CLAIMS

1. A method of designing a recombinant poxvirus, comprising performing by processing means (11) of a server (1) the steps of:
   (a) selecting a first subset of candidate peptides from a set of candidate peptides, wherein the candidate peptides of the first subset of candidate peptides present transmembrane scores below a transmembrane score threshold, wherein the transmembrane score of a candidate peptide is indicative of a probability that the candidate peptide bears at least one transmembrane segment;
   (b) determining an optimal distribution of the candidate peptides of the first subset of candidate peptides to one or more expression cassette among a plurality of possible distributions, wherein said determining comrpises, when the one or more expression cassettes comprises at least two expression cassettes, calculating for each possible distribution a range between hydropathy scores of the at least two expression cassettes and selecting as the optimal distribution the possible distribution having the lowest range;
   (c) for each of the one or more expression cassettes, determining an optimal slot assignment of the candidate peptides of the first subset of candidate peptides as function of a cassette slot occupancy rule so as to select a peptide fusion with a lowest transmembrane score, wherein said cassette slot occupancy rule defines possible slot positions of candidate peptides of the first subset of candidate peptides within an expression cassette according to transmembrane scores of the candidate peptides, and, in case of equal transmembrane scores, according to hydropathy scores of the candidate peptides;
   (d) determining a DNA transfer sequence comprising a nucleotide sequence of the one or more expression cassette for generation of said recombinant poxvirus.

2. The method of claim 1, wherein the candidate peptides of the first subset of candidate peptides present continuous regions below a homology threshold.

3. The method of claim 1, wherein the plurality of possible distributions does not exceed a given maximum number of possible distributions.

4. The method of claim 3, wherein step (a) comprises discarding candidate peptides

which transmembrane scores is above the transmembrane score threshold and/or which have a region of sequence identity above an identity threshold with another candidate peptide predicted to have a higher immunogenic potential, and selecting a second subset of candidate peptides wherein the candidate peptides of the second subset are neither discarded nor selected in the first subset.

5. The method of claim 4, further comprising, when for each possible distribution, at least one expression cassette presents an hydropathy score above a given threshold, reiterating step (b) with another plurality of possible distributions or replacing the candidate peptide from the first subset of candidate peptides presenting the highest hydropathy score by a candidate peptide from the second subset of candidate peptides, and reiterating step (a).

6. The method of any one of claims 1 to 5, wherein step (c) further comprises discarding any peptide fusion that displays at least one transmembrane patch with a score above a transmembrane patch score threshold.

7. The method of claim 6, wherein step (a) comprises discarding candidate peptides which transmembrane scores is above the transmembrane score threshold and/or which have a region of sequence identity above an identity threshold with another candidate peptide predicted to have a higher immunogenic potential, and selecting a second subset of candidate peptides wherein the candidate peptides of the second subset are neither discarded nor selected in the first subset.

8. The process of claim 7, wherein step (c) comprises, when at least one transmembrane domain is detected in any possible slot assignment of the candidate peptides in an expression cassette, replacing the candidate peptide from the first subset of candidate peptides presenting the highest transmembrane score, by a candidate peptide from the second subset, and repeating steps (b) then (c).

9. The method of claim 1, wherein the candidates peptides distributed to an expression cassette are classified in one of at least three classes and wherein said cassette slot

occupancy rule defines, for each slot position of an expression cassette, in which class a candidate peptide shall be classified to be assigned to this slot position.

10. The method of claim 1, wherein there is/are a single expression cassette when the number of candidate peptides in the first subset of candidate peptides is below 10, two expression cassettes when the number of candidate peptides in the first subset of candidate peptides is between 10 and 14, and three expression cassettes when the number of candidate peptides in the first subset of candidate peptides is between 15 and 30.

11. A method for preparing a therapeutic vaccine comprising a recombinant poxvirus, comprising:
    - performing the method of claim 1 to 9 for designing said recombinant poxvirus;
    - generating said recombinant poxvirus.

12. The method according to claim 11, wherein said process further comprises a manufacturing step of said recombinant poxvirus, wherein said manufacturing step comprises amplifying the recombinant poxvirus in a producer cell and recovering the amplified recombinant poxvirus.

13. The method according to any one of claims 11 and 12, wherein said recombinant poxvirus encodes neopeptides..