COMPOSITIONS AND METHODS FOR EXPRESSING THERAPEUTICS

CROSS-REFERENCE

[001] This application claims the benefit of US Provisional Application Serial Number 63/319,233 filed on March 11, 2022; US Provisional Application Serial Number 63/440,858 filed on January 24, 2023; and US Provisional Application Serial Number 63/441,643 filed on January 27, 2023, the entirety of which is hereby incorporated by reference herein.

INCORPORATION BY REFERENCE

[002] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference. To the extent publications and patents or patent applications incorporated by reference contradict the disclosure contained in the specification, the specification is intended to supersede and/or take precedence over any such contradictory material.

BACKGROUND

[003] Natriuretic peptide precursor C is a prohormone composed of 126 amino acids. Natriuretic peptide precursor C can be further cleaved to yield a receptor binding active version known as C-type natriuretic peptide (CNP), where the CNP can be any one of the three forms: CNP53 (CNP composed of 53 amino acids); CNP36 (CNP composed of 36 amino acids); or CNP22 (CNP composed of 22 amino acids). Upon the CNP binding to its cognate receptor, natriuretic peptide clearance receptor B (NPR-B) and NPR-C, the membrane associated guanylyl cyclase (GC) is activated and catalyzes enzymatic conversion of GTP into the cyclic guanylyl monophosphate (cGMP), the functional effector or the secondary messenger. Because of its ability to activate cGMP, CNP has been utilized as therapeutics.

SUMMARY

[004] However, cleaved CNP such as CNP53, CNP36, or CNP22 has a half-life of only a few minutes, which limits its use for treating a disease or condition. As such, there remains a need to engineer CNP to increase its stability. There also remains a need to engineer CNP for treating a disease or condition.

[004a] In one aspect, provided herein is an engineered polynucleotide comprising an AAV vector, said AAV vector comprises an expression cassette, wherein the expression cassette

encodes an engineered polypeptide comprising a natriuretic peptide covalently connected to an antibody or fragment thereof.

[004b] In another aspect, provided herein is use of an engineered polynucleotide in the manufacture of a medicament for treating a disease or condition in a subject, wherein the engineered polynucleotide is to be administered to the subject, wherein the engineered polynucleotide comprises a viral vector comprising an expression cassette for expressing an engineered polypeptide comprising an antibody or a fragment thereof operatively coupled to a natriuretic peptide in a cell of the subject, and wherein the cell expresses the engineered polypeptide.

[005] Described herein, in some aspects, is an engineered polynucleotide comprising a viral vector, said viral vector comprises an expression cassette, wherein the expression cassette encodes an engineered polypeptide comprising a natriuretic peptide covalently connected to