

SUMMARY

[005] In an aspect, the present disclosure provides a construct comprising a promoter sequence operably linked to a first set of one or more copies of coding sequences each encoding a viral accessory protein or a recombinant viral vector genome, wherein the construct further comprises two recombinase recognition sites in opposite orientations.

[006] In another aspectexample, the present disclosure provides a construct comprising a promoter sequence flanked by two sets of oppositely oriented coding sequences each encoding a viral accessory protein or a recombinant viral vector genome, wherein the promoter is capable of being inverted upon a recombination event inducible by a recombinase, wherein the promoter is operably linked to a first set of the two sets of oppositely oriented coding sequences prior to recombination and becomes operably linked to a second set of the two sets of oppositely oriented coding sequences post recombination. In another aspectexample, the construct of the present disclosure may further comprise one or more endonuclease recognition motifs.

[007] In another aspectexample, the present disclosure provides a method of producing a viral vector producer cell with an optimized stoichiometric ratio of viral vector genome and viral accessory proteins, wherein the method comprises:

- a. introducing a construct described here into a first clonal population of cells;
- b. transiently providing a recombinase to the first clonal population; and
- c. producing a second clonal population by inverting the promoter

[008] In another aspectexample, the present disclosure provides a method comprising:

- a. obtaining a first stable viral vector producer cell line;
- b. determining a viral titer from the first stable viral vector producer cell line; and
- c. engineering one or more elements in the stable viral vector producer cell line to produce a second stable viral vector producer cell line with a stoichiometric ratio of viral vector genome and one or more viral accessory proteins different from the corresponding stoichiometric ratio in the first stable viral vector producer cell line.

BRIEF DESCRIPTION OF THE DRAWINGS

[009] **Figure 1** provides an illustration of the genome organization of the HIV-1 Virus. The HIV-1 genome contains 9,749 bp. In addition to the *gag*, *pol*, and *env* genes common to