We claim:

1. A polypeptide comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 1, wherein

(a) residue 467 is Ser, residue 267 is Glu, and residue 271 is Asp; and

(b) the polypeptide comprises an amino acid change from SEQ ID NO: 1 at one or more residues selected from the group consisting of 221D/N/Q/H, 262E, 268S/T/A, 269L/T, 270A/T/V, 319A, 320M, 354A/E/Q/R/Y, 358N/S/Q/T, 368F/Q, 399Q, 402S/Q, 406S, 424K, 449E/N/Q, 461R, and 463A/L/M/Q/R/T/V, wherein the polypeptide has an improved gliadin endopeptidase activity over a polypeptide having the amino acid sequence set forth in SEQ ID NO: 1.

2. The polypeptide of claim 1, wherein the polypeptide comprises an amino acid change from SEQ ID NO: 1 at two or more residues selected from the group.

3. The polypeptide of claim 1, wherein the polypeptide comprises amino acid changes 358S and 463T, optionally, the polypeptide further comprises 399Q and 449Q.

4. The polypeptide of any one of claims 1-3, wherein the polypeptide comprises amino acid changes 262E, 269T, 354Q, 358S, 399Q, 449Q, and 463T, optionally, the polypeptide further comprises 320M.

5. The polypeptide of any one of claims 1-3, wherein the polypeptide comprises amino acid changes 262E, 269T, 270V, 354Q, 358S, 399Q, and A449Q.

6. The polypeptide of claim 1, wherein the polypeptide comprises amino acid changes 319A, 368F, 399Q, 449Q, and I463T, optionally, the polypeptide further comprises 320M.

7. The polypeptide of any one of claims 1-6, further comprising an amino acid change at one or more amino acid positions selected from the group consisting of 105H; 171R/A/S; 172R/A/S; 173R/S, 174S, and/or 456V.

8. A polypeptide comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 71, wherein

(a) residue 278 is Ser, residue 78 is Glu, and residue 82 is Asp; and

(b) the polypeptide comprises an amino acid change from SEQ ID NO: 71 at one or more residues selected from the group consisting of 32D/N/Q/H, 73E, 79S/T/A, 80L/T, 81A/T/V, 130A, 131M, 165E/Q/R/Y, 169S/Q/T, 179F/Q, 210Q, 213S/Q, 217S, 235K, 260E/N/Q, 272R, and 274A/L/M/Q/R/T/V, wherein the polypeptide has an improved gliadin endopeptidase activity over a polypeptide having an amino acid sequence set forth in SEQ ID NO: 71.

9. The polypeptide of any one of claims 11, wherein the polypeptide comprises an amino acid change from SEQ ID NO: 71 at two or more residues selected from the group.

10. The polypeptide of claim 8 or 9, wherein the polypeptide comprises amino acid changes 169S and 274T, optionally, wherein the polypeptide further comprises amino acid changes 210Q and 260Q.

11. The polypeptide of any one of claims 8-10, wherein the polypeptide comprises amino acid changes 73E, 80T, 165Q, 169S, 210Q, 260Q, and 274T, optionally, wherein the polypeptide further comprises 131M.

12. The polypeptide of claim 8 or 9, wherein the polypeptide comprises amino acid changes 73E, 80T, 81V, 165Q, 169S, 210Q, and 260Q.

13. The polypeptide of claim 8 or 9, wherein the polypeptide comprises amino acid changes 130A, 179F, 210Q, 260Q, and 274T, optionally, wherein the polypeptide comprises 131M.

14. The polypeptide of any one of claims 8-13, further comprising an amino acid change 267V from SEQ ID NO: 71.

15. The polypeptide of any one of claims 1-14, comprising the amino acid sequence selected from the group consisting of SEQ ID NOs: 2-42, 44-60, 72-112, 114-130, and 150-155.

16. The polypeptide of any one of claims 1-15, comprising the amino acid sequence selected from the group consisting of SEQ ID NOs: 2-42, 55-60, 72-112, 125-130, and 150-155.

17. The polypeptide of any one of claims 1-16, further comprising a histidine tag at the C-terminus of the polypeptide, including but not limited to the amino acid sequence GSTENLYFQSGALEHHHHHH (SEQ ID NO: 139).

18. The polypeptide of claim 17, wherein the histidine tag comprises a cleavable histidine tag, including but not limited to a cleavable histidine tag comprising the amino acid sequence X_NPQ(L/Q)PX_NHHHHHH (SEQ ID NO: 131), wherein X_N is an linker of between 1-25 amino acid residues.

19. The polypeptide of claim 18, wherein the cleavable histidine tag comprises the amino acid sequence GSSGSSGSQPQLPYGSSGSSGSHHHHHH (SEQ ID NO: 132).

20. The polypeptide of claim 15, comprising the amino acid sequence of SEQ ID NO:129.

21. The polypeptide of claim 1, comprising the amino acid sequence at least 99% identical to SEQ ID NO:59.

22. The polypeptide of claim 1, comprising the amino acid sequence at least 99% identical to SEQ ID NO:59, wherein said amino acid sequence comprises SEQ ID NO:129.

23. The polypeptide of claim 1, comprising the amino acid sequence at least 99% identical to SEQ ID NO:59, which comprises at least one amino acid deletion from SEQ ID NO:59.

24. A polypeptide comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 59, wherein

(a) residue 467 is Ser, residue 267 is Glu, and residue 271 is Asp; and

(b) the polypeptide comprises amino acids 262E, 269T, 320M, 354Q, 358S, 399Q, 449Q, and 463T.

25. The polypeptide of claim 24, wherein the polypeptide further comprises the amino acids 171R and 172R.

26. The polypeptide of claim 24 or 25, wherein the polypeptide comprises at least one amino acid deletion from SEQ NO: 59.

27. The polypeptide of any one of claims 24-26, wherein the polypeptide comprises the amino acid sequence of SEQ NO: 129.

28. A nucleic acid encoding the polypeptide of any one of claims 1-27.

29. A nucleic acid expression vector comprising the isolated nucleic acid of claim 28.

30. A recombinant host cell comprising the nucleic acid expression vector of claim 29.

31. A pharmaceutical composition, comprising the polypeptide of any one of claims 1-27, the nucleic acid of claim 28, the nucleic acid expression vector of claim 29, and/or the recombinant host cell of claim 30, and a pharmaceutically acceptable carrier.

32. Use of a polypeptide according to any one of claims 1-27 or the pharmaceutical composition of claim 31 in the manufacture of a medicament for treating celiac sprue or non-celiac gluten sensitivity (NCGS), wherein an effective amount of the polypeptide or the pharmaceutical composition to treat the celiac sprue or NCGS is to be administered to an individual with celiac sprue or NCGS.

33. The use of claim 32, wherein the polypeptide or the pharmaceutical composition is to be administered orally.

34. A polypeptide according to any one of claims 1-27 or the pharmaceutical composition of claim 31 for use in therapy.