underlined (SEQ ID NO: 2), the hinge region is shown in normal text (SEQ ID NO: 43), the ASTGS linker is shown in normal text (SEQ ID NO: 45), the Fc portion is italicized (SEQ ID NO: 3), and the WAP domain containing polypeptide is in bold font (SEQ ID NO: 12)

AAT-hFc1-Elafin (human IgG1 Fc)

EDPQGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVSIATAFAMLSLGTKADTHD
EILEGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFLSEGLKLVDKFLEDVKKLYHSEAFTVNFG
DTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFALVNYIFFKGKWERPFEVKDTEEEDFHVDQVTTVKVPMMK
RLGMFNIQHCKKLSSWVLLMKYLGNATAIFFLPDEGKLQHLENELTHDIITKFLENEDRRSASLHLPKLSITGT
YDLKSVLGQLGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDEKGTEAAGAMFLEAIPMSIPPEVKFNKPF
VFLMIEQNTKSPLFMGKVVNPTQK*EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVD*
VSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKA
KGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVD
*KSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*ASTGS**AVTGVPVKGQDTVKGRVPFNGQDPVKGQVSVKGQD**
KVKAQEPVKGPVSTKPGSCPIILIRCAMLNPPNRCLKDTDCPGIKKCCEGSCGMACFVPQ (SEQ ID
NO:29)

underlined and the albumin portion is italicized. For example, the polypeptide components can be directly attached.

[000160] An exemplary AAT-Albumin fusion protein is AAT-HSA, described herein. As shown below, the AAT polypeptide portion of the fusion protein is underlined (SEQ ID NO: 2), the ASTGS linker is shown in normal text (SEQ ID NO: 45), and the albumin polypeptide is italicized (SEQ ID NO: 14)

AAT-HSA

EDPQGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVSIATAFAMLSLGTKADTHD
EILEGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFLSEGLKLVDKFLEDVKKLYHSEAFTVNFG
DTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFALVNYIFFKGKWERPFEVKDTEEEDFHVDQVTTVKVPMMK
RLGMFNIQHCKKLSSWVLLMKYLGNATAIFFLPDEGKLQHLENELTHDIITKFLENEDRRSASLHLPKLSITGT
YDLKSVLGQLGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDEKGTEAAGAMFLEAIPMSIPPEVKFNKPF
VFLMIEQNTKSPLFMGKVVNPTQK*ASTGSDAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNE*
VTEFAKTCVADESAENCDKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPE
VDVMCTAFHDNEETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRDEGKASS
AKQRLKCASLQKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGDLLECADDRADLAKYICEN
QDSISSKLKECCEKPLLEKSHCIAEVENDEMPADLPSLAADFVESKDVCKNYAEAKDVFLGMFLYEYARRHPDY
SVVLLLRLAKTYETTLEKCCAAADPHECYAKVFDEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKV
PQVSTPTLVEVSRNLGKVGSKCCKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFS
ALEVDETYVPKEFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKADD
KETCFAEEGKKLVAASQAALGL (SEQ ID NO:30)

[000161] An exemplary AAT-Albumin fusion protein is AAT-HSA Domain 3, described herein. As shown below, the AAT polypeptide portion of the fusion protein is underlined (SEQ ID NO: 2), the ASTGS linker is shown in normal text (SEQ ID NO: 45), and the albumin polypeptide is italicized (SEQ ID NO: 15)

AAT-HSA Domain 3

EDPQGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVSIATAFAMLSLGTKADTHD
EILEGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFLSEGLKLVDKFLEDVKKLYHSEAFTVNFG
DTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFALVNYIFFKGKWERPFEVKDTEEEDFHVDQVTTVKVPMMK
RLGMFNIQHCKKLSSWVLLMKYLGNATAIFFLPDEGKLQHLENELTHDIITKFLENEDRRSASLHLPKLSITGT
YDLKSVLGQLGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDEKGTEAAGAMFLEAIPMSIPPEVKFNKPF
VFLMIEQNTKSPLFMGKVVNPTQK*ASTGSEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEV*
SRNLGKVGSKCCKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPK
EFNAETFTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKADDKETCFAEEGKK
LVA (SEQ ID NO:31)

SEQUENCE LISTING

<110> INHIBRX LLC
Eckelman, Brendan P.
Timmer, John C.
Nguy, Peter L.
Guenther, Grant B.
Deveraux, Quinn

<120> SERPIN FUSION POLYPEPTIDES AND METHODS OF USE THEREOF

<130> INHI-002/N01SG

<150> PCT/US2012/044730
<151> 2012-06-28

<150> US 61/502,055
<151> 2011-06-28

<150> US 61/570,394
<151> 2011-12-14

<150> US 61/577,204
<151> 2011-12-19

<150> US 61/638,168
<151> 2012-04-25

<160> 46

<170> PatentIn version 3.5

<210> 1
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> reactive site loop portion of the alpha-1 antitrypsin (AAT) protein

<400> 1

Gly Thr Glu Ala Ala Gly Ala Met Phe Leu Glu Ala Ile Pro Met Ser
1 5 10 15

Ile Pro Pro Glu Val Lys Phe Asn Lys
20 25

<210> 2
<211> 394
<212> PRT
<213> Homo sapiens

<400> 2

```
Glu Asp Pro Gln Gly Asp Ala Ala Gln Lys Thr Asp Thr Ser His His
1               5                  10                  15

Asp Gln Asp His Pro Thr Phe Asn Lys Ile Thr Pro Asn Leu Ala Glu
            20                  25                  30

Phe Ala Phe Ser Leu Tyr Arg Gln Leu Ala His Gln Ser Asn Ser Thr
        35                  40                  45

Asn Ile Phe Phe Ser Pro Val Ser Ile Ala Thr Ala Phe Ala Met Leu
    50                  55                  60

Ser Leu Gly Thr Lys Ala Asp Thr His Asp Glu Ile Leu Glu Gly Leu
65                  70                  75                  80

Asn Phe Asn Leu Thr Glu Ile Pro Glu Ala Gln Ile His Glu Gly Phe
                85                  90                  95

Gln Glu Leu Leu Arg Thr Leu Asn Gln Pro Asp Ser Gln Leu Gln Leu
            100                 105                 110

Thr Thr Gly Asn Gly Leu Phe Leu Ser Glu Gly Leu Lys Leu Val Asp
        115                 120                 125

Lys Phe Leu Glu Asp Val Lys Lys Leu Tyr His Ser Glu Ala Phe Thr
    130                 135                 140

Val Asn Phe Gly Asp Thr Glu Glu Ala Lys Lys Gln Ile Asn Asp Tyr
145                 150                 155                 160

Val Glu Lys Gly Thr Gln Gly Lys Ile Val Asp Leu Val Lys Glu Leu
                165                 170                 175

Asp Arg Asp Thr Val Phe Ala Leu Val Asn Tyr Ile Phe Phe Lys Gly
            180                 185                 190

Lys Trp Glu Arg Pro Phe Glu Val Lys Asp Thr Glu Glu Glu Asp Phe
        195                 200                 205

His Val Asp Gln Val Thr Thr Val Lys Val Pro Met Met Lys Arg Leu
    210                 215                 220
```

```
Gly Met Phe Asn Ile Gln His Cys Lys Lys Leu Ser Ser Trp Val Leu
225                 230                 235                 240

Leu Met Lys Tyr Leu Gly Asn Ala Thr Ala Ile Phe Phe Leu Pro Asp
                245                 250                 255

Glu Gly Lys Leu Gln His Leu Glu Asn Glu Leu Thr His Asp Ile Ile
            260                 265                 270

Thr Lys Phe Leu Glu Asn Glu Asp Arg Arg Ser Ala Ser Leu His Leu
        275                 280                 285

Pro Lys Leu Ser Ile Thr Gly Thr Tyr Asp Leu Lys Ser Val Leu Gly
    290                 295                 300

Gln Leu Gly Ile Thr Lys Val Phe Ser Asn Gly Ala Asp Leu Ser Gly
305                 310                 315                 320

Val Thr Glu Glu Ala Pro Leu Lys Leu Ser Lys Ala Val His Lys Ala
                325                 330                 335

Val Leu Thr Ile Asp Glu Lys Gly Thr Glu Ala Ala Gly Ala Met Phe
            340                 345                 350

Leu Glu Ala Ile Pro Met Ser Ile Pro Pro Glu Val Lys Phe Asn Lys
        355                 360                 365

Pro Phe Val Phe Leu Met Ile Glu Gln Asn Thr Lys Ser Pro Leu Phe
    370                 375                 380

Met Gly Lys Val Val Asn Pro Thr Gln Lys
385                 390
```

<210> 3
<211> 217
<212> PRT
<213> Homo sapiens

<400> 3

```
Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
1               5                   10                  15

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
            20                  25                  30
```

```
Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
        35                  40                  45

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
    50                  55                  60

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
65                  70                  75                  80

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
                85                  90                  95

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
            100                 105                 110

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu
        115                 120                 125

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
    130                 135                 140

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
145                 150                 155                 160

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
                165                 170                 175

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
            180                 185                 190

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
        195                 200                 205

Lys Ser Leu Ser Leu Ser Pro Gly Lys
    210                 215
```

<210> 4
<211> 216
<212> PRT
<213> Homo sapiens

<400> 4

```
Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
1               5                  10                  15

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
            20                  25                  30

Val Asp Val Ser His Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val
        35                  40                  45

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
    50                  55                  60

Phe Asn Ser Thr Phe Arg Val Val Ser Val Leu Thr Val Val His Gln
65                  70                  75                  80

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly
                85                  90                  95

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln Pro
            100                 105                 110

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr
        115                 120                 125

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
    130                 135                 140

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
145                 150                 155                 160

Lys Thr Thr Pro Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
                165                 170                 175

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
            180                 185                 190

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
        195                 200                 205

Ser Leu Ser Leu Ser Pro Gly Lys
    210                 215
```

<210> 5

<211> 217
<212> PRT
<213> Homo sapiens

<400> 5

```
Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
1               5                  10                  15

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
            20                  25                  30

Val Val Asp Val Ser His Glu Asp Pro Glu Val Gln Phe Lys Trp Tyr
        35                  40                  45

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
    50                  55                  60

Gln Tyr Asn Ser Thr Phe Arg Val Val Ser Val Leu Thr Val Leu His
65                  70                  75                  80

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
                85                  90                  95

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Thr Lys Gly Gln
            100                 105                 110

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met
        115                 120                 125

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
    130                 135                 140

Ser Asp Ile Ala Val Glu Trp Glu Ser Ser Gly Gln Pro Glu Asn Asn
145                 150                 155                 160

Tyr Asn Thr Thr Pro Pro Met Leu Asp Ser Asp Gly Ser Phe Phe Leu
                165                 170                 175

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Ile
            180                 185                 190

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn Arg Phe Thr Gln
        195                 200                 205
```

```
Lys Ser Leu Ser Leu Ser Pro Gly Lys
    210                 215


<210>  6
<211>  216
<212>  PRT
<213>  Homo sapiens

<400>  6

Ala Pro Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
1               5                   10                  15


Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
            20                  25                  30


Val Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr
        35                  40                  45


Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
    50                  55                  60


Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
65                  70                  75                  80


Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
                85                  90                  95


Gly Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
            100                 105                 110


Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met
        115                 120                 125


Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
    130                 135                 140


Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
145                 150                 155                 160


Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
                165                 170                 175


Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe
```

180 185 190

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
195 200 205

Ser Leu Ser Leu Ser Leu Gly Lys
210 215

<210> 7
<211> 218
<212> PRT
<213> Homo sapiens

<400> 7

Ile Ala Glu Leu Pro Pro Lys Val Ser Val Phe Val Pro Pro Arg Asp
1 5 10 15

Gly Phe Phe Gly Asn Pro Arg Lys Ser Lys Leu Ile Cys Gln Ala Thr
20 25 30

Gly Phe Ser Pro Arg Gln Ile Gln Val Ser Trp Leu Arg Glu Gly Lys
35 40 45

Gln Val Gly Ser Gly Val Thr Thr Asp Gln Val Gln Ala Glu Ala Lys
50 55 60

Glu Ser Gly Pro Thr Thr Tyr Lys Val Thr Ser Thr Leu Thr Ile Lys
65 70 75 80

Glu Ser Asp Trp Leu Gly Gln Ser Met Phe Thr Cys Arg Val Asp His
85 90 95

Arg Gly Leu Thr Phe Gln Gln Asn Ala Ser Ser Met Cys Val Pro Asp
100 105 110

Gln Asp Thr Ala Ile Arg Val Phe Ala Ile Pro Pro Ser Phe Ala Ser
115 120 125

Ile Phe Leu Thr Lys Ser Thr Lys Leu Thr Cys Leu Val Thr Asp Leu
130 135 140

Thr Thr Tyr Asp Ser Val Thr Ile Ser Trp Thr Arg Gln Asn Gly Glu
145 150 155 160

```
Ala Val Lys Thr His Thr Asn Ile Ser Glu Ser His Pro Asn Ala Thr
                165                 170                 175

Phe Ser Ala Val Gly Glu Ala Ser Ile Cys Glu Asp Asp Trp Asn Ser
            180                 185                 190

Gly Glu Arg Phe Thr Cys Thr Val Thr His Thr Asp Leu Pro Ser Pro
        195                 200                 205

Leu Lys Gln Thr Ile Ser Arg Pro Lys Gly
    210                 215
```

<210> 8
<211> 132
<212> PRT
<213> Homo sapiens

<400> 8

```
Met Lys Ser Ser Gly Leu Phe Pro Phe Leu Val Leu Leu Ala Leu Gly
1               5                   10                  15

Thr Leu Ala Pro Trp Ala Val Glu Gly Ser Gly Lys Ser Phe Lys Ala
            20                  25                  30

Gly Val Cys Pro Pro Lys Lys Ser Ala Gln Cys Leu Arg Tyr Lys Lys
        35                  40                  45

Pro Glu Cys Gln Ser Asp Trp Gln Cys Pro Gly Lys Lys Arg Cys Cys
    50                  55                  60

Pro Asp Thr Cys Gly Ile Lys Cys Leu Asp Pro Val Asp Thr Pro Asn
65                  70                  75                  80

Pro Thr Arg Arg Lys Pro Gly Lys Cys Pro Val Thr Tyr Gly Gln Cys
                85                  90                  95

Leu Met Leu Asn Pro Pro Asn Phe Cys Glu Met Asp Gly Gln Cys Lys
            100                 105                 110

Arg Asp Leu Lys Cys Cys Met Gly Met Cys Gly Lys Ser Cys Val Ser
        115                 120                 125

Pro Val Lys Ala
```

130

<210> 9
<211> 107
<212> PRT
<213> Homo sapiens

<400> 9

Ser Gly Lys Ser Phe Lys Ala Gly Val Cys Pro Pro Lys Lys Ser Ala
1 5 10 15

Gln Cys Leu Arg Tyr Lys Lys Pro Glu Cys Gln Ser Asp Trp Gln Cys
20 25 30

Pro Gly Lys Lys Arg Cys Cys Pro Asp Thr Cys Gly Ile Lys Cys Leu
35 40 45

Asp Pro Val Asp Thr Pro Asn Pro Thr Arg Arg Lys Pro Gly Lys Cys
50 55 60

Pro Val Thr Tyr Gly Gln Cys Leu Met Leu Asn Pro Pro Asn Phe Cys
65 70 75 80

Glu Met Asp Gly Gln Cys Lys Arg Asp Leu Lys Cys Cys Met Gly Met
85 90 95

Cys Gly Lys Ser Cys Val Ser Pro Val Lys Ala
100 105

<210> 10
<211> 51
<212> PRT
<213> Homo sapiens

<400> 10

Thr Arg Arg Lys Pro Gly Lys Cys Pro Val Thr Tyr Gly Gln Cys Leu
1 5 10 15

Met Leu Asn Pro Pro Asn Phe Cys Glu Met Asp Gly Gln Cys Lys Arg
20 25 30

Asp Leu Lys Cys Cys Met Gly Met Cys Gly Lys Ser Cys Val Ser Pro
35 40 45

Val Lys Ala
50

<210> 11
<211> 117
<212> PRT
<213> Homo sapiens

<400> 11

Met Arg Ala Ser Ser Phe Leu Ile Val Val Val Phe Leu Ile Ala Gly
1 5 10 15

Thr Leu Val Leu Glu Ala Ala Val Thr Gly Val Pro Val Lys Gly Gln
20 25 30

Asp Thr Val Lys Gly Arg Val Pro Phe Asn Gly Gln Asp Pro Val Lys
35 40 45

Gly Gln Val Ser Val Lys Gly Gln Asp Lys Val Lys Ala Gln Glu Pro
50 55 60

Val Lys Gly Pro Val Ser Thr Lys Pro Gly Ser Cys Pro Ile Ile Leu
65 70 75 80

Ile Arg Cys Ala Met Leu Asn Pro Pro Asn Arg Cys Leu Lys Asp Thr
85 90 95

Asp Cys Pro Gly Ile Lys Lys Cys Cys Glu Gly Ser Cys Gly Met Ala
100 105 110

Cys Phe Val Pro Gln
115

<210> 12
<211> 95
<212> PRT
<213> Homo sapiens

<400> 12

Ala Val Thr Gly Val Pro Val Lys Gly Gln Asp Thr Val Lys Gly Arg
1 5 10 15

Val Pro Phe Asn Gly Gln Asp Pro Val Lys Gly Gln Val Ser Val Lys
20 25 30

```
Gly Gln Asp Lys Val Lys Ala Gln Glu Pro Val Lys Gly Pro Val Ser
        35                  40                  45

Thr Lys Pro Gly Ser Cys Pro Ile Ile Leu Ile Arg Cys Ala Met Leu
    50                  55                  60

Asn Pro Pro Asn Arg Cys Leu Lys Asp Thr Asp Cys Pro Gly Ile Lys
65                  70                  75                  80

Lys Cys Cys Glu Gly Ser Cys Gly Met Ala Cys Phe Val Pro Gln
                85                  90                  95
```

<210> 13
<211> 49
<212> PRT
<213> Homo sapiens

<400> 13

```
Val Ser Thr Lys Pro Gly Ser Cys Pro Ile Ile Leu Ile Arg Cys Ala
1               5                   10                  15

Met Leu Asn Pro Pro Asn Arg Cys Leu Lys Asp Thr Asp Cys Pro Gly
            20                  25                  30

Ile Lys Lys Cys Cys Glu Gly Ser Cys Gly Met Ala Cys Phe Val Pro
        35                  40                  45

Gln
```

<210> 14
<211> 585
<212> PRT
<213> Homo sapiens

<400> 14

```
Asp Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu
1               5                   10                  15

Glu Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln
            20                  25                  30

Gln Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu
        35                  40                  45
```

```
Phe Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys
    50                  55                  60

Ser Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu
65                  70                  75                  80

Arg Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro
                85                  90                  95

Glu Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu
            100                 105                 110

Pro Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His
        115                 120                 125

Asp Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg
    130                 135                 140

Arg His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg
145                 150                 155                 160

Tyr Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala
                165                 170                 175

Cys Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser
            180                 185                 190

Ser Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu
        195                 200                 205

Arg Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro
    210                 215                 220

Lys Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys
225                 230                 235                 240

Val His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp
                245                 250                 255

Arg Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser
            260                 265                 270
```

```
Ser Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His
        275                 280                 285

Cys Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser
    290                 295                 300

Leu Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala
305                 310                 315                 320

Glu Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg
                325                 330                 335

Arg His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr
            340                 345                 350

Tyr Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu
        355                 360                 365

Cys Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro
    370                 375                 380

Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu
385                 390                 395                 400

Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro
                405                 410                 415

Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys
            420                 425                 430

Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys
        435                 440                 445

Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His
    450                 455                 460

Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser
465                 470                 475                 480

Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr
                485                 490                 495
```

```
Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp
            500                 505                 510

Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala
        515                 520                 525

Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu
    530                 535                 540

Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys
545                 550                 555                 560

Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val
                565                 570                 575

Ala Ala Ser Gln Ala Ala Leu Gly Leu
            580                 585
```

<210> 15
<211> 196
<212> PRT
<213> Homo sapiens

<400> 15

```
Glu Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln
1               5                   10                  15

Leu Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys
            20                  25                  30

Lys Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn
        35                  40                  45

Leu Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg
    50                  55                  60

Met Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys
65                  70                  75                  80

Val Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys
                85                  90                  95

Thr Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val
            100                 105                 110
```

```
Asp Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe
        115                 120                 125

His Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys
    130                 135                 140

Gln Thr Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys
145                 150                 155                 160

Glu Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys
                165                 170                 175

Cys Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys
            180                 185                 190

Lys Leu Val Ala
        195
```

<210> 16
<211> 626
<212> PRT
<213> Artificial Sequence

<220>
<223> AAT-hFc1 fusion protein

<400> 16

```
Glu Asp Pro Gln Gly Asp Ala Ala Gln Lys Thr Asp Thr Ser His His
1               5                   10                  15

Asp Gln Asp His Pro Thr Phe Asn Lys Ile Thr Pro Asn Leu Ala Glu
            20                  25                  30

Phe Ala Phe Ser Leu Tyr Arg Gln Leu Ala His Gln Ser Asn Ser Thr
        35                  40                  45

Asn Ile Phe Phe Ser Pro Val Ser Ile Ala Thr Ala Phe Ala Met Leu
    50                  55                  60

Ser Leu Gly Thr Lys Ala Asp Thr His Asp Glu Ile Leu Glu Gly Leu
65                  70                  75                  80

Asn Phe Asn Leu Thr Glu Ile Pro Glu Ala Gln Ile His Glu Gly Phe
```

```
                85                  90                  95

Gln Glu Leu Leu Arg Thr Leu Asn Gln Pro Asp Ser Gln Leu Gln Leu
            100                 105                 110

Thr Thr Gly Asn Gly Leu Phe Leu Ser Glu Gly Leu Lys Leu Val Asp
        115                 120                 125

Lys Phe Leu Glu Asp Val Lys Lys Leu Tyr His Ser Glu Ala Phe Thr
    130                 135                 140

Val Asn Phe Gly Asp Thr Glu Glu Ala Lys Lys Gln Ile Asn Asp Tyr
145                 150                 155                 160

Val Glu Lys Gly Thr Gln Gly Lys Ile Val Asp Leu Val Lys Glu Leu
                165                 170                 175

Asp Arg Asp Thr Val Phe Ala Leu Val Asn Tyr Ile Phe Phe Lys Gly
            180                 185                 190

Lys Trp Glu Arg Pro Phe Glu Val Lys Asp Thr Glu Glu Glu Asp Phe
        195                 200                 205

His Val Asp Gln Val Thr Thr Val Lys Val Pro Met Met Lys Arg Leu
    210                 215                 220

Gly Met Phe Asn Ile Gln His Cys Lys Lys Leu Ser Ser Trp Val Leu
225                 230                 235                 240

Leu Met Lys Tyr Leu Gly Asn Ala Thr Ala Ile Phe Phe Leu Pro Asp
                245                 250                 255

Glu Gly Lys Leu Gln His Leu Glu Asn Glu Leu Thr His Asp Ile Ile
            260                 265                 270

Thr Lys Phe Leu Glu Asn Glu Asp Arg Arg Ser Ala Ser Leu His Leu
        275                 280                 285

Pro Lys Leu Ser Ile Thr Gly Thr Tyr Asp Leu Lys Ser Val Leu Gly
    290                 295                 300

Gln Leu Gly Ile Thr Lys Val Phe Ser Asn Gly Ala Asp Leu Ser Gly
305                 310                 315                 320
```

```
Val Thr Glu Glu Ala Pro Leu Lys Leu Ser Lys Ala Val His Lys Ala
                325                 330                 335

Val Leu Thr Ile Asp Glu Lys Gly Thr Glu Ala Ala Gly Ala Met Phe
            340                 345                 350

Leu Glu Ala Ile Pro Met Ser Ile Pro Pro Glu Val Lys Phe Asn Lys
        355                 360                 365

Pro Phe Val Phe Leu Met Ile Glu Gln Asn Thr Lys Ser Pro Leu Phe
    370                 375                 380

Met Gly Lys Val Val Asn Pro Thr Gln Lys Glu Pro Lys Ser Cys Asp
385                 390                 395                 400

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
                405                 410                 415

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
            420                 425                 430

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
        435                 440                 445

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
    450                 455                 460

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
465                 470                 475                 480

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
                485                 490                 495

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
            500                 505                 510

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
        515                 520                 525

Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu
    530                 535                 540
```

```
Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
545                 550                 555                 560

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
                565                 570                 575

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
            580                 585                 590

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
        595                 600                 605

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
    610                 615                 620

Gly Lys
625
```

<210> 17
<211> 622
<212> PRT
<213> Artificial Sequence

<220>
<223> AAT-hFc2 fusion protein

<400> 17

```
Glu Asp Pro Gln Gly Asp Ala Ala Gln Lys Thr Asp Thr Ser His His
1               5                   10                  15

Asp Gln Asp His Pro Thr Phe Asn Lys Ile Thr Pro Asn Leu Ala Glu
            20                  25                  30

Phe Ala Phe Ser Leu Tyr Arg Gln Leu Ala His Gln Ser Asn Ser Thr
        35                  40                  45

Asn Ile Phe Phe Ser Pro Val Ser Ile Ala Thr Ala Phe Ala Met Leu
    50                  55                  60

Ser Leu Gly Thr Lys Ala Asp Thr His Asp Glu Ile Leu Glu Gly Leu
65                  70                  75                  80

Asn Phe Asn Leu Thr Glu Ile Pro Glu Ala Gln Ile His Glu Gly Phe
                85                  90                  95
```

```
Gln Glu Leu Leu Arg Thr Leu Asn Gln Pro Asp Ser Gln Leu Gln Leu
            100                 105                 110

Thr Thr Gly Asn Gly Leu Phe Leu Ser Glu Gly Leu Lys Leu Val Asp
        115                 120                 125

Lys Phe Leu Glu Asp Val Lys Lys Leu Tyr His Ser Glu Ala Phe Thr
    130                 135                 140

Val Asn Phe Gly Asp Thr Glu Glu Ala Lys Lys Gln Ile Asn Asp Tyr
145                 150                 155                 160

Val Glu Lys Gly Thr Gln Gly Lys Ile Val Asp Leu Val Lys Glu Leu
                165                 170                 175

Asp Arg Asp Thr Val Phe Ala Leu Val Asn Tyr Ile Phe Phe Lys Gly
            180                 185                 190

Lys Trp Glu Arg Pro Phe Glu Val Lys Asp Thr Glu Glu Glu Asp Phe
        195                 200                 205

His Val Asp Gln Val Thr Thr Val Lys Val Pro Met Met Lys Arg Leu
    210                 215                 220

Gly Met Phe Asn Ile Gln His Cys Lys Lys Leu Ser Ser Trp Val Leu
225                 230                 235                 240

Leu Met Lys Tyr Leu Gly Asn Ala Thr Ala Ile Phe Phe Leu Pro Asp
                245                 250                 255

Glu Gly Lys Leu Gln His Leu Glu Asn Glu Leu Thr His Asp Ile Ile
            260                 265                 270

Thr Lys Phe Leu Glu Asn Glu Asp Arg Arg Ser Ala Ser Leu His Leu
        275                 280                 285

Pro Lys Leu Ser Ile Thr Gly Thr Tyr Asp Leu Lys Ser Val Leu Gly
    290                 295                 300

Gln Leu Gly Ile Thr Lys Val Phe Ser Asn Gly Ala Asp Leu Ser Gly
305                 310                 315                 320
```

```
Val Thr Glu Glu Ala Pro Leu Lys Leu Ser Lys Ala Val His Lys Ala
                325                 330                 335

Val Leu Thr Ile Asp Glu Lys Gly Thr Glu Ala Ala Gly Ala Met Phe
            340                 345                 350

Leu Glu Ala Ile Pro Met Ser Ile Pro Pro Glu Val Lys Phe Asn Lys
        355                 360                 365

Pro Phe Val Phe Leu Met Ile Glu Gln Asn Thr Lys Ser Pro Leu Phe
    370                 375                 380

Met Gly Lys Val Val Asn Pro Thr Gln Lys Glu Arg Lys Cys Cys Val
385                 390                 395                 400

Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe
                405                 410                 415

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
            420                 425                 430

Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val
        435                 440                 445

Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
    450                 455                 460

Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Val Val Ser Val
465                 470                 475                 480

Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
                485                 490                 495

Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
            500                 505                 510

Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
        515                 520                 525

Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val
    530                 535                 540
```

```
Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
545                 550                 555                 560

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu Asp Ser Asp
                565                 570                 575

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
            580                 585                 590

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
        595                 600                 605

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
    610                 615                 620
```

<210> 18
<211> 626
<212> PRT
<213> Artificial Sequence

<220>
<223> AAT-MM-EL-hFc1 fusion protein

<400> 18

```
Glu Asp Pro Gln Gly Asp Ala Ala Gln Lys Thr Asp Thr Ser His His
1               5                   10                  15

Asp Gln Asp His Pro Thr Phe Asn Lys Ile Thr Pro Asn Leu Ala Glu
            20                  25                  30

Phe Ala Phe Ser Leu Tyr Arg Gln Leu Ala His Gln Ser Asn Ser Thr
        35                  40                  45

Asn Ile Phe Phe Ser Pro Val Ser Ile Ala Thr Ala Phe Ala Met Leu
    50                  55                  60

Ser Leu Gly Thr Lys Ala Asp Thr His Asp Glu Ile Leu Glu Gly Leu
65                  70                  75                  80

Asn Phe Asn Leu Thr Glu Ile Pro Glu Ala Gln Ile His Glu Gly Phe
                85                  90                  95

Gln Glu Leu Leu Arg Thr Leu Asn Gln Pro Asp Ser Gln Leu Gln Leu
            100                 105                 110
```

```
Thr Thr Gly Asn Gly Leu Phe Leu Ser Glu Gly Leu Lys Leu Val Asp
        115                 120                 125

Lys Phe Leu Glu Asp Val Lys Lys Leu Tyr His Ser Glu Ala Phe Thr
    130                 135                 140

Val Asn Phe Gly Asp Thr Glu Glu Ala Lys Lys Gln Ile Asn Asp Tyr
145                 150                 155                 160

Val Glu Lys Gly Thr Gln Gly Lys Ile Val Asp Leu Val Lys Glu Leu
                165                 170                 175

Asp Arg Asp Thr Val Phe Ala Leu Val Asn Tyr Ile Phe Phe Lys Gly
            180                 185                 190

Lys Trp Glu Arg Pro Phe Glu Val Lys Asp Thr Glu Glu Glu Asp Phe
        195                 200                 205

His Val Asp Gln Val Thr Thr Val Lys Val Pro Met Met Lys Arg Leu
    210                 215                 220

Gly Met Phe Asn Ile Gln His Cys Lys Lys Leu Ser Ser Trp Val Leu
225                 230                 235                 240

Leu Met Lys Tyr Leu Gly Asn Ala Thr Ala Ile Phe Phe Leu Pro Asp
                245                 250                 255

Glu Gly Lys Leu Gln His Leu Glu Asn Glu Leu Thr His Asp Ile Ile
            260                 265                 270

Thr Lys Phe Leu Glu Asn Glu Asp Arg Arg Ser Ala Ser Leu His Leu
        275                 280                 285

Pro Lys Leu Ser Ile Thr Gly Thr Tyr Asp Leu Lys Ser Val Leu Gly
    290                 295                 300

Gln Leu Gly Ile Thr Lys Val Phe Ser Asn Gly Ala Asp Leu Ser Gly
305                 310                 315                 320

Val Thr Glu Glu Ala Pro Leu Lys Leu Ser Lys Ala Val His Lys Ala
                325                 330                 335
```

```
Val Leu Thr Ile Asp Glu Lys Gly Thr Glu Ala Ala Gly Ala Glu Phe
            340                 345                 350

Leu Glu Ala Ile Pro Leu Ser Ile Pro Pro Glu Val Lys Phe Asn Lys
        355                 360                 365

Pro Phe Val Phe Leu Met Ile Glu Gln Asn Thr Lys Ser Pro Leu Phe
    370                 375                 380

Met Gly Lys Val Val Asn Pro Thr Gln Lys Glu Pro Lys Ser Cys Asp
385                 390                 395                 400

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
                405                 410                 415

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
            420                 425                 430

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
        435                 440                 445

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
    450                 455                 460

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
465                 470                 475                 480

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
                485                 490                 495

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
            500                 505                 510

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
        515                 520                 525

Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu
    530                 535                 540

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
545                 550                 555                 560

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
```

565 570 575

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
580 585 590

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
595 600 605

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
610 615 620

Gly Lys
625

<210> 19
<211> 622
<212> PRT
<213> Artificial Sequence

<220>
<223> AAT-MM-EL-hFc2 fusion protein

<400> 19

Glu Asp Pro Gln Gly Asp Ala Ala Gln Lys Thr Asp Thr Ser His His
1 5 10 15

Asp Gln Asp His Pro Thr Phe Asn Lys Ile Thr Pro Asn Leu Ala Glu
20 25 30

Phe Ala Phe Ser Leu Tyr Arg Gln Leu Ala His Gln Ser Asn Ser Thr
35 40 45

Asn Ile Phe Phe Ser Pro Val Ser Ile Ala Thr Ala Phe Ala Met Leu
50 55 60

Ser Leu Gly Thr Lys Ala Asp Thr His Asp Glu Ile Leu Glu Gly Leu
65 70 75 80

Asn Phe Asn Leu Thr Glu Ile Pro Glu Ala Gln Ile His Glu Gly Phe
85 90 95

Gln Glu Leu Leu Arg Thr Leu Asn Gln Pro Asp Ser Gln Leu Gln Leu
100 105 110

```
Thr Thr Gly Asn Gly Leu Phe Leu Ser Glu Gly Leu Lys Leu Val Asp
        115                 120                 125

Lys Phe Leu Glu Asp Val Lys Lys Leu Tyr His Ser Glu Ala Phe Thr
    130                 135                 140

Val Asn Phe Gly Asp Thr Glu Glu Ala Lys Lys Gln Ile Asn Asp Tyr
145                 150                 155                 160

Val Glu Lys Gly Thr Gln Gly Lys Ile Val Asp Leu Val Lys Glu Leu
                165                 170                 175

Asp Arg Asp Thr Val Phe Ala Leu Val Asn Tyr Ile Phe Phe Lys Gly
            180                 185                 190

Lys Trp Glu Arg Pro Phe Glu Val Lys Asp Thr Glu Glu Glu Asp Phe
        195                 200                 205

His Val Asp Gln Val Thr Thr Val Lys Val Pro Met Met Lys Arg Leu
    210                 215                 220

Gly Met Phe Asn Ile Gln His Cys Lys Lys Leu Ser Ser Trp Val Leu
225                 230                 235                 240

Leu Met Lys Tyr Leu Gly Asn Ala Thr Ala Ile Phe Phe Leu Pro Asp
                245                 250                 255

Glu Gly Lys Leu Gln His Leu Glu Asn Glu Leu Thr His Asp Ile Ile
            260                 265                 270

Thr Lys Phe Leu Glu Asn Glu Asp Arg Arg Ser Ala Ser Leu His Leu
        275                 280                 285

Pro Lys Leu Ser Ile Thr Gly Thr Tyr Asp Leu Lys Ser Val Leu Gly
    290                 295                 300

Gln Leu Gly Ile Thr Lys Val Phe Ser Asn Gly Ala Asp Leu Ser Gly
305                 310                 315                 320

Val Thr Glu Glu Ala Pro Leu Lys Leu Ser Lys Ala Val His Lys Ala
                325                 330                 335

Val Leu Thr Ile Asp Glu Lys Gly Thr Glu Ala Ala Gly Ala Glu Phe
```

```
            340                 345                 350

Leu Glu Ala Ile Pro Leu Ser Ile Pro Pro Glu Val Lys Phe Asn Lys
        355                 360                 365

Pro Phe Val Phe Leu Met Ile Glu Gln Asn Thr Lys Ser Pro Leu Phe
    370                 375                 380

Met Gly Lys Val Val Asn Pro Thr Gln Lys Glu Arg Lys Cys Cys Val
385                 390                 395                 400

Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe
                405                 410                 415

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
            420                 425                 430

Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val
        435                 440                 445

Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
    450                 455                 460

Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Val Val Ser Val
465                 470                 475                 480

Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
                485                 490                 495

Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
            500                 505                 510

Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
        515                 520                 525

Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val
    530                 535                 540

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
545                 550                 555                 560

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu Asp Ser Asp
                565                 570                 575
```

```
Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
            580                 585                 590

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
        595                 600                 605

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
    610                 615                 620
```

<210> 20
<211> 622
<212> PRT
<213> Artificial Sequence

<220>
<223> AAT-MM:LL-hFc2 fusion protein

<400> 20

```
Glu Asp Pro Gln Gly Asp Ala Ala Gln Lys Thr Asp Thr Ser His His
1               5                   10                  15

Asp Gln Asp His Pro Thr Phe Asn Lys Ile Thr Pro Asn Leu Ala Glu
            20                  25                  30

Phe Ala Phe Ser Leu Tyr Arg Gln Leu Ala His Gln Ser Asn Ser Thr
        35                  40                  45

Asn Ile Phe Phe Ser Pro Val Ser Ile Ala Thr Ala Phe Ala Met Leu
    50                  55                  60

Ser Leu Gly Thr Lys Ala Asp Thr His Asp Glu Ile Leu Glu Gly Leu
65                  70                  75                  80

Asn Phe Asn Leu Thr Glu Ile Pro Glu Ala Gln Ile His Glu Gly Phe
                85                  90                  95

Gln Glu Leu Leu Arg Thr Leu Asn Gln Pro Asp Ser Gln Leu Gln Leu
            100                 105                 110

Thr Thr Gly Asn Gly Leu Phe Leu Ser Glu Gly Leu Lys Leu Val Asp
        115                 120                 125

Lys Phe Leu Glu Asp Val Lys Lys Leu Tyr His Ser Glu Ala Phe Thr
```

```
    130                 135                 140

Val Asn Phe Gly Asp Thr Glu Glu Ala Lys Lys Gln Ile Asn Asp Tyr
145                 150                 155                 160

Val Glu Lys Gly Thr Gln Gly Lys Ile Val Asp Leu Val Lys Glu Leu
                165                 170                 175

Asp Arg Asp Thr Val Phe Ala Leu Val Asn Tyr Ile Phe Phe Lys Gly
            180                 185                 190

Lys Trp Glu Arg Pro Phe Glu Val Lys Asp Thr Glu Glu Glu Asp Phe
        195                 200                 205

His Val Asp Gln Val Thr Thr Val Lys Val Pro Met Met Lys Arg Leu
    210                 215                 220

Gly Met Phe Asn Ile Gln His Cys Lys Lys Leu Ser Ser Trp Val Leu
225                 230                 235                 240

Leu Met Lys Tyr Leu Gly Asn Ala Thr Ala Ile Phe Phe Leu Pro Asp
                245                 250                 255

Glu Gly Lys Leu Gln His Leu Glu Asn Glu Leu Thr His Asp Ile Ile
            260                 265                 270

Thr Lys Phe Leu Glu Asn Glu Asp Arg Arg Ser Ala Ser Leu His Leu
        275                 280                 285

Pro Lys Leu Ser Ile Thr Gly Thr Tyr Asp Leu Lys Ser Val Leu Gly
    290                 295                 300

Gln Leu Gly Ile Thr Lys Val Phe Ser Asn Gly Ala Asp Leu Ser Gly
305                 310                 315                 320

Val Thr Glu Glu Ala Pro Leu Lys Leu Ser Lys Ala Val His Lys Ala
                325                 330                 335

Val Leu Thr Ile Asp Glu Lys Gly Thr Glu Ala Ala Gly Ala Leu Phe
            340                 345                 350

Leu Glu Ala Ile Pro Leu Ser Ile Pro Pro Glu Val Lys Phe Asn Lys
        355                 360                 365
```

```
Pro Phe Val Phe Leu Met Ile Glu Gln Asn Thr Lys Ser Pro Leu Phe
    370                 375                 380

Met Gly Lys Val Val Asn Pro Thr Gln Lys Glu Arg Lys Cys Cys Val
385                 390                 395                 400

Glu Cys Pro Pro Cys Pro Ala Pro Pro Val Ala Gly Pro Ser Val Phe
                405                 410                 415

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
            420                 425                 430

Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val
        435                 440                 445

Gln Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
    450                 455                 460

Lys Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Val Val Ser Val
465                 470                 475                 480

Leu Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
                485                 490                 495

Lys Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
            500                 505                 510

Lys Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
        515                 520                 525

Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val
    530                 535                 540

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
545                 550                 555                 560

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu Asp Ser Asp
                565                 570                 575

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
            580                 585                 590
```

```
Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
        595                 600                 605

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
    610                 615                 620
```

<210> 21
<211> 1025
<212> PRT
<213> Artificial Sequence

<220>
<223> AAT-hFc1-AAT fusion protein

<400> 21

```
Glu Asp Pro Gln Gly Asp Ala Ala Gln Lys Thr Asp Thr Ser His His
1               5                   10                  15

Asp Gln Asp His Pro Thr Phe Asn Lys Ile Thr Pro Asn Leu Ala Glu
            20                  25                  30

Phe Ala Phe Ser Leu Tyr Arg Gln Leu Ala His Gln Ser Asn Ser Thr
        35                  40                  45

Asn Ile Phe Phe Ser Pro Val Ser Ile Ala Thr Ala Phe Ala Met Leu
    50                  55                  60

Ser Leu Gly Thr Lys Ala Asp Thr His Asp Glu Ile Leu Glu Gly Leu
65                  70                  75                  80

Asn Phe Asn Leu Thr Glu Ile Pro Glu Ala Gln Ile His Glu Gly Phe
                85                  90                  95

Gln Glu Leu Leu Arg Thr Leu Asn Gln Pro Asp Ser Gln Leu Gln Leu
            100                 105                 110

Thr Thr Gly Asn Gly Leu Phe Leu Ser Glu Gly Leu Lys Leu Val Asp
        115                 120                 125

Lys Phe Leu Glu Asp Val Lys Lys Leu Tyr His Ser Glu Ala Phe Thr
    130                 135                 140

Val Asn Phe Gly Asp Thr Glu Glu Ala Lys Lys Gln Ile Asn Asp Tyr
145                 150                 155                 160
```

```
Val Glu Lys Gly Thr Gln Gly Lys Ile Val Asp Leu Val Lys Glu Leu
                165                 170                 175

Asp Arg Asp Thr Val Phe Ala Leu Val Asn Tyr Ile Phe Phe Lys Gly
            180                 185                 190

Lys Trp Glu Arg Pro Phe Glu Val Lys Asp Thr Glu Glu Glu Asp Phe
        195                 200                 205

His Val Asp Gln Val Thr Thr Val Lys Val Pro Met Met Lys Arg Leu
    210                 215                 220

Gly Met Phe Asn Ile Gln His Cys Lys Lys Leu Ser Ser Trp Val Leu
225                 230                 235                 240

Leu Met Lys Tyr Leu Gly Asn Ala Thr Ala Ile Phe Phe Leu Pro Asp
                245                 250                 255

Glu Gly Lys Leu Gln His Leu Glu Asn Glu Leu Thr His Asp Ile Ile
            260                 265                 270

Thr Lys Phe Leu Glu Asn Glu Asp Arg Arg Ser Ala Ser Leu His Leu
        275                 280                 285

Pro Lys Leu Ser Ile Thr Gly Thr Tyr Asp Leu Lys Ser Val Leu Gly
    290                 295                 300

Gln Leu Gly Ile Thr Lys Val Phe Ser Asn Gly Ala Asp Leu Ser Gly
305                 310                 315                 320

Val Thr Glu Glu Ala Pro Leu Lys Leu Ser Lys Ala Val His Lys Ala
                325                 330                 335

Val Leu Thr Ile Asp Glu Lys Gly Thr Glu Ala Ala Gly Ala Met Phe
            340                 345                 350

Leu Glu Ala Ile Pro Met Ser Ile Pro Pro Glu Val Lys Phe Asn Lys
        355                 360                 365

Pro Phe Val Phe Leu Met Ile Glu Gln Asn Thr Lys Ser Pro Leu Phe
    370                 375                 380
```

```
Met Gly Lys Val Val Asn Pro Thr Gln Lys Glu Pro Lys Ser Cys Asp
385                 390                 395                 400

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
                405                 410                 415

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
            420                 425                 430

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
        435                 440                 445

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
    450                 455                 460

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
465                 470                 475                 480

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
                485                 490                 495

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
            500                 505                 510

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
        515                 520                 525

Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu
    530                 535                 540

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
545                 550                 555                 560

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
                565                 570                 575

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
            580                 585                 590

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
        595                 600                 605
```

```
Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
    610                 615                 620

Gly Lys Ala Ser Thr Gly Ser Glu Asp Pro Gln Gly Asp Ala Ala Gln
625                 630                 635                 640

Lys Thr Asp Thr Ser His His Asp Gln Asp His Pro Thr Phe Asn Lys
                645                 650                 655

Ile Thr Pro Asn Leu Ala Glu Phe Ala Phe Ser Leu Tyr Arg Gln Leu
            660                 665                 670

Ala His Gln Ser Asn Ser Thr Asn Ile Phe Phe Ser Pro Val Ser Ile
        675                 680                 685

Ala Thr Ala Phe Ala Met Leu Ser Leu Gly Thr Lys Ala Asp Thr His
    690                 695                 700

Asp Glu Ile Leu Glu Gly Leu Asn Phe Asn Leu Thr Glu Ile Pro Glu
705                 710                 715                 720

Ala Gln Ile His Glu Gly Phe Gln Glu Leu Leu Arg Thr Leu Asn Gln
                725                 730                 735

Pro Asp Ser Gln Leu Gln Leu Thr Thr Gly Asn Gly Leu Phe Leu Ser
            740                 745                 750

Glu Gly Leu Lys Leu Val Asp Lys Phe Leu Glu Asp Val Lys Lys Leu
        755                 760                 765

Tyr His Ser Glu Ala Phe Thr Val Asn Phe Gly Asp Thr Glu Glu Ala
    770                 775                 780

Lys Lys Gln Ile Asn Asp Tyr Val Glu Lys Gly Thr Gln Gly Lys Ile
785                 790                 795                 800

Val Asp Leu Val Lys Glu Leu Asp Arg Asp Thr Val Phe Ala Leu Val
                805                 810                 815

Asn Tyr Ile Phe Phe Lys Gly Lys Trp Glu Arg Pro Phe Glu Val Lys
            820                 825                 830

Asp Thr Glu Glu Glu Asp Phe His Val Asp Gln Val Thr Thr Val Lys
```

835 840 845

Val Pro Met Met Lys Arg Leu Gly Met Phe Asn Ile Gln His Cys Lys
850 855 860

Lys Leu Ser Ser Trp Val Leu Leu Met Lys Tyr Leu Gly Asn Ala Thr
865 870 875 880

Ala Ile Phe Phe Leu Pro Asp Glu Gly Lys Leu Gln His Leu Glu Asn
885 890 895

Glu Leu Thr His Asp Ile Ile Thr Lys Phe Leu Glu Asn Glu Asp Arg
900 905 910

Arg Ser Ala Ser Leu His Leu Pro Lys Leu Ser Ile Thr Gly Thr Tyr
915 920 925

Asp Leu Lys Ser Val Leu Gly Gln Leu Gly Ile Thr Lys Val Phe Ser
930 935 940

Asn Gly Ala Asp Leu Ser Gly Val Thr Glu Glu Ala Pro Leu Lys Leu
945 950 955 960

Ser Lys Ala Val His Lys Ala Val Leu Thr Ile Asp Glu Lys Gly Thr
965 970 975

Glu Ala Ala Gly Ala Met Phe Leu Glu Ala Ile Pro Met Ser Ile Pro
980 985 990

Pro Glu Val Lys Phe Asn Lys Pro Phe Val Phe Leu Met Ile Glu Gln
995 1000 1005

Asn Thr Lys Ser Pro Leu Phe Met Gly Lys Val Val Asn Pro Thr
1010 1015 1020

Gln Lys
1025

<210> 22
<211> 616
<212> PRT
<213> Artificial Sequence

<220>

<223> D2E7-Light Chain-AAT fusion protein

<400> 22

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                  10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Tyr
            20                  25                  30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Ala 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 Val Ala Thr Tyr Tyr Cys Gln Arg Tyr Asn Arg Ala Pro Tyr
                85                  90                  95

Thr Phe Gly Gln 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 Ser Gly Gly Gly Ser Glu Asp
```

```
    210                 215                 220

Pro Gln Gly Asp Ala Ala Gln Lys Thr Asp Thr Ser His His Asp Gln
225                 230                 235                 240

Asp His Pro Thr Phe Asn Lys Ile Thr Pro Asn Leu Ala Glu Phe Ala
                245                 250                 255

Phe Ser Leu Tyr Arg Gln Leu Ala His Gln Ser Asn Ser Thr Asn Ile
            260                 265                 270

Phe Phe Ser Pro Val Ser Ile Ala Thr Ala Phe Ala Met Leu Ser Leu
        275                 280                 285

Gly Thr Lys Ala Asp Thr His Asp Glu Ile Leu Glu Gly Leu Asn Phe
    290                 295                 300

Asn Leu Thr Glu Ile Pro Glu Ala Gln Ile His Glu Gly Phe Gln Glu
305                 310                 315                 320

Leu Leu Arg Thr Leu Asn Gln Pro Asp Ser Gln Leu Gln Leu Thr Thr
                325                 330                 335

Gly Asn Gly Leu Phe Leu Ser Glu Gly Leu Lys Leu Val Asp Lys Phe
            340                 345                 350

Leu Glu Asp Val Lys Lys Leu Tyr His Ser Glu Ala Phe Thr Val Asn
        355                 360                 365

Phe Gly Asp Thr Glu Glu Ala Lys Lys Gln Ile Asn Asp Tyr Val Glu
    370                 375                 380

Lys Gly Thr Gln Gly Lys Ile Val Asp Leu Val Lys Glu Leu Asp Arg
385                 390                 395                 400

Asp Thr Val Phe Ala Leu Val Asn Tyr Ile Phe Phe Lys Gly Lys Trp
                405                 410                 415

Glu Arg Pro Phe Glu Val Lys Asp Thr Glu Glu Glu Asp Phe His Val
            420                 425                 430

Asp Gln Val Thr Thr Val Lys Val Pro Met Met Lys Arg Leu Gly Met
        435                 440                 445
```

```
Phe Asn Ile Gln His Cys Lys Lys Leu Ser Ser Trp Val Leu Leu Met
    450                 455                 460

Lys Tyr Leu Gly Asn Ala Thr Ala Ile Phe Phe Leu Pro Asp Glu Gly
465                 470                 475                 480

Lys Leu Gln His Leu Glu Asn Glu Leu Thr His Asp Ile Ile Thr Lys
                485                 490                 495

Phe Leu Glu Asn Glu Asp Arg Arg Ser Ala Ser Leu His Leu Pro Lys
            500                 505                 510

Leu Ser Ile Thr Gly Thr Tyr Asp Leu Lys Ser Val Leu Gly Gln Leu
        515                 520                 525

Gly Ile Thr Lys Val Phe Ser Asn Gly Ala Asp Leu Ser Gly Val Thr
    530                 535                 540

Glu Glu Ala Pro Leu Lys Leu Ser Lys Ala Val His Lys Ala Val Leu
545                 550                 555                 560

Thr Ile Asp Glu Lys Gly Thr Glu Ala Ala Gly Ala Met Phe Leu Glu
                565                 570                 575

Ala Ile Pro Met Ser Ile Pro Pro Glu Val Lys Phe Asn Lys Pro Phe
            580                 585                 590

Val Phe Leu Met Ile Glu Gln Asn Thr Lys Ser Pro Leu Phe Met Gly
        595                 600                 605

Lys Val Val Asn Pro Thr Gln Lys
    610                 615
```

<210> 23
<211> 613
<212> PRT
<213> Artificial Sequence

<220>
<223> D2E7-Light Chain-AAT ASTGS Linker fusion protein

<400> 23

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
```

```
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Tyr
            20                  25                  30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Ala 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 Val Ala Thr Tyr Tyr Cys Gln Arg Tyr Asn Arg Ala Pro Tyr
                85                  90                  95

Thr Phe Gly Gln 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 Ser Thr Gly Ser Glu Asp Pro Gln Gly
    210                 215                 220

Asp Ala Ala Gln Lys Thr Asp Thr Ser His His Asp Gln Asp His Pro
225                 230                 235                 240
```

```
Thr Phe Asn Lys Ile Thr Pro Asn Leu Ala Glu Phe Ala Phe Ser Leu
                245                 250                 255

Tyr Arg Gln Leu Ala His Gln Ser Asn Ser Thr Asn Ile Phe Phe Ser
            260                 265                 270

Pro Val Ser Ile Ala Thr Ala Phe Ala Met Leu Ser Leu Gly Thr Lys
        275                 280                 285

Ala Asp Thr His Asp Glu Ile Leu Glu Gly Leu Asn Phe Asn Leu Thr
    290                 295                 300

Glu Ile Pro Glu Ala Gln Ile His Glu Gly Phe Gln Glu Leu Leu Arg
305                 310                 315                 320

Thr Leu Asn Gln Pro Asp Ser Gln Leu Gln Leu Thr Thr Gly Asn Gly
                325                 330                 335

Leu Phe Leu Ser Glu Gly Leu Lys Leu Val Asp Lys Phe Leu Glu Asp
            340                 345                 350

Val Lys Lys Leu Tyr His Ser Glu Ala Phe Thr Val Asn Phe Gly Asp
        355                 360                 365

Thr Glu Glu Ala Lys Lys Gln Ile Asn Asp Tyr Val Glu Lys Gly Thr
    370                 375                 380

Gln Gly Lys Ile Val Asp Leu Val Lys Glu Leu Asp Arg Asp Thr Val
385                 390                 395                 400

Phe Ala Leu Val Asn Tyr Ile Phe Phe Lys Gly Lys Trp Glu Arg Pro
                405                 410                 415

Phe Glu Val Lys Asp Thr Glu Glu Glu Asp Phe His Val Asp Gln Val
            420                 425                 430

Thr Thr Val Lys Val Pro Met Met Lys Arg Leu Gly Met Phe Asn Ile
        435                 440                 445

Gln His Cys Lys Lys Leu Ser Ser Trp Val Leu Leu Met Lys Tyr Leu
    450                 455                 460
```

```
Gly Asn Ala Thr Ala Ile Phe Phe Leu Pro Asp Glu Gly Lys Leu Gln
465                 470                 475                 480

His Leu Glu Asn Glu Leu Thr His Asp Ile Ile Thr Lys Phe Leu Glu
                485                 490                 495

Asn Glu Asp Arg Arg Ser Ala Ser Leu His Leu Pro Lys Leu Ser Ile
            500                 505                 510

Thr Gly Thr Tyr Asp Leu Lys Ser Val Leu Gly Gln Leu Gly Ile Thr
        515                 520                 525

Lys Val Phe Ser Asn Gly Ala Asp Leu Ser Gly Val Thr Glu Glu Ala
    530                 535                 540

Pro Leu Lys Leu Ser Lys Ala Val His Lys Ala Val Leu Thr Ile Asp
545                 550                 555                 560

Glu Lys Gly Thr Glu Ala Ala Gly Ala Met Phe Leu Glu Ala Ile Pro
                565                 570                 575

Met Ser Ile Pro Pro Glu Val Lys Phe Asn Lys Pro Phe Val Phe Leu
            580                 585                 590

Met Ile Glu Gln Asn Thr Lys Ser Pro Leu Phe Met Gly Lys Val Val
        595                 600                 605

Asn Pro Thr Gln Lys
    610
```

<210> 24
<211> 853
<212> PRT
<213> Artificial Sequence

<220>
<223> D2E7-Heavy Chain-AAT (G3S)2 Linker fusion protein

<400> 24

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
            20                  25                  30
```

```
Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ala Ile Thr Trp Asn Ser Gly His Ile Asp Tyr Ala Asp Ser Val
    50                  55                  60

Glu Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser 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 Lys Val Ser Tyr Leu Ser Thr Ala Ser Ser Leu Asp Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
        115                 120                 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
    130                 135                 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
    210                 215                 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
225                 230                 235                 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                 250                 255
```

```
Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
            260                 265                 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
    290                 295                 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305                 310                 315                 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
                325                 330                 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
            340                 345                 350

Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
        355                 360                 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
    370                 375                 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385                 390                 395                 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
                405                 410                 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
            420                 425                 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
        435                 440                 445

Pro Gly Lys Gly Gly Gly Ser Gly Gly Gly Ser Glu Asp Pro Gln Gly
    450                 455                 460

Asp Ala Ala Gln Lys Thr Asp Thr Ser His His Asp Gln Asp His Pro
465                 470                 475                 480
```

```
Thr Phe Asn Lys Ile Thr Pro Asn Leu Ala Glu Phe Ala Phe Ser Leu
                485                 490                 495

Tyr Arg Gln Leu Ala His Gln Ser Asn Ser Thr Asn Ile Phe Phe Ser
            500                 505                 510

Pro Val Ser Ile Ala Thr Ala Phe Ala Met Leu Ser Leu Gly Thr Lys
        515                 520                 525

Ala Asp Thr His Asp Glu Ile Leu Glu Gly Leu Asn Phe Asn Leu Thr
    530                 535                 540

Glu Ile Pro Glu Ala Gln Ile His Glu Gly Phe Gln Glu Leu Leu Arg
545                 550                 555                 560

Thr Leu Asn Gln Pro Asp Ser Gln Leu Gln Leu Thr Thr Gly Asn Gly
                565                 570                 575

Leu Phe Leu Ser Glu Gly Leu Lys Leu Val Asp Lys Phe Leu Glu Asp
            580                 585                 590

Val Lys Lys Leu Tyr His Ser Glu Ala Phe Thr Val Asn Phe Gly Asp
        595                 600                 605

Thr Glu Glu Ala Lys Lys Gln Ile Asn Asp Tyr Val Glu Lys Gly Thr
    610                 615                 620

Gln Gly Lys Ile Val Asp Leu Val Lys Glu Leu Asp Arg Asp Thr Val
625                 630                 635                 640

Phe Ala Leu Val Asn Tyr Ile Phe Phe Lys Gly Lys Trp Glu Arg Pro
                645                 650                 655

Phe Glu Val Lys Asp Thr Glu Glu Glu Asp Phe His Val Asp Gln Val
            660                 665                 670

Thr Thr Val Lys Val Pro Met Met Lys Arg Leu Gly Met Phe Asn Ile
        675                 680                 685

Gln His Cys Lys Lys Leu Ser Ser Trp Val Leu Leu Met Lys Tyr Leu
    690                 695                 700

Gly Asn Ala Thr Ala Ile Phe Phe Leu Pro Asp Glu Gly Lys Leu Gln
```

705 710 715 720

His Leu Glu Asn Glu Leu Thr His Asp Ile Ile Thr Lys Phe Leu Glu
725 730 735

Asn Glu Asp Arg Arg Ser Ala Ser Leu His Leu Pro Lys Leu Ser Ile
740 745 750

Thr Gly Thr Tyr Asp Leu Lys Ser Val Leu Gly Gln Leu Gly Ile Thr
755 760 765

Lys Val Phe Ser Asn Gly Ala Asp Leu Ser Gly Val Thr Glu Glu Ala
770 775 780

Pro Leu Lys Leu Ser Lys Ala Val His Lys Ala Val Leu Thr Ile Asp
785 790 795 800

Glu Lys Gly Thr Glu Ala Ala Gly Ala Met Phe Leu Glu Ala Ile Pro
805 810 815

Met Ser Ile Pro Pro Glu Val Lys Phe Asn Lys Pro Phe Val Phe Leu
820 825 830

Met Ile Glu Gln Asn Thr Lys Ser Pro Leu Phe Met Gly Lys Val Val
835 840 845

Asn Pro Thr Gln Lys
850

<210> 25
<211> 850
<212> PRT
<213> Artificial Sequence

<220>
<223> D2E7-Heavy Chain-AAT ASTGS Linker fusion protein

<400> 25

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
20 25 30

```
Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ala Ile Thr Trp Asn Ser Gly His Ile Asp Tyr Ala Asp Ser Val
    50                  55                  60

Glu Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser 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 Lys Val Ser Tyr Leu Ser Thr Ala Ser Ser Leu Asp Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
        115                 120                 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
    130                 135                 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
    210                 215                 220

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
225                 230                 235                 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
                245                 250                 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
```

```
            260                 265                 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
        275                 280                 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
    290                 295                 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
305                 310                 315                 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
                325                 330                 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
            340                 345                 350

Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
        355                 360                 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
    370                 375                 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
385                 390                 395                 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
                405                 410                 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
            420                 425                 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
        435                 440                 445

Pro Gly Lys Ala Ser Thr Gly Ser Glu Asp Pro Gln Gly Asp Ala Ala
    450                 455                 460

Gln Lys Thr Asp Thr Ser His His Asp Gln Asp His Pro Thr Phe Asn
465                 470                 475                 480

Lys Ile Thr Pro Asn Leu Ala Glu Phe Ala Phe Ser Leu Tyr Arg Gln
                485                 490                 495
```

```
Leu Ala His Gln Ser Asn Ser Thr Asn Ile Phe Phe Ser Pro Val Ser
            500                 505                 510

Ile Ala Thr Ala Phe Ala Met Leu Ser Leu Gly Thr Lys Ala Asp Thr
        515                 520                 525

His Asp Glu Ile Leu Glu Gly Leu Asn Phe Asn Leu Thr Glu Ile Pro
    530                 535                 540

Glu Ala Gln Ile His Glu Gly Phe Gln Glu Leu Leu Arg Thr Leu Asn
545                 550                 555                 560

Gln Pro Asp Ser Gln Leu Gln Leu Thr Thr Gly Asn Gly Leu Phe Leu
                565                 570                 575

Ser Glu Gly Leu Lys Leu Val Asp Lys Phe Leu Glu Asp Val Lys Lys
            580                 585                 590

Leu Tyr His Ser Glu Ala Phe Thr Val Asn Phe Gly Asp Thr Glu Glu
        595                 600                 605

Ala Lys Lys Gln Ile Asn Asp Tyr Val Glu Lys Gly Thr Gln Gly Lys
    610                 615                 620

Ile Val Asp Leu Val Lys Glu Leu Asp Arg Asp Thr Val Phe Ala Leu
625                 630                 635                 640

Val Asn Tyr Ile Phe Phe Lys Gly Lys Trp Glu Arg Pro Phe Glu Val
                645                 650                 655

Lys Asp Thr Glu Glu Glu Asp Phe His Val Asp Gln Val Thr Thr Val
            660                 665                 670

Lys Val Pro Met Met Lys Arg Leu Gly Met Phe Asn Ile Gln His Cys
        675                 680                 685

Lys Lys Leu Ser Ser Trp Val Leu Leu Met Lys Tyr Leu Gly Asn Ala
    690                 695                 700

Thr Ala Ile Phe Phe Leu Pro Asp Glu Gly Lys Leu Gln His Leu Glu
705                 710                 715                 720
```

```
Asn Glu Leu Thr His Asp Ile Ile Thr Lys Phe Leu Glu Asn Glu Asp
                725                 730                 735

Arg Arg Ser Ala Ser Leu His Leu Pro Lys Leu Ser Ile Thr Gly Thr
            740                 745                 750

Tyr Asp Leu Lys Ser Val Leu Gly Gln Leu Gly Ile Thr Lys Val Phe
        755                 760                 765

Ser Asn Gly Ala Asp Leu Ser Gly Val Thr Glu Glu Ala Pro Leu Lys
    770                 775                 780

Leu Ser Lys Ala Val His Lys Ala Val Leu Thr Ile Asp Glu Lys Gly
785                 790                 795                 800

Thr Glu Ala Ala Gly Ala Met Phe Leu Glu Ala Ile Pro Met Ser Ile
                805                 810                 815

Pro Pro Glu Val Lys Phe Asn Lys Pro Phe Val Phe Leu Met Ile Glu
            820                 825                 830

Gln Asn Thr Lys Ser Pro Leu Phe Met Gly Lys Val Val Asn Pro Thr
        835                 840                 845

Gln Lys
    850
```

<210> 26
<211> 869
<212> PRT
<213> Artificial Sequence

<220>
<223> TNFR2-ECD-Fc1-AAT(G3S)2 Linker fusion protein

<400> 26

```
Leu Pro Ala Gln Val Ala Phe Thr Pro Tyr Ala Pro Glu Pro Gly Ser
1               5                   10                  15

Thr Cys Arg Leu Arg Glu Tyr Tyr Asp Gln Thr Ala Gln Met Cys Cys
            20                  25                  30

Ser Lys Cys Ser Pro Gly Gln His Ala Lys Val Phe Cys Thr Lys Thr
        35                  40                  45
```

```
Ser Asp Thr Val Cys Asp Ser Cys Glu Asp Ser Thr Tyr Thr Gln Leu
    50                  55                  60

Trp Asn Trp Val Pro Glu Cys Leu Ser Cys Gly Ser Arg Cys Ser Ser
65                  70                  75                  80

Asp Gln Val Glu Thr Gln Ala Cys Thr Arg Glu Gln Asn Arg Ile Cys
                85                  90                  95

Thr Cys Arg Pro Gly Trp Tyr Cys Ala Leu Ser Lys Gln Glu Gly Cys
            100                 105                 110

Arg Leu Cys Ala Pro Leu Arg Lys Cys Arg Pro Gly Phe Gly Val Ala
        115                 120                 125

Arg Pro Gly Thr Glu Thr Ser Asp Val Val Cys Lys Pro Cys Ala Pro
    130                 135                 140

Gly Thr Phe Ser Asn Thr Thr Ser Ser Thr Asp Ile Cys Arg Pro His
145                 150                 155                 160

Gln Ile Cys Asn Val Val Ala Ile Pro Gly Asn Ala Ser Met Asp Ala
                165                 170                 175

Val Cys Thr Ser Thr Ser Pro Thr Arg Ser Met Ala Pro Gly Ala Val
            180                 185                 190

His Leu Pro Gln Pro Val Ser Thr Arg Ser Gln His Thr Gln Pro Thr
        195                 200                 205

Pro Glu Pro Ser Thr Ala Pro Ser Thr Ser Phe Leu Leu Pro Met Gly
    210                 215                 220

Pro Ser Pro Pro Ala Glu Gly Ser Thr Gly Asp Glu Pro Lys Ser Cys
225                 230                 235                 240

Asp Lys Thr His Thr Cys Pro* Pro Cys Pro Ala Pro Glu Leu Leu Gly
                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 Gln Val Lys Phe Asn Trp Tyr Val Asp Gly Val Gln Val
    290                 295                 300

His Asn Ala Lys Thr Lys Pro Arg Glu Gln Gln Tyr Asn Ser Thr Tyr
305                 310                 315                 320

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asn Trp Leu Asp Gly
                325                 330                 335

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
            340                 345                 350

Glu Lys Thr Ile Ser Lys Ala 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

Val 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 Lys Gly Gly Gly Ser Gly Gly Gly Ser Glu Asp Pro Gln Gly
465                 470                 475                 480

Asp Ala Ala Gln Lys Thr Asp Thr Ser His His Asp Gln Asp His Pro
                485                 490                 495
```

Thr Phe Asn Lys Ile Thr Pro Asn Leu Ala Glu Phe Ala Phe Ser Leu
500 505 510

Tyr Arg Gln Leu Ala His Gln Ser Asn Ser Thr Asn Ile Phe Phe Ser
515 520 525

Pro Val Ser Ile Ala Thr Ala Phe Ala Met Leu Ser Leu Gly Thr Lys
530 535 540

Ala Asp Thr His Asp Glu Ile Leu Glu Gly Leu Asn Phe Asn Leu Thr
545 550 555 560

Glu Ile Pro Glu Ala Gln Ile His Glu Gly Phe Gln Glu Leu Leu Arg
565 570 575

Thr Leu Asn Gln Pro Asp Ser Gln Leu Gln Leu Thr Thr Gly Asn Gly
580 585 590

Leu Phe Leu Ser Glu Gly Leu Lys Leu Val Asp Lys Phe Leu Glu Asp
595 600 605

Val Lys Lys Leu Tyr His Ser Glu Ala Phe Thr Val Asn Phe Gly Asp
610 615 620

Thr Glu Glu Ala Lys Lys Gln Ile Asn Asp Tyr Val Glu Lys Gly Thr
625 630 635 640

Gln Gly Lys Ile Val Asp Leu Val Lys Glu Leu Asp Arg Asp Thr Val
645 650 655

Phe Ala Leu Val Asn Tyr Ile Phe Phe Lys Gly Lys Trp Glu Arg Pro
660 665 670

Phe Glu Val Lys Asp Thr Glu Glu Glu Asp Phe His Val Asp Gln Val
675 680 685

Thr Thr Val Lys Val Pro Met Met Lys Arg Leu Gly Met Phe Asn Ile
690 695 700

Gln His Cys Lys Lys Leu Ser Ser Trp Val Leu Leu Met Lys Tyr Leu
705 710 715 720

Gly Asn Ala Thr Ala Ile Phe Phe Leu Pro Asp Glu Gly Lys Leu Gln

```
                725                 730                 735

His Leu Glu Asn Glu Leu Thr His Asp Ile Ile Thr Lys Phe Leu Glu
            740                 745                 750

Asn Glu Asp Arg Arg Ser Ala Ser Leu His Leu Pro Lys Leu Ser Ile
        755                 760                 765

Thr Gly Thr Tyr Asp Leu Lys Ser Val Leu Gly Gln Leu Gly Ile Thr
    770                 775                 780

Lys Val Phe Ser Asn Gly Ala Asp Leu Ser Gly Val Thr Glu Glu Ala
785                 790                 795                 800

Pro Leu Lys Leu Ser Lys Ala Val His Lys Ala Val Leu Thr Ile Asp
                805                 810                 815

Glu Lys Gly Thr Glu Ala Ala Gly Ala Met Phe Leu Glu Ala Ile Pro
            820                 825                 830

Met Ser Ile Pro Pro Glu Val Lys Phe Asn Lys Pro Phe Val Phe Leu
        835                 840                 845

Met Ile Glu Gln Asn Thr Lys Ser Pro Leu Phe Met Gly Lys Val Val
    850                 855                 860

Asn Pro Thr Gln Lys
865
```

<210> 27
<211> 866
<212> PRT
<213> Artificial Sequence

<220>
<223> TNFR2-ECD-Fc1-AAT ASTGS Linker fusion protein

<400> 27

```
Leu Pro Ala Gln Val Ala Phe Thr Pro Tyr Ala Pro Glu Pro Gly Ser
1               5                   10                  15

Thr Cys Arg Leu Arg Glu Tyr Tyr Asp Gln Thr Ala Gln Met Cys Cys
            20                  25                  30
```

```
Ser Lys Cys Ser Pro Gly Gln His Ala Lys Val Phe Cys Thr Lys Thr
        35                  40                  45

Ser Asp Thr Val Cys Asp Ser Cys Glu Asp Ser Thr Tyr Thr Gln Leu
    50                  55                  60

Trp Asn Trp Val Pro Glu Cys Leu Ser Cys Gly Ser Arg Cys Ser Ser
65                  70                  75                  80

Asp Gln Val Glu Thr Gln Ala Cys Thr Arg Glu Gln Asn Arg Ile Cys
                85                  90                  95

Thr Cys Arg Pro Gly Trp Tyr Cys Ala Leu Ser Lys Gln Glu Gly Cys
            100                 105                 110

Arg Leu Cys Ala Pro Leu Arg Lys Cys Arg Pro Gly Phe Gly Val Ala
        115                 120                 125

Arg Pro Gly Thr Glu Thr Ser Asp Val Val Cys Lys Pro Cys Ala Pro
    130                 135                 140

Gly Thr Phe Ser Asn Thr Thr Ser Ser Thr Asp Ile Cys Arg Pro His
145                 150                 155                 160

Gln Ile Cys Asn Val Val Ala Ile Pro Gly Asn Ala Ser Met Asp Ala
                165                 170                 175

Val Cys Thr Ser Thr Ser Pro Thr Arg Ser Met Ala Pro Gly Ala Val
            180                 185                 190

His Leu Pro Gln Pro Val Ser Thr Arg Ser Gln His Thr Gln Pro Thr
        195                 200                 205

Pro Glu Pro Ser Thr Ala Pro Ser Thr Ser Phe Leu Leu Pro Met Gly
    210                 215                 220

Pro Ser Pro Pro Ala Glu Gly Ser Thr Gly Asp Glu Pro Lys Ser Cys
225                 230                 235                 240

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
                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 Gln Val Lys Phe Asn Trp Tyr Val Asp Gly Val Gln Val
    290                 295                 300

His Asn Ala Lys Thr Lys Pro Arg Glu Gln Gln Tyr Asn Ser Thr Tyr
305                 310                 315                 320

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asn Trp Leu Asp Gly
                325                 330                 335

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
            340                 345                 350

Glu Lys Thr Ile Ser Lys Ala 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

Val 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 Lys Ala Ser Thr Gly Ser Glu Asp Pro Gln Gly Asp Ala Ala
465                 470                 475                 480

Gln Lys Thr Asp Thr Ser His His Asp Gln Asp His Pro Thr Phe Asn
                485                 490                 495
```

```
Lys Ile Thr Pro Asn Leu Ala Glu Phe Ala Phe Ser Leu Tyr Arg Gln
            500                 505                 510

Leu Ala His Gln Ser Asn Ser Thr Asn Ile Phe Phe Ser Pro Val Ser
        515                 520                 525

Ile Ala Thr Ala Phe Ala Met Leu Ser Leu Gly Thr Lys Ala Asp Thr
    530                 535                 540

His Asp Glu Ile Leu Glu Gly Leu Asn Phe Asn Leu Thr Glu Ile Pro
545                 550                 555                 560

Glu Ala Gln Ile His Glu Gly Phe Gln Glu Leu Leu Arg Thr Leu Asn
                565                 570                 575

Gln Pro Asp Ser Gln Leu Gln Leu Thr Thr Gly Asn Gly Leu Phe Leu
            580                 585                 590

Ser Glu Gly Leu Lys Leu Val Asp Lys Phe Leu Glu Asp Val Lys Lys
        595                 600                 605

Leu Tyr His Ser Glu Ala Phe Thr Val Asn Phe Gly Asp Thr Glu Glu
    610                 615                 620

Ala Lys Lys Gln Ile Asn Asp Tyr Val Glu Lys Gly Thr Gln Gly Lys
625                 630                 635                 640

Ile Val Asp Leu Val Lys Glu Leu Asp Arg Asp Thr Val Phe Ala Leu
                645                 650                 655

Val Asn Tyr Ile Phe Phe Lys Gly Lys Trp Glu Arg Pro Phe Glu Val
            660                 665                 670

Lys Asp Thr Glu Glu Glu Asp Phe His Val Asp Gln Val Thr Thr Val
        675                 680                 685

Lys Val Pro Met Met Lys Arg Leu Gly Met Phe Asn Ile Gln His Cys
    690                 695                 700

Lys Lys Leu Ser Ser Trp Val Leu Leu Met Lys Tyr Leu Gly Asn Ala
705                 710                 715                 720
```

```
Thr Ala Ile Phe Phe Leu Pro Asp Glu Gly Lys Leu Gln His Leu Glu
                725                 730                 735

Asn Glu Leu Thr His Asp Ile Ile Thr Lys Phe Leu Glu Asn Glu Asp
            740                 745                 750

Arg Arg Ser Ala Ser Leu His Leu Pro Lys Leu Ser Ile Thr Gly Thr
        755                 760                 765

Tyr Asp Leu Lys Ser Val Leu Gly Gln Leu Gly Ile Thr Lys Val Phe
    770                 775                 780

Ser Asn Gly Ala Asp Leu Ser Gly Val Thr Glu Glu Ala Pro Leu Lys
785                 790                 795                 800

Leu Ser Lys Ala Val His Lys Ala Val Leu Thr Ile Asp Glu Lys Gly
                805                 810                 815

Thr Glu Ala Ala Gly Ala Met Phe Leu Glu Ala Ile Pro Met Ser Ile
            820                 825                 830

Pro Pro Glu Val Lys Phe Asn Lys Pro Phe Val Phe Leu Met Ile Glu
        835                 840                 845

Gln Asn Thr Lys Ser Pro Leu Phe Met Gly Lys Val Val Asn Pro Thr
    850                 855                 860

Gln Lys
865
```

<210> 28
<211> 738
<212> PRT
<213> Artificial Sequence

<220>
<223> AAT-hFc1-SLPI fusion protein

<400> 28

```
Glu Asp Pro Gln Gly Asp Ala Ala Gln Lys Thr Asp Thr Ser His His
1               5                  10                  15

Asp Gln Asp His Pro Thr Phe Asn Lys Ile Thr Pro Asn Leu Ala Glu
            20                  25                  30
```

```
Phe Ala Phe Ser Leu Tyr Arg Gln Leu Ala His Gln Ser Asn Ser Thr
        35                  40                  45

Asn Ile Phe Phe Ser Pro Val Ser Ile Ala Thr Ala Phe Ala Met Leu
    50                  55                  60

Ser Leu Gly Thr Lys Ala Asp Thr His Asp Glu Ile Leu Glu Gly Leu
65                  70                  75                  80

Asn Phe Asn Leu Thr Glu Ile Pro Glu Ala Gln Ile His Glu Gly Phe
                85                  90                  95

Gln Glu Leu Leu Arg Thr Leu Asn Gln Pro Asp Ser Gln Leu Gln Leu
            100                 105                 110

Thr Thr Gly Asn Gly Leu Phe Leu Ser Glu Gly Leu Lys Leu Val Asp
        115                 120                 125

Lys Phe Leu Glu Asp Val Lys Lys Leu Tyr His Ser Glu Ala Phe Thr
    130                 135                 140

Val Asn Phe Gly Asp Thr Glu Glu Ala Lys Lys Gln Ile Asn Asp Tyr
145                 150                 155                 160

Val Glu Lys Gly Thr Gln Gly Lys Ile Val Asp Leu Val Lys Glu Leu
                165                 170                 175

Asp Arg Asp Thr Val Phe Ala Leu Val Asn Tyr Ile Phe Phe Lys Gly
            180                 185                 190

Lys Trp Glu Arg Pro Phe Glu Val Lys Asp Thr Glu Glu Glu Asp Phe
        195                 200                 205

His Val Asp Gln Val Thr Thr Val Lys Val Pro Met Met Lys Arg Leu
    210                 215                 220

Gly Met Phe Asn Ile Gln His Cys Lys Lys Leu Ser Ser Trp Val Leu
225                 230                 235                 240

Leu Met Lys Tyr Leu Gly Asn Ala Thr Ala Ile Phe Phe Leu Pro Asp
                245                 250                 255
```

```
Glu Gly Lys Leu Gln His Leu Glu Asn Glu Leu Thr His Asp Ile Ile
            260                 265                 270

Thr Lys Phe Leu Glu Asn Glu Asp Arg Arg Ser Ala Ser Leu His Leu
        275                 280                 285

Pro Lys Leu Ser Ile Thr Gly Thr Tyr Asp Leu Lys Ser Val Leu Gly
    290                 295                 300

Gln Leu Gly Ile Thr Lys Val Phe Ser Asn Gly Ala Asp Leu Ser Gly
305                 310                 315                 320

Val Thr Glu Glu Ala Pro Leu Lys Leu Ser Lys Ala Val His Lys Ala
                325                 330                 335

Val Leu Thr Ile Asp Glu Lys Gly Thr Glu Ala Ala Gly Ala Met Phe
            340                 345                 350

Leu Glu Ala Ile Pro Met Ser Ile Pro Pro Glu Val Lys Phe Asn Lys
        355                 360                 365

Pro Phe Val Phe Leu Met Ile Glu Gln Asn Thr Lys Ser Pro Leu Phe
    370                 375                 380

Met Gly Lys Val Val Asn Pro Thr Gln Lys Glu Pro Lys Ser Cys Asp
385                 390                 395                 400

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
                405                 410                 415

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
            420                 425                 430

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
        435                 440                 445

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
    450                 455                 460

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
465                 470                 475                 480
```

```
Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
                485                 490                 495

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
            500                 505                 510

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
        515                 520                 525

Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu
    530                 535                 540

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
545                 550                 555                 560

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
                565                 570                 575

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
            580                 585                 590

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
        595                 600                 605

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
    610                 615                 620

Gly Lys Ala Ser Thr Gly Ser Ser Gly Lys Ser Phe Lys Ala Gly Val
625                 630                 635                 640

Cys Pro Pro Lys Lys Ser Ala Gln Cys Leu Arg Tyr Lys Lys Pro Glu
                645                 650                 655

Cys Gln Ser Asp Trp Gln Cys Pro Gly Lys Lys Arg Cys Cys Pro Asp
            660                 665                 670

Thr Cys Gly Ile Lys Cys Leu Asp Pro Val Asp Thr Pro Asn Pro Thr
        675                 680                 685

Arg Arg Lys Pro Gly Lys Cys Pro Val Thr Tyr Gly Gln Cys Leu Met
    690                 695                 700

Leu Asn Pro Pro Asn Phe Cys Glu Met Asp Gly Gln Cys Lys Arg Asp
```

705 710 715 720

Leu Lys Cys Cys Met Gly Met Cys Gly Lys Ser Cys Val Ser Pro Val
725 730 735

Lys Ala

<210> 29
<211> 726
<212> PRT
<213> Artificial Sequence

<220>
<223> AAT-hFc1-Elafin fusion protein

<400> 29

Glu Asp Pro Gln Gly Asp Ala Ala Gln Lys Thr Asp Thr Ser His His
1 5 10 15

Asp Gln Asp His Pro Thr Phe Asn Lys Ile Thr Pro Asn Leu Ala Glu
20 25 30

Phe Ala Phe Ser Leu Tyr Arg Gln Leu Ala His Gln Ser Asn Ser Thr
35 40 45

Asn Ile Phe Phe Ser Pro Val Ser Ile Ala Thr Ala Phe Ala Met Leu
50 55 60

Ser Leu Gly Thr Lys Ala Asp Thr His Asp Glu Ile Leu Glu Gly Leu
65 70 75 80

Asn Phe Asn Leu Thr Glu Ile Pro Glu Ala Gln Ile His Glu Gly Phe
85 90 95

Gln Glu Leu Leu Arg Thr Leu Asn Gln Pro Asp Ser Gln Leu Gln Leu
100 105 110

Thr Thr Gly Asn Gly Leu Phe Leu Ser Glu Gly Leu Lys Leu Val Asp
115 120 125

Lys Phe Leu Glu Asp Val Lys Lys Leu Tyr His Ser Glu Ala Phe Thr
130 135 140

```
Val Asn Phe Gly Asp Thr Glu Glu Ala Lys Lys Gln Ile Asn Asp Tyr
145                 150                 155                 160

Val Glu Lys Gly Thr Gln Gly Lys Ile Val Asp Leu Val Lys Glu Leu
                165                 170                 175

Asp Arg Asp Thr Val Phe Ala Leu Val Asn Tyr Ile Phe Phe Lys Gly
            180                 185                 190

Lys Trp Glu Arg Pro Phe Glu Val Lys Asp Thr Glu Glu Glu Asp Phe
        195                 200                 205

His Val Asp Gln Val Thr Thr Val Lys Val Pro Met Met Lys Arg Leu
    210                 215                 220

Gly Met Phe Asn Ile Gln His Cys Lys Lys Leu Ser Ser Trp Val Leu
225                 230                 235                 240

Leu Met Lys Tyr Leu Gly Asn Ala Thr Ala Ile Phe Phe Leu Pro Asp
                245                 250                 255

Glu Gly Lys Leu Gln His Leu Glu Asn Glu Leu Thr His Asp Ile Ile
            260                 265                 270

Thr Lys Phe Leu Glu Asn Glu Asp Arg Arg Ser Ala Ser Leu His Leu
        275                 280                 285

Pro Lys Leu Ser Ile Thr Gly Thr Tyr Asp Leu Lys Ser Val Leu Gly
    290                 295                 300

Gln Leu Gly Ile Thr Lys Val Phe Ser Asn Gly Ala Asp Leu Ser Gly
305                 310                 315                 320

Val Thr Glu Glu Ala Pro Leu Lys Leu Ser Lys Ala Val His Lys Ala
                325                 330                 335

Val Leu Thr Ile Asp Glu Lys Gly Thr Glu Ala Ala Gly Ala Met Phe
            340                 345                 350

Leu Glu Ala Ile Pro Met Ser Ile Pro Pro Glu Val Lys Phe Asn Lys
        355                 360                 365

Pro Phe Val Phe Leu Met Ile Glu Gln Asn Thr Lys Ser Pro Leu Phe
```

```
    370                 375                 380

Met Gly Lys Val Val Asn Pro Thr Gln Lys Glu Pro Lys Ser Cys Asp
385                 390                 395                 400

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
                405                 410                 415

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
            420                 425                 430

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
        435                 440                 445

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
    450                 455                 460

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
465                 470                 475                 480

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
                485                 490                 495

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
            500                 505                 510

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
        515                 520                 525

Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu
    530                 535                 540

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
545                 550                 555                 560

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
                565                 570                 575

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
            580                 585                 590

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
        595                 600                 605
```

```
Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
    610                 615                 620

Gly Lys Ala Ser Thr Gly Ser Ala Val Thr Gly Val Pro Val Lys Gly
625                 630                 635                 640

Gln Asp Thr Val Lys Gly Arg Val Pro Phe Asn Gly Gln Asp Pro Val
                645                 650                 655

Lys Gly Gln Val Ser Val Lys Gly Gln Asp Lys Val Lys Ala Gln Glu
            660                 665                 670

Pro Val Lys Gly Pro Val Ser Thr Lys Pro Gly Ser Cys Pro Ile Ile
        675                 680                 685

Leu Ile Arg Cys Ala Met Leu Asn Pro Pro Asn Arg Cys Leu Lys Asp
    690                 695                 700

Thr Asp Cys Pro Gly Ile Lys Lys Cys Cys Glu Gly Ser Cys Gly Met
705                 710                 715                 720

Ala Cys Phe Val Pro Gln
                725
```

<210> 30
<211> 984
<212> PRT
<213> Artificial Sequence

<220>
<223> AAT-HSA fusion protein

<400> 30

```
Glu Asp Pro Gln Gly Asp Ala Ala Gln Lys Thr Asp Thr Ser His His
1               5                   10                  15

Asp Gln Asp His Pro Thr Phe Asn Lys Ile Thr Pro Asn Leu Ala Glu
            20                  25                  30

Phe Ala Phe Ser Leu Tyr Arg Gln Leu Ala His Gln Ser Asn Ser Thr
        35                  40                  45

Asn Ile Phe Phe Ser Pro Val Ser Ile Ala Thr Ala Phe Ala Met Leu
```

```
    50                  55                  60

Ser Leu Gly Thr Lys Ala Asp Thr His Asp Glu Ile Leu Glu Gly Leu
65                  70                  75                  80

Asn Phe Asn Leu Thr Glu Ile Pro Glu Ala Gln Ile His Glu Gly Phe
                85                  90                  95

Gln Glu Leu Leu Arg Thr Leu Asn Gln Pro Asp Ser Gln Leu Gln Leu
            100                 105                 110

Thr Thr Gly Asn Gly Leu Phe Leu Ser Glu Gly Leu Lys Leu Val Asp
        115                 120                 125

Lys Phe Leu Glu Asp Val Lys Lys Leu Tyr His Ser Glu Ala Phe Thr
    130                 135                 140

Val Asn Phe Gly Asp Thr Glu Glu Ala Lys Lys Gln Ile Asn Asp Tyr
145                 150                 155                 160

Val Glu Lys Gly Thr Gln Gly Lys Ile Val Asp Leu Val Lys Glu Leu
                165                 170                 175

Asp Arg Asp Thr Val Phe Ala Leu Val Asn Tyr Ile Phe Phe Lys Gly
            180                 185                 190

Lys Trp Glu Arg Pro Phe Glu Val Lys Asp Thr Glu Glu Glu Asp Phe
        195                 200                 205

His Val Asp Gln Val Thr Thr Val Lys Val Pro Met Met Lys Arg Leu
    210                 215                 220

Gly Met Phe Asn Ile Gln His Cys Lys Lys Leu Ser Ser Trp Val Leu
225                 230                 235                 240

Leu Met Lys Tyr Leu Gly Asn Ala Thr Ala Ile Phe Phe Leu Pro Asp
                245                 250                 255

Glu Gly Lys Leu Gln His Leu Glu Asn Glu Leu Thr His Asp Ile Ile
            260                 265                 270

Thr Lys Phe Leu Glu Asn Glu Asp Arg Arg Ser Ala Ser Leu His Leu
        275                 280                 285
```

```
Pro Lys Leu Ser Ile Thr Gly Thr Tyr Asp Leu Lys Ser Val Leu Gly
    290                 295                 300

Gln Leu Gly Ile Thr Lys Val Phe Ser Asn Gly Ala Asp Leu Ser Gly
305                 310                 315                 320

Val Thr Glu Glu Ala Pro Leu Lys Leu Ser Lys Ala Val His Lys Ala
                325                 330                 335

Val Leu Thr Ile Asp Glu Lys Gly Thr Glu Ala Ala Gly Ala Met Phe
            340                 345                 350

Leu Glu Ala Ile Pro Met Ser Ile Pro Pro Glu Val Lys Phe Asn Lys
        355                 360                 365

Pro Phe Val Phe Leu Met Ile Glu Gln Asn Thr Lys Ser Pro Leu Phe
    370                 375                 380

Met Gly Lys Val Val Asn Pro Thr Gln Lys Ala Ser Thr Gly Ser Asp
385                 390                 395                 400

Ala His Lys Ser Glu Val Ala His Arg Phe Lys Asp Leu Gly Glu Glu
                405                 410                 415

Asn Phe Lys Ala Leu Val Leu Ile Ala Phe Ala Gln Tyr Leu Gln Gln
            420                 425                 430

Cys Pro Phe Glu Asp His Val Lys Leu Val Asn Glu Val Thr Glu Phe
        435                 440                 445

Ala Lys Thr Cys Val Ala Asp Glu Ser Ala Glu Asn Cys Asp Lys Ser
    450                 455                 460

Leu His Thr Leu Phe Gly Asp Lys Leu Cys Thr Val Ala Thr Leu Arg
465                 470                 475                 480

Glu Thr Tyr Gly Glu Met Ala Asp Cys Cys Ala Lys Gln Glu Pro Glu
                485                 490                 495

Arg Asn Glu Cys Phe Leu Gln His Lys Asp Asp Asn Pro Asn Leu Pro
            500                 505                 510
```

```
Arg Leu Val Arg Pro Glu Val Asp Val Met Cys Thr Ala Phe His Asp
        515                 520                 525

Asn Glu Glu Thr Phe Leu Lys Lys Tyr Leu Tyr Glu Ile Ala Arg Arg
    530                 535                 540

His Pro Tyr Phe Tyr Ala Pro Glu Leu Leu Phe Phe Ala Lys Arg Tyr
545                 550                 555                 560

Lys Ala Ala Phe Thr Glu Cys Cys Gln Ala Ala Asp Lys Ala Ala Cys
                565                 570                 575

Leu Leu Pro Lys Leu Asp Glu Leu Arg Asp Glu Gly Lys Ala Ser Ser
            580                 585                 590

Ala Lys Gln Arg Leu Lys Cys Ala Ser Leu Gln Lys Phe Gly Glu Arg
        595                 600                 605

Ala Phe Lys Ala Trp Ala Val Ala Arg Leu Ser Gln Arg Phe Pro Lys
    610                 615                 620

Ala Glu Phe Ala Glu Val Ser Lys Leu Val Thr Asp Leu Thr Lys Val
625                 630                 635                 640

His Thr Glu Cys Cys His Gly Asp Leu Leu Glu Cys Ala Asp Asp Arg
                645                 650                 655

Ala Asp Leu Ala Lys Tyr Ile Cys Glu Asn Gln Asp Ser Ile Ser Ser
            660                 665                 670

Lys Leu Lys Glu Cys Cys Glu Lys Pro Leu Leu Glu Lys Ser His Cys
        675                 680                 685

Ile Ala Glu Val Glu Asn Asp Glu Met Pro Ala Asp Leu Pro Ser Leu
    690                 695                 700

Ala Ala Asp Phe Val Glu Ser Lys Asp Val Cys Lys Asn Tyr Ala Glu
705                 710                 715                 720

Ala Lys Asp Val Phe Leu Gly Met Phe Leu Tyr Glu Tyr Ala Arg Arg
                725                 730                 735
```

```
His Pro Asp Tyr Ser Val Val Leu Leu Leu Arg Leu Ala Lys Thr Tyr
            740                 745                 750

Glu Thr Thr Leu Glu Lys Cys Cys Ala Ala Ala Asp Pro His Glu Cys
        755                 760                 765

Tyr Ala Lys Val Phe Asp Glu Phe Lys Pro Leu Val Glu Glu Pro Gln
    770                 775                 780

Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu Gly Glu Tyr
785                 790                 795                 800

Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys Val Pro Gln
                805                 810                 815

Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu Gly Lys Val
            820                 825                 830

Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met Pro Cys Ala
        835                 840                 845

Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val Leu His Glu
    850                 855                 860

Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr Glu Ser Leu
865                 870                 875                 880

Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp Glu Thr Tyr
                885                 890                 895

Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His Ala Asp Ile
            900                 905                 910

Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln Thr Ala Leu
        915                 920                 925

Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu Gln Leu Lys
    930                 935                 940

Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys Cys Lys Ala
945                 950                 955                 960

Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys Leu Val Ala
```

965 970 975

Ala Ser Gln Ala Ala Leu Gly Leu
980

<210> 31
<211> 595
<212> PRT
<213> Artificial Sequence

<220>
<223> AAT-HSA Domain 3 fusion protein

<400> 31

Glu Asp Pro Gln Gly Asp Ala Ala Gln Lys Thr Asp Thr Ser His His
1 5 10 15

Asp Gln Asp His Pro Thr Phe Asn Lys Ile Thr Pro Asn Leu Ala Glu
20 25 30

Phe Ala Phe Ser Leu Tyr Arg Gln Leu Ala His Gln Ser Asn Ser Thr
35 40 45

Asn Ile Phe Phe Ser Pro Val Ser Ile Ala Thr Ala Phe Ala Met Leu
50 55 60

Ser Leu Gly Thr Lys Ala Asp Thr His Asp Glu Ile Leu Glu Gly Leu
65 70 75 80

Asn Phe Asn Leu Thr Glu Ile Pro Glu Ala Gln Ile His Glu Gly Phe
85 90 95

Gln Glu Leu Leu Arg Thr Leu Asn Gln Pro Asp Ser Gln Leu Gln Leu
100 105 110

Thr Thr Gly Asn Gly Leu Phe Leu Ser Glu Gly Leu Lys Leu Val Asp
115 120 125

Lys Phe Leu Glu Asp Val Lys Lys Leu Tyr His Ser Glu Ala Phe Thr
130 135 140

Val Asn Phe Gly Asp Thr Glu Glu Ala Lys Lys Gln Ile Asn Asp Tyr
145 150 155 160

```
Val Glu Lys Gly Thr Gln Gly Lys Ile Val Asp Leu Val Lys Glu Leu
                165                 170                 175

Asp Arg Asp Thr Val Phe Ala Leu Val Asn Tyr Ile Phe Phe Lys Gly
            180                 185                 190

Lys Trp Glu Arg Pro Phe Glu Val Lys Asp Thr Glu Glu Glu Asp Phe
        195                 200                 205

His Val Asp Gln Val Thr Thr Val Lys Val Pro Met Met Lys Arg Leu
    210                 215                 220

Gly Met Phe Asn Ile Gln His Cys Lys Lys Leu Ser Ser Trp Val Leu
225                 230                 235                 240

Leu Met Lys Tyr Leu Gly Asn Ala Thr Ala Ile Phe Phe Leu Pro Asp
                245                 250                 255

Glu Gly Lys Leu Gln His Leu Glu Asn Glu Leu Thr His Asp Ile Ile
            260                 265                 270

Thr Lys Phe Leu Glu Asn Glu Asp Arg Arg Ser Ala Ser Leu His Leu
        275                 280                 285

Pro Lys Leu Ser Ile Thr Gly Thr Tyr Asp Leu Lys Ser Val Leu Gly
    290                 295                 300

Gln Leu Gly Ile Thr Lys Val Phe Ser Asn Gly Ala Asp Leu Ser Gly
305                 310                 315                 320

Val Thr Glu Glu Ala Pro Leu Lys Leu Ser Lys Ala Val His Lys Ala
                325                 330                 335

Val Leu Thr Ile Asp Glu Lys Gly Thr Glu Ala Ala Gly Ala Met Phe
            340                 345                 350

Leu Glu Ala Ile Pro Met Ser Ile Pro Pro Glu Val Lys Phe Asn Lys
        355                 360                 365

Pro Phe Val Phe Leu Met Ile Glu Gln Asn Thr Lys Ser Pro Leu Phe
    370                 375                 380

Met Gly Lys Val Val Asn Pro Thr Gln Lys Ala Ser Thr Gly Ser Glu
```

385 390 395 400

Glu Pro Gln Asn Leu Ile Lys Gln Asn Cys Glu Leu Phe Glu Gln Leu
405 410 415

Gly Glu Tyr Lys Phe Gln Asn Ala Leu Leu Val Arg Tyr Thr Lys Lys
420 425 430

Val Pro Gln Val Ser Thr Pro Thr Leu Val Glu Val Ser Arg Asn Leu
435 440 445

Gly Lys Val Gly Ser Lys Cys Cys Lys His Pro Glu Ala Lys Arg Met
450 455 460

Pro Cys Ala Glu Asp Tyr Leu Ser Val Val Leu Asn Gln Leu Cys Val
465 470 475 480

Leu His Glu Lys Thr Pro Val Ser Asp Arg Val Thr Lys Cys Cys Thr
485 490 495

Glu Ser Leu Val Asn Arg Arg Pro Cys Phe Ser Ala Leu Glu Val Asp
500 505 510

Glu Thr Tyr Val Pro Lys Glu Phe Asn Ala Glu Thr Phe Thr Phe His
515 520 525

Ala Asp Ile Cys Thr Leu Ser Glu Lys Glu Arg Gln Ile Lys Lys Gln
530 535 540

Thr Ala Leu Val Glu Leu Val Lys His Lys Pro Lys Ala Thr Lys Glu
545 550 555 560

Gln Leu Lys Ala Val Met Asp Asp Phe Ala Ala Phe Val Glu Lys Cys
565 570 575

Cys Lys Ala Asp Asp Lys Glu Thr Cys Phe Ala Glu Glu Gly Lys Lys
580 585 590

Leu Val Ala
595

<210> 32
<211> 25

<212> PRT
<213> Artificial Sequence

<220>
<223> reactive site loop of a variant of the fusion alpha-1 antitrypsin polypeptide

<400> 32

Gly Thr Glu Ala Ala Gly Ala Glu Phe Leu Glu Ala Ile Pro Leu Ser
1 5 10 15

Ile Pro Pro Glu Val Lys Phe Asn Lys
20 25

<210> 33
<211> 25
<212> PRT
<213> Artificial Sequence

<220>
<223> reactive site loop of a variant of the fusion alpha-1 antitrypsin polypeptide

<400> 33

Gly Thr Glu Ala Ala Gly Ala Leu Phe Leu Glu Ala Ile Pro Leu Ser
1 5 10 15

Ile Pro Pro Glu Val Lys Phe Asn Lys
20 25

<210> 34
<211> 394
<212> PRT
<213> Artificial Sequence

<220>
<223> alpha-1 antitrypsin polypeptide portion of the AAT-MM-EL-hFc1 fusion protein

<400> 34

Glu Asp Pro Gln Gly Asp Ala Ala Gln Lys Thr Asp Thr Ser His His
1 5 10 15

Asp Gln Asp His Pro Thr Phe Asn Lys Ile Thr Pro Asn Leu Ala Glu
20 25 30

Phe Ala Phe Ser Leu Tyr Arg Gln Leu Ala His Gln Ser Asn Ser Thr
35 40 45

```
Asn Ile Phe Phe Ser Pro Val Ser Ile Ala Thr Ala Phe Ala Met Leu
    50                  55                  60

Ser Leu Gly Thr Lys Ala Asp Thr His Asp Glu Ile Leu Glu Gly Leu
65                  70                  75                  80

Asn Phe Asn Leu Thr Glu Ile Pro Glu Ala Gln Ile His Glu Gly Phe
                85                  90                  95

Gln Glu Leu Leu Arg Thr Leu Asn Gln Pro Asp Ser Gln Leu Gln Leu
            100                 105                 110

Thr Thr Gly Asn Gly Leu Phe Leu Ser Glu Gly Leu Lys Leu Val Asp
        115                 120                 125

Lys Phe Leu Glu Asp Val Lys Lys Leu Tyr His Ser Glu Ala Phe Thr
    130                 135                 140

Val Asn Phe Gly Asp Thr Glu Glu Ala Lys Lys Gln Ile Asn Asp Tyr
145                 150                 155                 160

Val Glu Lys Gly Thr Gln Gly Lys Ile Val Asp Leu Val Lys Glu Leu
                165                 170                 175

Asp Arg Asp Thr Val Phe Ala Leu Val Asn Tyr Ile Phe Phe Lys Gly
            180                 185                 190

Lys Trp Glu Arg Pro Phe Glu Val Lys Asp Thr Glu Glu Glu Asp Phe
        195                 200                 205

His Val Asp Gln Val Thr Thr Val Lys Val Pro Met Met Lys Arg Leu
    210                 215                 220

Gly Met Phe Asn Ile Gln His Cys Lys Lys Leu Ser Ser Trp Val Leu
225                 230                 235                 240

Leu Met Lys Tyr Leu Gly Asn Ala Thr Ala Ile Phe Phe Leu Pro Asp
                245                 250                 255

Glu Gly Lys Leu Gln His Leu Glu Asn Glu Leu Thr His Asp Ile Ile
            260                 265                 270
```

```
Thr Lys Phe Leu Glu Asn Glu Asp Arg Arg Ser Ala Ser Leu His Leu
        275                 280                 285

Pro Lys Leu Ser Ile Thr Gly Thr Tyr Asp Leu Lys Ser Val Leu Gly
    290                 295                 300

Gln Leu Gly Ile Thr Lys Val Phe Ser Asn Gly Ala Asp Leu Ser Gly
305                 310                 315                 320

Val Thr Glu Glu Ala Pro Leu Lys Leu Ser Lys Ala Val His Lys Ala
                325                 330                 335

Val Leu Thr Ile Asp Glu Lys Gly Thr Glu Ala Ala Gly Ala Glu Phe
            340                 345                 350

Leu Glu Ala Ile Pro Leu Ser Ile Pro Pro Glu Val Lys Phe Asn Lys
        355                 360                 365

Pro Phe Val Phe Leu Met Ile Glu Gln Asn Thr Lys Ser Pro Leu Phe
    370                 375                 380

Met Gly Lys Val Val Asn Pro Thr Gln Lys
385                 390
```

<210> 35
<211> 394
<212> PRT
<213> Artificial Sequence

<220>
<223> AAT polypeptide portion of the AAT-MM-LL-hFc1 fusion protein

<400> 35

```
Glu Asp Pro Gln Gly Asp Ala Ala Gln Lys Thr Asp Thr Ser His His
1               5                   10                  15

Asp Gln Asp His Pro Thr Phe Asn Lys Ile Thr Pro Asn Leu Ala Glu
            20                  25                  30

Phe Ala Phe Ser Leu Tyr Arg Gln Leu Ala His Gln Ser Asn Ser Thr
        35                  40                  45

Asn Ile Phe Phe Ser Pro Val Ser Ile Ala Thr Ala Phe Ala Met Leu
    50                  55                  60
```

```
Ser Leu Gly Thr Lys Ala Asp Thr His Asp Glu Ile Leu Glu Gly Leu
65                  70                  75                  80

Asn Phe Asn Leu Thr Glu Ile Pro Glu Ala Gln Ile His Glu Gly Phe
                85                  90                  95

Gln Glu Leu Leu Arg Thr Leu Asn Gln Pro Asp Ser Gln Leu Gln Leu
            100                 105                 110

Thr Thr Gly Asn Gly Leu Phe Leu Ser Glu Gly Leu Lys Leu Val Asp
        115                 120                 125

Lys Phe Leu Glu Asp Val Lys Lys Leu Tyr His Ser Glu Ala Phe Thr
    130                 135                 140

Val Asn Phe Gly Asp Thr Glu Glu Ala Lys Lys Gln Ile Asn Asp Tyr
145                 150                 155                 160

Val Glu Lys Gly Thr Gln Gly Lys Ile Val Asp Leu Val Lys Glu Leu
                165                 170                 175

Asp Arg Asp Thr Val Phe Ala Leu Val Asn Tyr Ile Phe Phe Lys Gly
            180                 185                 190

Lys Trp Glu Arg Pro Phe Glu Val Lys Asp Thr Glu Glu Glu Asp Phe
        195                 200                 205

His Val Asp Gln Val Thr Thr Val Lys Val Pro Met Met Lys Arg Leu
    210                 215                 220

Gly Met Phe Asn Ile Gln His Cys Lys Lys Leu Ser Ser Trp Val Leu
225                 230                 235                 240

Leu Met Lys Tyr Leu Gly Asn Ala Thr Ala Ile Phe Phe Leu Pro Asp
                245                 250                 255

Glu Gly Lys Leu Gln His Leu Glu Asn Glu Leu Thr His Asp Ile Ile
            260                 265                 270

Thr Lys Phe Leu Glu Asn Glu Asp Arg Arg Ser Ala Ser Leu His Leu
        275                 280                 285
```

```
Pro Lys Leu Ser Ile Thr Gly Thr Tyr Asp Leu Lys Ser Val Leu Gly
    290                 295                 300

Gln Leu Gly Ile Thr Lys Val Phe Ser Asn Gly Ala Asp Leu Ser Gly
305                 310                 315                 320

Val Thr Glu Glu Ala Pro Leu Lys Leu Ser Lys Ala Val His Lys Ala
                325                 330                 335

Val Leu Thr Ile Asp Glu Lys Gly Thr Glu Ala Ala Gly Ala Leu Phe
            340                 345                 350

Leu Glu Ala Ile Pro Leu Ser Ile Pro Pro Glu Val Lys Phe Asn Lys
        355                 360                 365

Pro Phe Val Phe Leu Met Ile Glu Gln Asn Thr Lys Ser Pro Leu Phe
    370                 375                 380

Met Gly Lys Val Val Asn Pro Thr Gln Lys
385                 390
```

<210> 36
<211> 626
<212> PRT
<213> Artificial Sequence

<220>
<223> AAT-MM-LL-hFc1 fusion protein

<400> 36

```
Glu Asp Pro Gln Gly Asp Ala Ala Gln Lys Thr Asp Thr Ser His His
1               5                   10                  15

Asp Gln Asp His Pro Thr Phe Asn Lys Ile Thr Pro Asn Leu Ala Glu
            20                  25                  30

Phe Ala Phe Ser Leu Tyr Arg Gln Leu Ala His Gln Ser Asn Ser Thr
        35                  40                  45

Asn Ile Phe Phe Ser Pro Val Ser Ile Ala Thr Ala Phe Ala Met Leu
    50                  55                  60

Ser Leu Gly Thr Lys Ala Asp Thr His Asp Glu Ile Leu Glu Gly Leu
65                  70                  75                  80
```

```
Asn Phe Asn Leu Thr Glu Ile Pro Glu Ala Gln Ile His Glu Gly Phe
                85                  90                  95

Gln Glu Leu Leu Arg Thr Leu Asn Gln Pro Asp Ser Gln Leu Gln Leu
            100                 105                 110

Thr Thr Gly Asn Gly Leu Phe Leu Ser Glu Gly Leu Lys Leu Val Asp
        115                 120                 125

Lys Phe Leu Glu Asp Val Lys Lys Leu Tyr His Ser Glu Ala Phe Thr
    130                 135                 140

Val Asn Phe Gly Asp Thr Glu Glu Ala Lys Lys Gln Ile Asn Asp Tyr
145                 150                 155                 160

Val Glu Lys Gly Thr Gln Gly Lys Ile Val Asp Leu Val Lys Glu Leu
                165                 170                 175

Asp Arg Asp Thr Val Phe Ala Leu Val Asn Tyr Ile Phe Phe Lys Gly
            180                 185                 190

Lys Trp Glu Arg Pro Phe Glu Val Lys Asp Thr Glu Glu Glu Asp Phe
        195                 200                 205

His Val Asp Gln Val Thr Thr Val Lys Val Pro Met Met Lys Arg Leu
    210                 215                 220

Gly Met Phe Asn Ile Gln His Cys Lys Lys Leu Ser Ser Trp Val Leu
225                 230                 235                 240

Leu Met Lys Tyr Leu Gly Asn Ala Thr Ala Ile Phe Phe Leu Pro Asp
                245                 250                 255

Glu Gly Lys Leu Gln His Leu Glu Asn Glu Leu Thr His Asp Ile Ile
            260                 265                 270

Thr Lys Phe Leu Glu Asn Glu Asp Arg Arg Ser Ala Ser Leu His Leu
        275                 280                 285

Pro Lys Leu Ser Ile Thr Gly Thr Tyr Asp Leu Lys Ser Val Leu Gly
    290                 295                 300
```

```
Gln Leu Gly Ile Thr Lys Val Phe Ser Asn Gly Ala Asp Leu Ser Gly
305                 310                 315                 320

Val Thr Glu Glu Ala Pro Leu Lys Leu Ser Lys Ala Val His Lys Ala
                325                 330                 335

Val Leu Thr Ile Asp Glu Lys Gly Thr Glu Ala Ala Gly Ala Leu Phe
            340                 345                 350

Leu Glu Ala Ile Pro Leu Ser Ile Pro Pro Glu Val Lys Phe Asn Lys
        355                 360                 365

Pro Phe Val Phe Leu Met Ile Glu Gln Asn Thr Lys Ser Pro Leu Phe
    370                 375                 380

Met Gly Lys Val Val Asn Pro Thr Gln Lys Glu Pro Lys Ser Cys Asp
385                 390                 395                 400

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
                405                 410                 415

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
            420                 425                 430

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
        435                 440                 445

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
    450                 455                 460

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
465                 470                 475                 480

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
                485                 490                 495

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
            500                 505                 510

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
        515                 520                 525
```

```
Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu
    530                 535                 540

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
545                 550                 555                 560

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
                565                 570                 575

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
            580                 585                 590

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
        595                 600                 605

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
    610                 615                 620

Gly Lys
625
```

<210> 37
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> D2E7-VK portion of a fusion protein

<400> 37

```
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Tyr
            20                  25                  30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Ala 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 Val Ala Thr Tyr Tyr Cys Gln Arg Tyr Asn Arg Ala Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 38
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> antibody constant region of a fusion protein

<400> 38

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
1 5 10 15

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
20 25 30

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
35 40 45

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
50 55 60

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
65 70 75 80

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
85 90 95

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
100 105

<210> 39
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<223> D2E7-VH portion of a fusion protein

<400> 39

```
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1               5                  10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
            20                  25                  30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45

Ser Ala Ile Thr Trp Asn Ser Gly His Ile Asp Tyr Ala Asp Ser Val
    50                  55                  60

Glu Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser 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 Lys Val Ser Tyr Leu Ser Thr Ala Ser Ser Leu Asp Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Leu
        115
```

<210> 40
<211> 335
<212> PRT
<213> Artificial Sequence

<220>
<223> antibody constant region of a fusion protein

<400> 40

```
Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
1               5                  10                  15

Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
            20                  25                  30

Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
        35                  40                  45

Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
    50                  55                  60
```

```
Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
65                  70                  75                  80

Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
                85                  90                  95

Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His
            100                 105                 110

Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val
        115                 120                 125

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
    130                 135                 140

Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
145                 150                 155                 160

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
                165                 170                 175

Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
            180                 185                 190

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
        195                 200                 205

Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
    210                 215                 220

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
225                 230                 235                 240

Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
                245                 250                 255

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
            260                 265                 270

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
        275                 280                 285
```

```
Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
    290                 295                 300

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
305                 310                 315                 320

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
                325                 330                 335
```

<210> 41
<211> 235
<212> PRT
<213> Artificial Sequence

<220>
<223> TNFR2-ECD portion of a fusion protein

<400> 41

```
Leu Pro Ala Gln Val Ala Phe Thr Pro Tyr Ala Pro Glu Pro Gly Ser
1               5                   10                  15

Thr Cys Arg Leu Arg Glu Tyr Tyr Asp Gln Thr Ala Gln Met Cys Cys
            20                  25                  30

Ser Lys Cys Ser Pro Gly Gln His Ala Lys Val Phe Cys Thr Lys Thr
        35                  40                  45

Ser Asp Thr Val Cys Asp Ser Cys Glu Asp Ser Thr Tyr Thr Gln Leu
    50                  55                  60

Trp Asn Trp Val Pro Glu Cys Leu Ser Cys Gly Ser Arg Cys Ser Ser
65                  70                  75                  80

Asp Gln Val Glu Thr Gln Ala Cys Thr Arg Glu Gln Asn Arg Ile Cys
                85                  90                  95

Thr Cys Arg Pro Gly Trp Tyr Cys Ala Leu Ser Lys Gln Glu Gly Cys
            100                 105                 110

Arg Leu Cys Ala Pro Leu Arg Lys Cys Arg Pro Gly Phe Gly Val Ala
        115                 120                 125

Arg Pro Gly Thr Glu Thr Ser Asp Val Val Cys Lys Pro Cys Ala Pro
    130                 135                 140
```

```
Gly Thr Phe Ser Asn Thr Thr Ser Ser Thr Asp Ile Cys Arg Pro His
145                 150                 155                 160

Gln Ile Cys Asn Val Val Ala Ile Pro Gly Asn Ala Ser Met Asp Ala
                165                 170                 175

Val Cys Thr Ser Thr Ser Pro Thr Arg Ser Met Ala Pro Gly Ala Val
            180                 185                 190

His Leu Pro Gln Pro Val Ser Thr Arg Ser Gln His Thr Gln Pro Thr
        195                 200                 205

Pro Glu Pro Ser Thr Ala Pro Ser Thr Ser Phe Leu Leu Pro Met Gly
    210                 215                 220

Pro Ser Pro Pro Ala Glu Gly Ser Thr Gly Asp
225                 230                 235
```

<210> 42
<211> 232
<212> PRT
<213> Artificial Sequence

<220>
<223> antibody constant region of a fusion protein

<400> 42

```
Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
1               5                   10                  15

Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
            20                  25                  30

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
        35                  40                  45

Val Asp Val Ser His Glu Asp Pro Gln Val Lys Phe Asn Trp Tyr Val
    50                  55                  60

Asp Gly Val Gln Val His Asn Ala Lys Thr Lys Pro Arg Glu Gln Gln
65                  70                  75                  80

Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
                85                  90                  95
```

```
Asn Trp Leu Asp Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
            100                 105                 110

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
        115                 120                 125

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr
    130                 135                 140

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
145                 150                 155                 160

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
                165                 170                 175

Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
            180                 185                 190

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
        195                 200                 205

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
    210                 215                 220

Ser Leu Ser Leu Ser Pro Gly Lys
225                 230
```

<210> 43
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> hinge region

<400> 43

```
Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro
1               5                   10                  15
```

<210> 44
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> hinge region

<400> 44

Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro
1 5 10

<210> 45
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> ASTGS linker

<400> 45

Ala Ser Thr Gly Ser
1 5

<210> 46
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> (G3S)2 linker

<400> 46

Gly Gly Gly Ser Gly Gly Gly Ser
1 5

CLAIMS

1. An isolated fusion protein comprising at least one human serpin polypeptide comprising a human alpha-1 antitrypsin (AAT) polypeptide comprising the amino acid sequence of SEQ ID NO:1 operably linked an immunoglobulin Fc polypeptide comprising the amino acid sequence of SEQ ID NO: 6.

2. An isolated fusion protein comprising at least one human alpha-1 antitrypsin (AAT) polypeptide comprising the amino acid sequence of SEQ ID NO: 32 or SEQ ID NO: 33 operably linked to an immunoglobulin Fc polypeptide comprising the amino acid sequence of SEQ ID NO: 6.

3. The isolated fusion protein of claim 1, wherein AAT polypeptide comprises the amino acid sequence of SEQ ID NO: 2.

4. The isolated fusion protein of claim 1, wherein the serpin polypeptide and the immunoglobulin Fc polypeptide are operably linked via a hinge region, a linker region, or both a hinge region and linker region.

5. The isolated fusion protein of claim 2, wherein the AAT polypeptide and the immunoglobulin Fc polypeptide are operably linked via a hinge region, a linker region, or both a hinge region and linker region.

6. The isolated fusion protein of claim 4, wherein the hinge region, the linker region or both the hinge region and the linker region comprise a peptide sequence.

7. The isolated fusion protein of claim 5, wherein the hinge region, the linker region or both the hinge region and the linker region comprise a peptide sequence.

8. The isolated fusion protein of claim 6, wherein the peptide sequence comprises the amino acid sequence of SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 45, or SEQ ID NO: 46.

9. The isolated fusion protein of claim 7, wherein the peptide sequence comprises the amino acid sequence of SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 45, or SEQ ID NO: 46.

10. The isolated fusion protein of claim 1, wherein the fusion protein further comprises a WAP domain-containing polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 9-13.

11. The isolated fusion protein of claim 2, wherein the fusion protein further comprises a SLPI polypeptide comprising the amino acid sequence of SEQ ID NO: 9 or SEQ ID NO:10.

12. The isolated fusion protein of claim 1, wherein the immunoglobulin Fc polypeptide is modified to enhance FcRn binding.

13. The isolated fusion protein of claim 1, wherein the immunoglobulin Fc polypeptide comprises at least one mutation at a position selected from the group consisting of: Met252, Ser254, Thr256, Met428, and Asn434.

14. The isolated fusion protein of claim 1, wherein the immunoglobulin Fc polypeptide comprises at least one of the following mutations: Met252Tyr, Ser254Thr, Thr256Glu, Met428Leu or Asn434Ser.

15. The isolated fusion protein of claim 10, wherein the immunoglobulin Fc polypeptide is modified to enhance FcRn binding.

16. The isolated fusion protein of claim 10, wherein the immunoglobulin Fc polypeptide comprises at least one mutation at a position selected from the group consisting of: Met252, Ser254, Thr256, Met428, and Asn434.

17. The isolated fusion protein of claim 10, wherein the immunoglobulin Fc polypeptide comprises at least one of the following mutations: Met252Tyr, Ser254Thr, Thr256Glu, Met428Leu or Asn434Ser.

18. Use of the fusion protein of claim 1 or claim 2 in the manufacture of a medicament for treating or alleviating a symptom of a disease or disorder associated with aberrant serine protease expression or activit1y in a subject in need thereof.

19. Use of the fusion protein of claim 1 or claim 2 in the manufacture of a medicament for treating or alleviating inflammation or a symptom of an inflammatory disease or disorder while reducing the risk of infection, in a subject in need thereof.

20. Use of the fusion protein of claim 1 or claim 2 in the manufacture of a medicament for reducing the risk of infection in a subject in need thereof.

21. The use of the fusion protein of any one of claims 18-20, wherein the subject is a human.

22. The use of the fusion protein of claim 19, wherein the inflammatory disease or disorder is selected from the following: emphysema, chronic obstructive pulmonary disease (COPD), acute respiratory distress syndrome (ARDS), allergic asthma, cystic fibrosis, cancers of the lung, ischemia-reperfusion injury, ischemia/reperfusion injury following cardiac transplantation, myocardial infarction, rheumatoid arthritis, septic arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, psoriasis, type I and/or type II diabetes, pneumonia, sepsis, graft versus host disease (GVHD), wound healing, Systemic lupus erythematosus, and Multiple sclerosis.

23. The use of the fusion protein of claim 20, wherein the infection is selected from bacterial infections, fungal infections, or viral infections.