This technical problem is solved by the provision of the embodiments as defined in the claims.

Other and further aspects, features and advantages of the present invention will be apparent from the following description of the presently preferred embodiments of the invention. These embodiments are given for the purpose of disclosure.

BRIEF SUMMARY OF THE INVENTION

In one aspect, provided herein is 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 comprises, 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.

In another aspect, provided herein is 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.

According to a first ~~aspect~~example, the present ~~invention~~disclosure is related to a process for designing a recombinant poxvirus, said recombinant poxvirus comprising one or more expression cassettes, each for expression of a fusion of one or a plurality of peptides, characterized in that it comprises performing by processing means of a server the steps of:

(a) selecting a first subset of candidate peptides, wherein said peptides present transmembrane scores below a TMS threshold;

(b) determining an optimal distribution of the candidate peptides from said first subset to the expression cassette(s) among a plurality of possible distributions, wherein said optimal distribution presents, if there are at least two expression cassettes, the lowest range between the hydropathy scores of at least two expression cassettes;

(c) for each expression cassette, determining an optimal slot assignment of the candidate peptides as function of cassette slot occupancy rule and selecting the peptide fusion with the lowest TM score;

(d) determining a DNA transfer sequence comprising the nucleotide sequence of the one or more expression cassette(s) for generation of said recombinant poxvirus.

According to advantageous and non-limiting features:

Said peptides of step (a) present continuous regions below a homology threshold.

Step (a) comprises discarding peptides if they present transmembrane scores above a TMS threshold and/or an homologous region with a higher ranked candidate according to a predicted immunogenic potential above an homology threshold, and selecting a second subset of the identified set of candidate peptides as candidate peptides neither disclosed nor selected in the first subset.

Step (b) comprises, if the number of possible distributions exceeds a given maximum number function of resources of the processing means of the server, attempting to determine said optimal distribution of the candidate peptides from said first subset to the expression cassette(s) among at least one iteration of said maximum number of possible distributions among the plurality of possible distributions

Step (b) comprises, if for each possible distribution of an iteration of said maximum number of possible distributions, at least one expression cassette presents an hydropathy score above a given threshold, either considering another iteration of said maximum number 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, and proceeding again with a peptide selection.

Step (c) further comprises discarding any peptide fusion that displays at least one TM patch with a score above a TMSK7 threshold.

Step (c) comprises, if 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).

Said cassette slot occupancy rule defines possible slot positions of candidate peptides within a cassette according to transmembrane scores of the peptides, and, in case of equal transmembrane scores, according to their hydropathy scores.

The candidates peptides distributed to an expression cassette are classified according to at least three classes of risk of not generating or producing any recombinant poxvirus, wherein said cassette slot occupancy rule defining, for each slot positions of a cassette, what class a candidate peptide shall have to be assigned to this slot position.

Said optimal slot assignment of the candidate peptides distributed to an expression cassette presents a transmembrane score below a given threshold.

There is/are a single expression cassette if the number of selected candidate peptides is below 10, two expression cassettes if the number of selected candidate peptides is between 10 and 14, and three expression cassettes if the number of selected candidate peptides is between 15 and 30.

According to a second ~~aspect~~example, the ~~invention~~disclosure is related to a process for preparing a therapeutic vaccine comprising a recombinant poxvirus, comprising:

- performing the process according to the first ~~aspect~~example for designing said recombinant poxvirus;
- generating said recombinant poxvirus.

According to advantageous and non-limiting features:

Said process further comprises a manufacturing step of said recombinant poxvirus, wherein said manufacturing step comprises an amplification step in a suitable producer cell to a suitable scale, a step of recovery of the produced recombinant poxvirus from the cell culture and an optional step of purification of the recovered recombinant poxvirus.

Said recombinant poxvirus encodes neopeptides and is for use as a personalized cancer vaccine.

According to a third ~~aspect~~example, the ~~invention~~disclosure is related to a personalized cancer vaccine obtained according to the process according to the second ~~aspect~~example, wherein said personalized cancer vaccine is a composition comprising a therapeutically effective amount of said recombinant poxvirus and a pharmaceutically acceptable vehicle, preferably for use in a subject in need thereof for treating a cancer or preventing its relapse in a subject.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 represents the general scheme of a process according to the invention for designing a recombinant poxvirus for expression of fusion(s) of peptide(s). The main steps (a) to (d) are indicated in grey boxes (HSK7: fusion hydropathy score; HSK7Thresh: HSK7 threshold; TM patch: transmembrane patch; TMSK7: fusion TMS threshold).

Figure 2 represents an architecture for performing the process according to the invention involving a server 1, data processing means 11, storage means 12 and an interface 13.

Figure 3 is a flowchart illustrating an embodiment of a step (a) of selecting the candidate peptides suitable for expression by the recombinant poxvirus in the process according to the invention (TMS: transmembrane score; TMSThresh: peptide TMS threshold; N: number of total candidate peptides; Nmax: maximal number of peptides).

Figure 4 is a flowchart illustrating an embodiment of a step (b) of determining an optimal inter-cassette distribution of the candidate peptides in the process according to the