REGENERATIVE POLYPEPTIDES AND USES THEREOF

REFERENCE TO SEQUENCE LISTING, TABLE OR COMPUTER PROGRAM

[0001] The official copy of the Sequence Listing is submitted concurrently with the specification as an ASCII formatted text file via EFS-Web, with a file name of "JTI021_ST25.txt", a creation date of June 7, 2022, and a size of 101,574 bytes. The Sequence Listing filed via EFS-Web is part of the specification and is incorporated in its entirety by reference herein.

BACKGROUND

[0002] As the average life span increases, increasing emphasis is placed upon "healthy aging." Individuals would like to live more active lifestyles as they age, and as a result, many aging disorders can have a significant impact on the quality of life of aging individuals. Treatments directed to regenerative ends have utility for treating aging diseases. Additionally, many treatments for aging disorders can be applicable to younger individuals who have suffered illness, injury, or who possess genetic or developmental defects leading to premature tissue loss, wasting, or weakening.

SUMMARY

[0003] As individuals age, tissue progenitor cells lose their regenerative potential.

[0004] Described herein are polypeptides comprising an IGF2 amino acid sequence and an amino acid sequence from a heterologous polypeptide useful for the treatment of soft-tissue and muscle diseases, disorders, and injuries. Also described herein mutations within the IGF2 amino acid sequence improved the stability of the molecule by reducing backbone cleavage. Also described herein are mutations within IGF2 sequences that block cleavage of its peptide backbone. Also described are methods of treating muscle and soft-tissue diseases comprising administering the polypeptides and/or synergistic compositions.

[0004a] In one aspect, provided herein is an IGF2 fusion polypeptide, wherein the amino acid sequence of the polypeptide is 100% identical to SEQ ID NO: 34 and 6 amino acids are deleted from the N-terminus of SEQ ID NO: 34.

[0004b] In another aspect, provided herein is a use of the IGF2 fusion polypeptide as described herein in the manufacture of a medicament for treating a muscle or soft-tissue disorder or condition in a subject, wherein a therapeutically effective amount of the polypeptide is to be administered to the subject.

[0004c] In another aspect, provided herein is the IGF2 fusion polypeptide as described herein, for use in therapy.

BRIEF DESCRIPTION OF THE DRAWINGS

[0005] **FIG. 1A** depicts purified IGF2-hFcm promoted differentiation of human myoblast cells

[0006] **FIG. 1B** depicts purified IGF2-LhFc4 promoted differentiation of human myoblast cells

[0007] **FIG. 2A** purified HSA-L-IGF2R61A promoted differentiation of human myoblast cells.

[0008] **FIG. 2B** depicts IGF2 and IGF2 receptors were expressed in human myoblast

[0009] **FIG. 2C** depicts IGF2 and IGF2 receptors were expressed in human myoblast

[0010] **FIG. 3A** depicts sodium butyrate enhanced muscle fusion