CONTROLLED EXPRESSION OF TRANSGENES USING CLOSED-ENDED DNA (CEDNA) VECTORS

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims benefit under 35 U.S.C. § 119(e) of U.S. Provisional Application Nos. 62/633,882 filed February 22, 2018; 62/633,757 filed February 22, 2018; 62/633,795 filed February 22, 2018; and 62/746,762, filed October 17, 2018, the contents of each are incorporated herein by reference in their entireties.

[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 February 21, 2019, is named 080170-091190-WOPT_SL.txt and is 116,872 bytes in size.

TECHNICAL FIELD

[0003] The present invention relates to the field of gene therapy, including capsid-free vectors for controlled expression of a transgene or isolated polynucleotides in a subject or cell. The technology described herein relates to methods of controlled expression of a transgene *in vivo* from a capsid-free DNA vectors with closed ends (ceDNA) vector where the expression level can be sustained at desired level for a predetermined time or increased with one or more subsequent administrations (e.g., a booster administration, or re-dose).

BACKGROUND

[0004] Gene therapy aims to improve clinical outcomes for patients suffering from either genetic mutations or acquired diseases caused by an aberration in the gene expression profile. Gene therapy includes the treatment or prevention of medical conditions resulting from defective genes or abnormal regulation or expression, e.g. underexpression or overexpression, that can result in a disorder, disease, malignancy, etc. For example, a disease or disorder caused by a defective gene might be treated, prevented or ameliorated by delivery of a corrective genetic material to a patient, by altering or silencing a defective gene, or delivering a therapeutic antibody, e.g., resulting in the therapeutic expression of the genetic material within the patient.

[0005] The basis of gene therapy is to supply a transcription cassette with an active gene product (sometimes referred to as a transgene), e.g., that can result in a positive gain-of-function effect, a negative loss-of-function effect, or another outcome. Gene therapy can also be used to treat a disease or malignancy caused by other factors. Human monogenic disorders can be treated by the delivery and expression of a normal gene to the target cells. Delivery and expression of a corrective gene in the