CLAIMS

1. A method of increasing the hydrodynamic size or hydrodynamic volume of a human growth hormone (hGH) polypeptide, the method comprising:

   (a) attaching one chorionic gonadotropin carboxy terminal peptide (CTP) unit to the amino terminus of the hGH polypeptide and two CTP units in tandem to the carboxy terminus of the hGH polypeptide to generate a CTP-modified hGH polypeptide; and

   (b) expressing the CTP-modified hGH polypeptide in a host cell, wherein the expressing comprises glycosylation of the CTP units of the CTP-modified hGH polypeptide,

   wherein the amino acid sequence of the CTP-modified hGH polypeptide is set forth in amino acids 27 to 301 of SEQ ID NO:11, and

   wherein the glycosylated CTP units incrementally increase the hydrodynamic size or hydrodynamic volume of the hGH polypeptide by about 28 to 40 kilodaltons (kDa) per each glycosylated CTP unit.

2. The method of claim 1, wherein the glycosylation is O-glycosylation.

3. The method of claim 2, wherein the O-glycosylation is a GalNAc attachment to serine (Ser) or threonine (Thr) in the protein chain of the CTP-modified hGH polypeptide by an α-glycosidic linkage.

4. The method of claim 2, wherein the O-glycosylation is core 1 glycosylation, O-fucosylation, O-mannosylation, or O-glycosylation.

5. The method of any one of claims 2 to 4, wherein the O-glycosylation is followed by the addition of one to sixty galactose molecules to the CTP-modified hGH polypeptide.

6. The method of any one of claims 2 to 5, wherein the O-glycosylation is followed by the addition of one to 120 sialic acid molecules to the CTP-modified hGH polypeptide.

7. The method of any one of claims 1 to 6, wherein the increasing the hydrodynamic size or hydrodynamic volume

   (a) increases the retention time of the hGH polypeptide in a biological sample;

   (b) increases the bioavailability of the hGH polypeptide;

(c) increases the bioactivity of the hGH polypeptide;

(d) reduces the administration frequency of the hGH polypeptide;

(e) extends the area under the curve (AUC) of the hGH polypeptide; or

(f) any combination thereof.

8. The method of claim 7, wherein the biological sample is blood, cerebro-spinal fluid (CSF), lymph, or sera.

9. The method of any one of claims 1 to 8, wherein the amino acid sequence of at least one of the CTP units is selected from the group consisting of SEQ ID NO: 1 and SEQ ID NO: 2.

10. The method of any one of claims 1 to 9, wherein at least one of the CTP units is attached to the hGH polypeptide via a linker.

11. The method of claim 10, wherein the linker is a peptide bond.

12. The method of any one of claims 1 to 11, wherein the CTP-modified hGH polypeptide is encoded by the nucleotide sequence set forth in nucleotides 89 to 913 of SEQ ID NO: 16.

13. The method of any one of claims 1 to 12, wherein the host cell is a Chinese Hamster Ovary (CHO) cell.

14. The method of any one of claims 1 to 13, wherein any one of the CTP units contributes about 29 kDa to the hydrodynamic size or hydrodynamic volume of the CTP-modified hGH polypeptide.