(YTE) or Met428Leu, Asn434Ser (LS) which enhance FcRn binding are boxed, in bold text, and shaded in grey. 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. For example, the polypeptide components can be directly attached.

**[00131]** An exemplary SLPI-Fc fusion protein is the SLPI-hFc. As shown below, the SLPI polypeptide portion of the fusion protein is shown in bold (SEQ ID NO: 2), the WAP domain is underlined, the hinge region is shown in normal text (SEQ ID NO: 48), and the IgG-Fc polypeptide portion of the fusion protein is italicized (SEQ ID NO: 7).

**SLPI-hFc1 (human IgG1 Fc, long Hinge) (SEQ ID NO:16)**

**SGKSFKAGVCPPKKSAQCLRYKKPECQSDWQCPGKKRCCPDTCGIKCLDPVDTPNPTRRKPGKCPVT YGQCLMLNPPNFCEMDGQCKRDLKCCMGMCGKSCVSPVKA**EPKSCDKTHTCPPCP*APELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSD IAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL SPGK***(SEQ ID NO:16)**

**[00132]** An exemplary SLPI-Fc fusion protein is the SLPI-hFc2 (human IgG2 Fc, long Hinge). As shown below, the SLPI polypeptide portion of the fusion protein is shown in bold (SEQ ID NO: 2), the WAP domain is underlined, the hinge region is shown in normal text (SEQ ID NO: 49), and the IgG-Fc polypeptide portion of the fusion protein is italicized (SEQ ID NO: 8).

**SLPI-hFc2 (human IgG2 Fc, long Hinge) (SEQ ID NO:17)**

**SGKSFKAGVCPPKKSAQCLRYKKPECQSDWQCPGKKRCCPDTCGIKCLDPVDTPNPTRRKPGKCPVT YGQCLMLNPPNFCEMDGQCKRDLKCCMGMCGKSCVSPVKA**ERKCCVECPPCP*APPVAGPSVFLFPPK PKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTFRVVSVLTVVHQDW LNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK* (SEQ ID NO:17)

**[00133]** An exemplary SLPI-Fc fusion protein is the SLPI-ML-hFc1. As shown below, the SLPI polypeptide portion of the fusion protein is shown in bold (SEQ ID NO: 39), the WAP domain is underlined, the hinge region is shown in normal text (SEQ ID NO: 48), the IgG-Fc polypeptide portion of the fusion protein is italicized (SEQ ID NO: 7), and Met98Leu (ML) mutation in SLPI is boxed.

**SLPI-ML-hFc1 (human IgG1 Fc, Met98Leu) (SEQ ID NO:18)**

**SGKSFKAGVCPPKKSAQCLRYKKPECQSDWQCPGKKRCCPDTCGIKCLDPVDTPNPTRRKPGKCPVT YGQCLMLNPPNFCEMDGQCKRDLKCCMGLCGKSCVSPVKA**EPKSCDKTHTCPPCP*APELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSD IAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL SPGK* **(SEQ ID NO:18)**

**[00134]** An exemplary SLPI-Fc fusion protein is the SLPI-hFc1-YTE. As shown below, the SLPI polypeptide portion of the fusion protein is shown in bold (SEQ ID NO: 39), the WAP domain is underlined, the hinge region is shown in normal text (SEQ ID NO: 48), the IgG-Fc polypeptide portion of the fusion protein is italicized (SEQ ID NO: 40), and the Fc mutations Met252Tyr, Ser254Thr, Thr256Glu (YTE) are boxed, in bold text, and shaded in grey.

**SLPI-hFc1-YTE (human IgG1 Fc, Met252Tyr, Ser254Thr, Thr256Glu) (SEQ ID NO:19)**

**SGKSFKAGVCPPKKSAQCLRYKKPECQSDWQCPGKKRCCPDTCGIKCLDPVDTPNPTRRKPGKCPVT YGQCLMLNPPNFCEMDGQCKRDLKCCMGLCGKSCVSPVKA**EPKSCDKTHTCPPCP*APELLGGPSVFL FPPKPKDTLYITREPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTV LHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPS DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLS LSPGK* **(SEQ ID NO:19)**

**[00135]** An exemplary SLPI-Fc fusion protein is the SLPI-hFc1-LS. As shown below, the SLPI polypeptide portion of the fusion protein is shown in bold (SEQ ID NO: 39), the WAP domain is underlined, the hinge region is shown in normal text (SEQ ID NO: 48), the IgG-Fc polypeptide portion of the fusion protein is italicized (SEQ ID NO: 41), and Met428Leu, Asn434Ser (LS) which enhance FcRn binding are boxed, in bold text, and shaded in grey.

**SLPI-hFc1-LS (human IgG1 Fc, Met428Leu, Asn434Ser)**

**SGKSFKAGVCPPKKSAQCLRYKKPECQSDWQCPGKKRCCPDTCGIKCLDPVDTPNPTRRKPGKCPVT YGQCLMLNPPNFCEMDGQCKRDLKCCMGLCGKSCVSPVKA**EPKSCDKTHTCPPCP*APELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSD IAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKSLS LSPGK* **(SEQ ID NO:20)**

**[00136]** An exemplary Elafin-Fc fusion protein is the Elafin-hFc1. As shown below, the Elafin polypeptide portion of the fusion protein is shown in bold (SEQ ID NO: 5), the WAP domain is underlined, the hinge region is shown in normal text (SEQ ID NO: 48), the IgG-Fc polypeptide portion of the fusion protein is italicized (SEQ ID NO: 41), and the Asn434Ser (LS) which enhance FcRn binding are boxed, in bold text, and shaded in grey.

**Elafin-hFc1 (human IgG1)**

**AVTGVPVKGQDTVKGRVPFNGQDPVKGQVSVKGQDKVKAQEPVKGPVSTKPGSCPIILIRCAMLNPP NRCLKDTDCPGIKKCCEGSCGMACFVPQ**EPKSCDKTHTCPPCP*APELLGGPSVFLFPPKPKDTLMIS RTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKC KVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVLHEALHSHYTQKSLSLSPGK* **(SEQ ID NO:21)**

**[00137]** An exemplary SLPI-Fc fusion protein is the SLPI-hFc1-SLPI. As shown below, the SLPI polypeptide portion of the fusion protein is shown in bold (SEQ ID NO: 39), the WAP domain is underlined, the hinge region is shown in normal text (SEQ ID NO: 48), the IgG-Fc polypeptide portion of the fusion protein is italicized (SEQ ID NO: 7), and the ASTGS linker is shown in normal text (SEQ ID NO: 50).

**SLPI-hFc1-SLPI (human IgG1)**

**SGKSFKAGVCPPKKSAQCLRYKKPECQSDWQCPGKKRCCPDTCGIKCLDPVDTPNPTRRKPGKCPVT YGQCLMLNPPNFCEMDGQCKRDLKCCMGLCGKSCVSPVKA**EPKSCDKTHTCPPCP*APELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSD IAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL*

*SPGK*ASTGS**SGKSFKAGVCPPKKSAQCLRYKKPECQSDWQCPGKKRCCPDTCGIKCLDPVDTPNPTR RKPGKCPVTYGQCLMLNPPNFCEMDGQCKRDLKCCMGLCGKSCVSPVKA**(SEQ ID NO:22)

**[00138]** An exemplary Elafin-Fc fusion protein is the Elafin-hFc1-Elafin. As shown below, the Elafin polypeptide portion of the fusion protein is shown in bold (SEQ ID NO: 5), the WAP domain is underlined, the hinge region is shown in normal text (SEQ ID NO: 48), the IgG-Fc polypeptide portion of the fusion protein is italicized (SEQ ID NO: 7), and the ASTGS linker is shown in normal text (SEQ ID NO: 50).

**Elafin-hFc1-Elafin (human IgG1)**

**AVTGVPVKGQDTVKGRVPFNGQDPVKGQVSVKGQDKVKAQEPVKGPVSTKPGSCPIILIRCAMLNPP NRCLKDTDCPGIKKCCEGSCGMACFVPQ**EPKSCDKTHTCPPCP*APELLGGPSVFLFPPKPKDTLMIS RTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKC KVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*ASTGS**AVT GVPVKGQDTVKGRVPFNGQDPVKGQVSVKGQDKVKAQEPVKGPVSTKPGSCPIILIRCAMLNPPNRC LKDTDCPGIKKCCEGSCGMACFVPQ**(SEQ ID NO:23)

**[00139]** An exemplary Elafin-Fc fusion protein is the Elafin-hFc1-SLPI. As shown below, the SLPI polypeptide (SEQ ID NO: 39) portion of the fusion protein is shown in bold, with the WAP domain underlined, the Elafin (SEQ ID NO: 5) polypeptide portion of the fusion protein is shown in bold and italics, the WAP domain is underlined, the IgG-Fc polypeptide portion of the fusion protein is italicized (SEQ ID NO: 7), the hinge region is shown in normal text (SEQ ID NO: 48), and the ASTGS linker is shown in normal text (SEQ ID NO: 50).

**Elafin-hFc1-SLPI (human IgG1)**

***AVTGVPVKGQDTVKGRVPFNGQDPVKGQVSVKGQDKVKAQEPVKGPVSTKPGSCPIILIRCAMLNPP NRCLKDTDCPGIKKCCEGSCGMACFVPQ***EPKSCDKTHTCPPCP*APELLGGPSVFLFPPKPKDTLMIS RTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKC KVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*ASTGS**SGK SFKAGVCPPKKSAQCLRYKKPECQSDWQCPGKKRCCPDTCGIKCLDPVDTPNPTRRKPGKCPVTYGQ CLMLNPPNFCEMDGQCKRDLKCCMGLCGKSCVSPVKA**(SEQ ID NO:24)

**[00140]** An exemplary SLPI-Fc fusion protein is the SLPI-hFc1-Elafin. As shown below, the SLPI (SEQ ID NO: 39) portion of the fusion protein is shown in bold, with the WAP domain underlined, the Elafin (SEQ ID NO: 5) polypeptide portion of the fusion protein is shown in bold and italics, the WAP domain is underlined, and the IgG-Fc polypeptide portion of the fusion protein is italicized (SEQ ID NO: 7), the hinge region is shown in normal text (SEQ ID NO: 48), and the ASTGS linker is shown in normal text (SEQ ID NO: 50).

**SLPI-hFc1-Elafin (human IgG1)**

**SGKSFKAGVCPPKKSAQCLRYKKPECQSDWQCPGKKRCCPDTCGIKCLDPVDTPNPTRRKPGKCPVT YGQCLMLNPPNFCEMDGQCKRDLKCCMGLCGKSCVSPVKA**EPKSCDKTHTCPPCP*APELLGGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSD IAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL SPGK*ASTGS***AVTGVPVKGQDTVKGRVPFNGQDPVKGQVSVKGQDKVKAQEPVKGPVSTKPGSCPIIL IRCAMLNPPNRCLKDTDCPGIKKCCEGSCGMACFVPQ**(SEQ ID NO:25)

**[00141]** These exemplary SLPI-Fc and Elafin-Fc fusion proteins were made using the following techniques.

**[00142]** The genes encoding human SLPI and Elafin were PCR amplified from human spleen cDNA (Zyagen). Specific point mutations within the gene encoding SLPI, Elafin or the Fc region were generated by overlapping PCR. The SLPI or Elafin 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 SLPI or Elafin gene insertion site. In some cases, these vectors were further modified, wherein the gene encoding a linker sequence and either SLPI or Elafin was cloned in frame to the 3' end of the CH3 domain, to generate SLPI-Fc-SLPI, Elafin-Fc-Elafin, SLPI-Fc-Elafin, or Elafin-Fc-SLPI. 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 SLPI-Fc and Elafin-Fc fusion proteins were purified from the expression cell supernatant by protein A chromatography. Figure 1B shows a reducing SDS-PAGE gel of the Elafin-Fc (SEQ ID NO:21, lane 1) and SLPI-Fc (SEQ ID NO:16, lane 2) fusion

*VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVF*
*SCSVMHEALHNHYTQKSLSLSPGK*ASTGS**SGKSFKAGVCPPKKSAQCLRYKKPECQSDWQC**
**PGKKRCCPDTCGIKCLDPVDTPNPTRRKPGKCPVTYGQCLMLNPPNFCEMDGQCKRDLKCC**
**MGMCGKSCVSPVKA** (SEQ ID NO: 29)

**[00151]** An exemplary SLPI-TNFα Targeting Molecule fusion protein is TNFR2-ECD-Fc1-SLPI$(G_3S)_2$ Linker. As shown below, the SLPI polypeptide portion of the fusion protein is in bold text (SEQ ID NO: 2), the WAP domain is underlined, the Fc polypeptide portion is italicized (SEQ ID NO: 47), the TNFR2-ECD is shaded in grey and in bold text (SEQ ID NO: 46), the hinge region is shown in normal text (SEQ ID NO: 48), and the $(G_3S)_2$ linker is shown in normal text (SEQ ID NO: 51).

**TNFR2-ECD-Fc1-SLPI$(G_3S)_2$ Linker**

**LPAQVAFTPYAPEPGSTCRLREYYDQTAQMCCSKCSPGQHAKVFCTKTSDTVCDSCEDSTYTQLWNWVP**
**ECLSCGSRCSSDQVETQACTREQNRICTCRPGWYCALSKQEGCRLCAPLRKCRPGFGVARPGTETSDVV**
**CKPCAPGTFSNTTSSTDICRPHQICNVVAIPGNASMDAVCTSTSPTRSMAPGAVHLPQPVSTRSQHTQP**
**TPEPSTAPSTSFLLPMGPSPPAEGSTGD**EPKSCDKTHTCPPCP*APELLGGPSVFLFPPKPKDTLMISRT*
*PEVTCVVVDVSHEDPQVKFNWYVDGVQVHNAKTKPREQQYNSTYRVVSVLTVLHQNWLDGKEYKCKVSN*
*KALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTT*
*PPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*GGGSGGGS**SGKSFKAG**
**VCPPKKSAQCLRYKKPECQSDWQCPGKKRCCPDTCGIKCLDPVDTPNPTRRKPGKCPVTYGQCLMLNPP**
**NFCEMDGQCKRDLKCCMGMCGKSCVSPVKA** (SEQ ID NO: 30)

**[00152]** An exemplary SLPI-TNFα Targeting Molecule fusion protein is TNFR2-ECD-Fc1-SLPI ASTGS Linker. As shown below, the SLPI polypeptide portion of the fusion protein is in bold text (SEQ ID NO: 2), the WAP domain is underlined, the Fc polypeptide portion is italicized (SEQ ID NO: 47), the TNFR2-ECD is shaded in grey and in bold text (SEQ ID NO: 46), the hinge region is shown in normal text (SEQ ID NO: 48), and the ASTGS linker is shown in normal text (SEQ ID NO: 50).

**TNFR2-ECD-Fc1-SLPI ASTGS Linker**

**LPAQVAFTPYAPEPGSTCRLREYYDQTAQMCCSKCSPGQHAKVFCTKTSDTVCDSCEDSTYTQLWNWVP**
**ECLSCGSRCSSDQVETQACTREQNRICTCRPGWYCALSKQEGCRLCAPLRKCRPGFGVARPGTETSDVV**
**CKPCAPGTFSNTTSSTDICRPHQICNVVAIPGNASMDAVCTSTSPTRSMAPGAVHLPQPVSTRSQHTQP**

**TPEPSTAPSTSFLLPMGPSPPAEGSTGD**EPKSCDKTHTCPPCP*APELLGGPSVFLFPPKPKDTLMISRT*
*PEVTCVVVDVSHEDPQVKFNWYVDGVQVHNAKTKPREQQYNSTYRVVSVLTVLHQNWLDGKEYKCKVSN*
*KALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTT*
*PPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK*ASTGS**SGKSFKAGVCP**
**PKKSAQCLRYKKPECQSDWQCPGKKRCCPDTCGIKCLDPVDTPNPTRRKPGKCPVTYGQCLMLNPPNFC**
**EMDGQCKRDLKCCMGMCGKSCVSPVKA** (SEQ ID NO: 31)

**[00153]** These exemplary SLPI-TNFα targeting molecule fusion proteins were made using the following techniques.

**[00154]** 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 SLPI 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-SLPI), or the CL domain of the D2E7 light chain gene (D2E7-LC-SLPI) 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 SLPI 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-SLPI).

**[00155]** The D2E7-HC-SLPI expression vector was co-transfected with either the D2E7-LC or the D2E7-LC-SLPI expression vector into mammalian cells (specifically HEK293 or CHO cells) to generate the D2E7 antibody with SLPI fused to the C-terminus of the heavy chain or to the C-terminus of both the heavy chain and light chain, respectively.

**[00159]** An exemplary AAT-Fc-SLPI fusion protein is AAT-hFc1-SLPI (human IgG1 Fc). As shown below, the AAT polypeptide portion of the fusion protein is shown in bold text and shaded in grey (SEQ ID NO: 13), the Fc portion is italicized (SEQ ID NO: 7), the SLPI portion is in bold text (SEQ ID NO: 2), the WAP domain containing polypeptide is underlined (SEQ ID NO: 3), the hinge region is shown in normal text (SEQ ID NO: 48), and the ASTGS linker is shown in normal text (SEQ ID NO: 50).

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

**EDPQGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVSIATAFAMLSLGTK ADTHDEILEGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFLSEGLKLVDKFLEDVKKLY HSEAFTVNFGDTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFALVNYIFFKGKWERPFEVKDTEEED FHVDQVTTVKVPMMKRLGMFNIQHCKKLSSWVLLMKYLGNATAIFFLPDEGKLQHLENELTHDIITKFL ENEDRRSASLHLPKLSITGTYDLKSVLGQLGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDEKGT EAAGAMFLEAIPMSIPPEVKFNKPFVFLMIEQNTKSPLFMGKVVNPTQK**EPKSCDKTHTCPPCP*APELL GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVS VLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLS LSPGK*ASTGS**SGKSFKAGVCPPKKSAQCLRYKKPECQSDWQCPGKKRCCPDTCGIKCLDPVDTPNPTRR KPGKCPVTYGQCLMLNPPNFCEMDGQCKRDLKCCMGMCGKSCVSPVKA**(SEQ ID NO: 32)

**[00160]** An exemplary AAT-Fc-Elafin fusion protein is AAT-hFc1-Elafin. As shown below, the AAT polypeptide portion of the fusion protein is shown in bold text and shaded in grey (SEQ ID NO: 13), the Fc portion is italicized (SEQ ID NO: 7), the Elafin portion is in bold text (SEQ ID NO: 5), the WAP domain containing polypeptide is underlined (SEQ ID NO: 6), the hinge region is shown in normal text (SEQ ID NO: 48), and the ASTGS linker is shown in normal text (SEQ ID NO: 50).

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

**EDPQGDAAQKTDTSHHDQDHPTFNKITPNLAEFAFSLYRQLAHQSNSTNIFFSPVSIATAFAMLSLGTK ADTHDEILEGLNFNLTEIPEAQIHEGFQELLRTLNQPDSQLQLTTGNGLFLSEGLKLVDKFLEDVKKLY HSEAFTVNFGDTEEAKKQINDYVEKGTQGKIVDLVKELDRDTVFALVNYIFFKGKWERPFEVKDTEEED FHVDQVTTVKVPMMKRLGMFNIQHCKKLSSWVLLMKYLGNATAIFFLPDEGKLQHLENELTHDIITKFL ENEDRRSASLHLPKLSITGTYDLKSVLGQLGITKVFSNGADLSGVTEEAPLKLSKAVHKAVLTIDEKGT EAAGAMFLEAIPMSIPPEVKFNKPFVFLMIEQNTKSPLFMGKVVNPTQK**EPKSCDKTHTCPPCP*APELL GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVS*

*VLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFY*
*PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLS*
*LSPGK*ASTGS**AVTGVPVKGQDTVKGRVPFNGQDPVKGQVSVKGQDKVKAQEPVKGPVSTKPGSCPIILI**
**RCAMLNPPNRCLKDTDCPGIKKCCEGSCGMACFVPQ**(SEQ ID NO: 33)

**[00161]** The genes encoding the SLPI and Elafin were PCR amplified from human spleen cDNA (Zyagen). These genes and flanking linker sequences were cloned in frame into mammalian expression vectors containing the genes encoding AAT and an Ig Fc region, wherein a mammalian secretion precedes the AAT 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. Figure 3B shows a reducing SDS-PAGE gel of the purified fusion proteins: AAT-Fc-Elafin (SEQ ID NO: 33, lane 1) and AAT-Fc-SLPI (SEQ ID NO: 32, lane 2).

**[00162]** The purified AAT-Fc-WAP domain fusion proteins were tested for activity by determining their ability to inhibit neutrophil elastase. Human serum derived AAT (sdAAT) was used as a positive control in these assays. (Figure 3C). Relative to serum derived AAT, the AAT-Fc-WAP targeting molecule fusion proteins display enhanced potency of NE inhibition of neutrophil elastase. NE inhibition assays were conducted as described above.

**Example 4 SLPI-Albumin and Elafin-Albumin**

**[00163]** The studies presented herein describe several, non-limiting examples of recombinant AAT derivatives comprising human SLPI 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 in

## CLAIMS

1. An isolated fusion protein comprising at least one human whey acidic protein (WAP) domain-containing polypeptide comprising a human secretory leukocyte proteinase inhibitor (SLPI) polypeptide comprising the amino acid sequence of SEQ ID NO: 3 operably linked to an immunoglobulin Fc polypeptide comprising the amino acid sequence of SEQ ID NO: 10.

2. An isolated fusion protein comprising at least one human secretory leukocyte proteinase inhibitor (SLPI) polypeptide comprising the amino acid sequence of SEQ ID NO: 1, SEQ ID NO: 2 or SEQ ID NO: 39 operably linked to an immunoglobulin Fc polypeptide comprising the amino acid sequence of SEQ ID NO: 10.

3. The isolated fusion protein of claim 1, wherein 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.

4. The isolated fusion protein of claim 2, wherein 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.

5. The isolated fusion protein of claim 3, wherein the hinge region, the linker region or both the hinge region and the linker region comprise an amino acid sequence selected from the group consisting of SEQ ID NO: 48, SEQ ID NO: 49, SEQ ID NO: 50, and SEQ ID NO: 51.

6. The isolated fusion protein of claim 4, wherein the peptide sequence comprises the amino acid sequence of SEQ ID NO: 48, SEQ ID NO: 49, SEQ ID NO: 50, or SEQ ID NO: 51.

7. The isolated fusion protein of claim 1, wherein the immunoglobulin Fc polypeptide is modified to enhance FcRn binding.

8. 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.

9. 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.

10. The isolated fusion protein of claim 2, wherein the immunoglobulin Fc polypeptide is modified to enhance FcRn binding.

11. The isolated fusion protein of claim 2, 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.

12. The isolated fusion protein of claim 2, wherein the immunoglobulin Fc polypeptide comprises at least one of the following mutations: Met252Tyr, Ser254Thr, Thr256Glu, Met428Leu or Asn434Ser.

13. The isolated fusion protein of claim 2, wherein the human secretory leukocyte proteinase inhibitor (SLPI) polypeptide comprises of the amino acid sequence of SEQ ID NO: 3 operably linked to an immunoglobulin Fc polypeptide comprising the amino acid sequence of SEQ ID NO: 10.

14. The isolated fusion protein of claim 1, wherein the fusion protein further comprises a serpin polypeptide comprising the amino acid sequence of SEQ ID NO: 13 or SEQ ID NO: 38.

15. The isolated fusion protein of claim 2, wherein the fusion protein comprises a serpin polypeptide comprising the amino acid sequence of SEQ ID NO: 13 or SEQ ID NO: 38.

16. 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 selected from the group consisting of alpha-1-antitrypsin (AAT) deficiency, 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, arthritis, rheumatoid arthritis, septic arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, psoriasis, type I and/or type II diabetes, bacterial infections, fungal infections, viral infections, pneumonia, sepsis, graft versus host disease (GVHD), wound healing, Systemic lupus erythematosis, and multiple sclerosis in a subject in need thereof.

17. The use of the fusion protein of claim 16, wherein the subject is a human.