

CLAIMS:

1. A polypeptide comprising an amino acid sequence of the formula:

(AA1)_a-(AA2)_b-(AA3)_c-(AA4)_d-(AA5)_e-(AA6)_f-(AA7)_g-(AA8)_h-(AA9)_i-
 T10-Q11-L12-Q13-L14-E15-H16-L17-(AA18)-L19-D20-L21-(AA22)-
 5 M23-I24-L25-N26-G27-I28-N29-N30-Y31-K32-N33-P34-(AA35)-L36-
 T37-(AA38)-(AA39)-L40-T41-F42-K43-F44-Y45-M46-P47-K48-K49-
 A50-T51-E52-L53-K54-(AA55)-L56-Q57-C58-L59-E60-E61-E62-L63-
 K64-P65-L66-E67-E68-(AA69)-L70-N71-L72-A73-(AA74)-S75-K76-
 N77-F78-H79-(AA80)-(AA81)-P82-R83-D84-(AA85)-(AA86)-S87-N88-
 10 (AA89)-N90-(AA91)-(AA92)-V93-L94-E95-L96-(AA97)-G98-S99-E100-
 T101-T102-F103-(AA104)-C105-E106-Y107-A108-(AA109)-E110-T111-
 A112-(AA113)-I114-V115-E116-F117-L118-N119-R120-W121-I122-
 T123-F124-(AA125)-(AA126)-S127-I128-I129-(AA130)-T131-L132-T133

15 wherein:

- each of a, b, c, d, e, f, g, h, and i is individually selected from 0 or 1;
- AA1 is A (wild type, a=1) or deleted (a=0);
- AA2 is P (wild type, b=1) or deleted (b=0);
- AA3 is T (wild type, c=1), C, A, G, Q, E, N, D, R, K, P, or deleted (c=0);
- 20 • AA4 is S (wild type, d=1) or deleted (d=0);
- AA5 is S (wild type, e=1) or deleted (e=0);
- AA6 is S (wild type, f=1) or deleted (f=0);
- AA7 is T (wild type, g=1) or deleted (g=0);
- AA8 is K (wild type, h=1) or deleted (h=0);
- 25 • AA9 is K (wild type, i=1) or deleted (i=0);
- AA18 is L (wild type) or R, L, G, M, F, E, H, W, K, Q, S, V, I, Y, H, D or T;
- AA22 is Q (wild type) or F, E, G, A, L, M, F, W, K, S, V, I, Y, H, R, N, D, T, or F;
- AA35 is K (wildtype) or E;
- 30 • AA38 is R (wild type), W or G;
- AA39 is M (wildtype), L or V;

- AA55 is H (wildtype) or Y;
 - AA69 is V (wildtype) or A;
 - AA74 is Q (wild type), P, N, H, S;
 - AA80 is L (wild type), F or V;
 - 5 • AA81 is R (wild type), I, D or T;
 - AA85 is L (wild type) or V;
 - AA86 is I (wild type) or V;
 - AA89 is I (wild type) or V;
 - AA92 is I (wild type) or F;
 - 10 • AA97 is K (wild type) or Q;
 - AA104 is M (wild type) or A;
 - AA109 is D (wildtype), C or a non-natural amino acid with an activated side chain;
 - AA113 is T (wild type) or N;
 - 15 • AA125 is C (wild type), A or S;
 - AA126 is Q (wild type) or H, M, K, C, D, E, G, I, R, S, or T; and
 - AA130 is S (wild type), T, G or R.; and
- with the proviso that if AA18 is R and AA22 is E, then AA126 is not H, M, K, C, D, E, G, I, R, S, or T.
- 20 2. The polypeptide of claim 1 wherein
 - AA18 is selected from the group consisting of L (wild type) or R, L, G, M, F, E, H, W, K, Q, S, V, I, Y, H, D or T;
 - AA22 is selected from the group consisting of Q (wild type) or F, E, G, A, L, M, F, W, K, S, V, I, Y, H, R, N, D, T, or F; and
 - 25 • AA126 is selected from the group consisting of Q (wild type) or H, M, K, C, D, E, G, I, R, S, or T.
 3. The polypeptide of Claims 1 or 2 wherein a=0.
 4. The polypeptide of any one of claims 1-3 wherein said polypeptide comprises a set of mutations selected from the group consisting of: L18R, Q22E and Q126M; L18R, Q22E Q126T; L18R; Q22E; Q126H; L18R, and Q126H; Q22E, and Q126H; L18G, Q22E and Q126H; L18A, Q22E and Q126H; L18M, Q22E and Q126H; L18F, Q22E and Q126H; L18W, Q22E and Q126H; L18K, Q22E and Q126H; L18Q, Q22E and Q126H; L18E, Q22E

- and Q126H; L18S, Q22E and Q126H; L18V, Q22E and Q126H; L18I, Q22E and Q126H; L18Y, Q22E and Q126H; L18H, Q22E and Q126H; L18N, Q22E and Q126H; L18D, Q22E and Q126H; L18T, Q22E and Q126H; L18R, Q22G and Q126H; L18R, Q22A and Q126H; L18R, Q22L and Q126H; L18R, Q22M and Q126H; L18R, Q22F and Q126H; L18R, Q22W and Q126H; L18R, Q22K and Q126H; L18R, Q22S and Q126H; L18R, Q22V and Q126H; L18R, Q22I and Q126H; L18R Q22Y and Q126H; L18R Q22H and Q126H; L18R Q22R and Q126H; L18R Q22N and Q126H; L18R Q22D and Q126H; and L18R Q22T and Q126H.
- 5 5. The polypeptide of any one of claims 1-4 wherein the polypeptide is
10 PEGylated.
6. The polypeptide of any one of claims 1-5 wherein the polypeptide is PEGylated and the PEG component of such PEGylated polypeptide has a molecular weight of from about 10kD to about 70kD.
7. The polypeptide of any one of claims 1-6 wherein the polypeptide is a fusion
15 protein.
8. The polypeptide of Claim 7 wherein the fusion protein comprises an Fc domain.
9. A nucleic acid encoding a polypeptide of any one of claims 1-8.
10. The nucleic acid of claim 9 wherein the nucleic acid is DNA.
- 20 11. A recombinant expression vector comprising the nucleic acid of Claim 9 or
10. 10.
12. The vector of claim 11 wherein said vector is a viral vector.
13. The vector of claim 11 wherein said vector is a non-viral vector.
14. A host cell transformed with a vector of any one of claims 11-13.
- 25 15. A pharmaceutical formulation comprising a polypeptide of any one of claims 1-8, the nucleic acids of claims 9 and 10 or a vector of claims 11-13.
16. A method of treating a mammalian subject suffering from an autoimmune or inflammatory disease, disorder or condition or viral infection, the method comprising administering a therapeutically-effective amount of pharmaceutical formulation of claim 15.
- 30 17. The method of claim 16 further comprising administering one or more supplementary agents selected from the group consisting of a corticosteroid, a Janus kinase

inhibitor, a calcineurin inhibitor, a mTor inhibitor, an IMDH inhibitor, a biologic, a vaccine, and a therapeutic antibody.

18. The method of claim 17 wherein the therapeutic antibody is an antibody that binds a protein selected from the group consisting of BlyS, CD11a, CD20, CD25, CD3, CD52, IgEIL-12/IL-23, IL-17a, IL-1 β , IL-4R α , IL-5, IL-6R, integrin- α 4 β 7, RANKL, TNF α , VEGF-A, and VLA-4.

19. The method of any one of claims 16-18 wherein the disease, disorder or condition is selected from viral infections, heliobacter pylori infection, HTLV, organ rejection, graft versus host disease, autoimmune thyroid disease, multiple sclerosis, allergy, asthma, neurodegenerative diseases including Alzheimer's disease, systemic lupus erythramatosis (SLE), autoinflammatory diseases, inflammatory bowel disease (IBD), Crohn's disease, diabetes, cartilage inflammation, arthritis, rheumatoid arthritis, juvenile arthritis, juvenile rheumatoid arthritis, juvenile rheumatoid arthritis, polyarticular juvenile rheumatoid arthritis, systemic onset juvenile rheumatoid arthritis, juvenile ankylosing spondylitis, juvenile enteropathic arthritis, juvenile reactive arthritis, juvenile Reiter's Syndrome, SEA Syndrome, juvenile dermatomyositis, juvenile psoriatic arthritis, juvenile scleroderma, juvenile systemic lupus erythematosus, juvenile vasculitis, pauciarticular rheumatoidarthritis, polyarticular rheumatoidarthritis, systemic onset rheumatoidarthritis, ankylosing spondylitis, enteropathic arthritis, reactive arthritis, Reiter's syndrome, SEA Syndrome, psoriasis, psoriatic arthritis, dermatitis (eczema), exfoliative dermatitis or atopic dermatitis, pityriasis rubra pilaris, pityriasis rosacea, parapsoriasis, pityriasis lichenoiders, lichen planus, lichen nitidus, ichthyosiform dermatosis, keratodermas, dermatosis, alopecia areata, pyoderma gangrenosum, vitiligo, pemphigoid, urticaria, prokeratosis, rheumatoid arthritis; seborrheic dermatitis, solar dermatitis; seborrheic keratosis, senile keratosis, actinic keratosis, photo-induced keratosis, keratosis follicularis; acne vulgaris; keloids; nevi; warts including verruca, condyloma or condyloma acuminatum, and human papilloma viral (HPV) infections.