CLAIMS

1. A recombinant pro-protein comprising:
   a. a recombinant polypeptide comprising a cleavable moiety that is a substrate for a protease, wherein the cleavable moiety comprises the amino acid sequence selected from the group consisting of SEQ ID NO: 198 (ALFKSSFP) or a functional variant of SEQ ID NO: 198 (ALFKSSFP) in which one or two amino acids are substituted in SEQ ID NO: 198 (ALFKSSFP); wherein the functional variant of SEQ ID NO: 198 is a substrate for Cathepsin L; and
   b. a polypeptide with biological activity.

2. The recombinant pro-protein of claim 1, wherein the polypeptide with biological activity comprises a cytokine, chemokine, growth factor, a soluble receptor, antigen-binding polypeptide, an antibody or an antigen-binding portion thereof, or a combination thereof.

3. The recombinant pro-protein of claim 1, wherein the cleavable moiety that is a substrate for a protease SEQ ID NO: 198 (ALFKSSFP) in which one or two amino acids are substituted in SEQ ID NO: 198 (ALFKSSFP) with the provison that the amino acid at positions 4 and 5 of SEQ ID NO: 198 (ALFKSSFP) are not substituted.

4. The recombiant pro-protein of claim 1, wherein the cleavable moiety that is a substrate for a protease links the polypeptide with biological activity to another amino acid sequence.

5. The recombinant pro-protein of claim 1, wherein the polypeptide with biological activity has attenuated biological activity, and wherein cleavage of the cleavable moiety by the protease produces a polypeptide with biological activity that is not attenuated.

6. The recombinant pro-protein of claim 1, further comprising a blocking moiety selected from a steric blocking moiety, a specific blocking moiety, and a combination thereof.

7. The recombinant pro-protein of claim 6, wherein the blocking moiety comprises a steric blocking moiety that comprises human serum albumin (HSA), an anti-HSA antibody, an immunoglobulin Fc, or a fragment of any of the foregoing .

8. The recombinant pro-protein of claim 6, wherein the blocking moiety comprises a specific blocking moiety that comprises an antibody that has binding specificity for the biologically active

polypeptide or an antigen-binding fragment thereof, or the ligand-binding portion of a receptor that has binding specificity for the biologically active polypeptide or a ligand-binding fragment thereof.

9. The recombinant pro-protein of claim 1, further comprising a half-life extension domain.

10. The recombinant pro-protein of claim 5, wherein the polypeptide with biological activity comprises at least one of an extracellular domain, a transmembrane domain, and an intracellular domain.

11. The recombinant pro-protein of claim 1, wherein the polypeptide with biological activity comprises at least one of an extracellular domain, a transmembrane domain, and an intracellular domain.

12. The recombinant pro-protein of claim 1, wherein the polypeptide with biological activity comprises a cell surface receptor, a chimeric antigen receptor (CAR), or a T Cell Receptor (TCR) subunit.

13. The recombinant pro-protein of claim 1, wherein the polypeptide with biological activity comprises an antigen-binding polypeptide, an antibody or an antigen-binding portion thereof.

14. The recombinant pro-protein of claim 1, wherein one or two amino acid substitutions in the functional variant of SEQ ID NO: 198 are conservative substitutions.

15. The recombinant pro-protein of claim 1, wherein the functional variant of SEQ ID NO: 198 (ALFKSSFP) comprises the amino acid sequence of SEQ ID NO: 199, SEQ ID NO: 370, SEQ ID NO: 381, SEQ ID NO: 382, SEQ ID NO: 383, or SEQ ID NO: 390.

16. A nucleic acid composition comprising one or more nucleic acids encoding a recombinant pro-protein comprising:

a. a recombinant polypeptide comprising, a cleavable moiety that is a substrate for a protease, wherein the cleavable moiety comprises the amino acid sequence of SEQ ID NO: 198 (ALFKSSFP) or a functional variant of SEQ ID NO: 198 (ALFKSSFP) in which one or two amino acids are substituted in SEQ ID NO: 198 (ALFKSSFP); wherein the functional variant of SEQ ID NO: 198 is a substrate for

Cathepsin L; and

b. a polypeptide with biological activity.

17. The nucleic acid composition of claim 16, wherein the polypeptide with biological activity comprises a cytokine, chemokine, growth factor, a soluble receptor, antigen-binding polypeptide, an antibody or an antigen-binding portion thereof, or a combination thereof.

18. The nucleic acid composition of claim 16, wherein the cleavable moiety that is a substrate for a protease comprises an amino acid sequence at least 85% identical to SEQ ID NO: 198 (ALFKSSFP) in which one or two amino acids are substituted in SEQ ID NO: 198 (ALFKSSFP) with the provison that the amino acid at positions 4 and 5 of SEQ ID NO: 198 (ALFKSSFP) are not substituted.

19. The nucleic acid composition of claim 16, wherein the cleavable moiety that is a substrate for a protease links the polypeptide with biological activity to another amino acid sequence.

20. The nucleic acid composition of claim 16, wherein the polypeptide with biological activity has attenuated biological activity, and wherein cleavage of the cleavable moiety by the protease produces a polypeptide with biological activity that is not attenuated.

21. The nucleic acid composition of claim 16, wherein the one or more nucleic acids further encode a blocking moiety selected from a steric blocking moiety, a specific blocking moiety, and a combination thereof.

22. The nucleic acid composition of claim 21, wherein the blocking moiety comprises a steric blocking moiety that comprises human serum albumin (HSA), an anti-HSA antibody, an immunoglobulin Fc, or a fragment thereof.

23. The nucleic acid composition of claim 21, wherein the blocking moiety comprises a specific blocking moiety that comprises an antibody that has binding specificity for the biologically active polypeptide or an antigen-binding fragment thereof, or the ligand-binding portion of a receptor that has binding specificity for the biologically active polypeptide or a ligand-binding fragment thereof.

24. The nucleic acid composition of claim 16, wherein the one or more nucleic acids further encodes a half-life extension domain.

25. The nucleic acid composition of claim 16, wherein the polypeptide with biological activity comprises at least one of an extracellular domain, a transmembrane domain, and an intracellular domain.

26. The nucleic acid composition of claim 16, wherein the polypeptide with biological activity comprises a cell surface receptor, a chimeric antigen receptor (CAR), or a T Cell Receptor (TCR) subunit.

27. The nucleic acid of claim 16, wherein one or two amino acid substitutions in the functional variant of SEQ ID NO: 198 (ALFKSSFP) are conservative substitutions.

28. The nucleic acid of claim 16, wherein the functional variant of SEQ ID NO: 198 (ALFKSSFP) comprises the amino acid sequence of SEQ ID NO: 199, SEQ ID NO: 370, SEQ ID NO: 381, SEQ ID NO: 382, SEQ ID NO: 383, or SEQ ID NO: 390.

29. A vector comprising the nucleic acid composition of claim 16.

30. The vector of claim 29, wherein the vector is a viral vector.

31. A host cell comprising the nucleic acid of claim 16.