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 selected from the group consisting of SEQ ID NO: 198, SEQ ID NO: 199, SEQ ID NO: 381 or an amino acid sequence at least at least 85% identical to an amino acid sequence selected from the group consisting of SEQ ID NO: 198, SEQ ID NO: 199, SEQ ID NO: 381; 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 comprises an amino acid sequence at least 85% identical to SEQ ID NO: 198 or SEQ ID NO: 381, and wherein the amino acid at P1 is Lys (K) and the amino acid at P1' is Ser (S).

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

5. The recombinant pro-protein of claim 1, wherein the pro-protein 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 comprises human serum albumin (HSA), an anti-HSA antibody, an immunoglobulin Fc, or a fragment thereof.

8. The recombinant pro-protein of claim 6, wherein the blocking moiety comprises a specific blocking moiety 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. 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, SEQ ID NO: 199, SEQ ID NO: 381, or an amino acid sequence at least at least 85% identical to the amino acid sequence of SEQ ID NO: 198, SEQ ID NO: 199, SEQ ID NO: 381; and

b. a polypeptide with biological activity.

15. The nucleic acid composition of claim 14, 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.

16. The nucleic acid composition of claim 14, 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, or SEQ ID NO: 381, and wherein the amino acid at P1 is Lys (K) and the amino acid at P1’ is Ser (S).

17. The nucleic acid composition of claim 14, wherein the cleavable moiety that is a substrate for a protease links the polypeptide with biological activity to another to another amino acid sequence.

18. The nucleic acid composition of claim 14, wherein the pro-protein has attenuated biological activity, and wherein cleavage of the cleavable moiety by the protease produces a polypeptide with biological activity that is not attenuated.

19. The nucleic acid composition of claim 14, 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.

20. The nucleic acid composition of claim 19, wherein the blocking moiety comprises a steric blocking moiety comprises human serum albumin (HSA), an anti-HSA antibody, an immunoglobulin Fc, or a fragment thereof.

21. The nucleic acid composition of claim 19, wherein the blocking moiety comprises a specific blocking moiety 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.

22. The nucleic acid composition of claim 1, wherein the one or more nucleic acids further encodes a half-life extension domain.

23. The nucleic acid composition of claim 1, wherein the polypeptide with biological activity comprises at least one of an extracellular domain, a transmembrane domain, and an intracellular domain.

24. The nucleic acid composition 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.

25. A vector comprising the nucleic acid composition of claim 1.

26. The vector of claim 25, wherein the vector is a viral vector.

27. A host cell comprising the nucleic acid of claim 1.

28. A polypeptide comprising a protease cleavable amino acid sequence of SEQ ID NO:198, SEQ ID NO: 199, SEQ ID NO: 381 or an amino acid sequence that has at least about 85% identity to SEQ ID NO:198, SEQ ID NO: 199, or SEQ ID NO: 381.