PCT PATENT APPLICATION

TNFSF-L FUSION PROTEINS AND USES THEREOF

CROSS-REFERENCE

[0001] This application claims the benefit of U.S. Provisional Application No. 63/211,766 filed June 17, 2021, which is incorporated by reference herein in its entirety.

SEQUENCE LISTING

[0002] The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on June 14, 2022, is named 199249-715601_SL.txt and is 45,505 bytes in size**.**

BACKGROUND

[0003] The TNF superfamily (TNFSF) is made up of proteins important for the development and functioning of many mammalian systems, including the immune, hematological, and skeletal systems. TNFSF proteins are ligands for a corresponding set of receptors of the TNF receptor superfamily (TNFS). TNFSF members are generally expressed as Type II membrane proteins, with the exception of lymphotoxin-alpha which is produced as a secreted protein.

[0004] To produce soluble forms of TNFSF proteins, generally, the membrane protein is often expressed in a cell line possessing a protease capable of separating the TNFSF extracellular domain from the transmembrane domain or a truncated form of the TNFSF protein is produced which has the extracellular domain plus a signal sequence. In either case, certain soluble forms of TNFSF ligand (TNFSF-L) proteins are often unstable in solution as homotrimers composed solely of the extracellular domain. Thus, there is a need for more stable forms of these important signaling proteins.

BRIEF SUMMARY

[0004a] In one aspect, provided herein is a composition, wherein the composition comprises: a vector; and a nucleic acid encoding for a fusion protein, wherein the fusion protein comprises: a TNF-superfamily ligand (TNFSF-L) or functional variant thereof; and a plurality of domains from a collectin family protein, wherein the plurality of domains from the collectin family protein comprises: an oligomerization domain or functional variant thereof; and a neck domain or functional variant thereof, wherein the oligomerization domain or functional variant thereof and the neck domain or functional variant thereof are closer in sequence proximity compared to their location in the collectin family protein.

[0004b] In another aspect, provided herein is use of a pharmaceutical composition in the manufacture of a medicament for treatment of cancer, wherein the pharmaceutical composition comprises: the composition, fusion protein, or oncolytic virus as described herein, and a pharmaceutically acceptable carrier, and wherein the pharmaceutical composition is to be administered to a subject in an amount sufficient for treatment of a cancer.

[0004c] In another aspect, provided herein is the pharmaceutical composition comprising the composition, fusion protein, or oncolytic virus as described herein and a pharmaceutically acceptable carrier for use in therapy.

[0005] Provided herein are compositions, wherein the composition comprises a nucleic acid, wherein the nucleic acid encodes for a fusion protein, wherein the fusion protein comprises: a TNF-superfamily ligand (TNFSF-L) or functional variant thereof; and a plurality of domains from a collectin family protein, wherein the plurality of domains from the collectin family protein comprises: an oligomerization domain or functional variant thereof; and a neck domain or functional variant thereof, wherein the oligomerization domain or functional variant thereof and the neck domain or functional variant thereof are closer in sequence proximity compared to their location in the collectin family protein. Further provided are compositions, wherein the fusion protein comprises, in N-terminal to C-terminal order: the oligomerization domain or