not require the addition of any prodrug, that also contributes to the ease of use and safety of the present invention.

Based on these results, one may anticipate that the oncolytic viruses of the invention may be successfully used as an alternative to the other existing oncolytic viruses, and may have a better efficiency profile. The oncolytic viruses of the invention can also be exploited in combination with additional anticancer therapy/ies.

SUMMARY

In one aspect, the present disclosure refers to an oncolytic poxvirus defective in the J2R locus comprising a nucleotide sequence encoding a cytidine deaminase (CDAse) polypeptide. In another aspect, the present disclosure refers to a process for preparing an oncolytic poxvirus, in which process: (i) An oncolytic poxvirus as disclosed herein is introduced into a producer cell selected from the group consisting of HeLa, 293 cells, HER96, PER-C6, Vero, CV1, BSC1, BHK-21 and CEF cells; (ii) said producer cell is cultured under conditions which are appropriate for enabling said oncolytic poxvirus to be produced, and; (iii) said oncolytic poxvirus is recovered from the cell culture. In another aspect, the present disclosure refers to a composition comprising the oncolytic poxvirus as disclosed herein, or the oncolytic poxvirus prepared as disclosed herein, which further comprises a pharmaceutically acceptable vehicle, wherein said composition preferably comprises a dose of oncolytic virus comprised between 10^6 and $5x10^9$ PFU, and wherein said oncolytic virus is preferably formulated for parenteral route administration with a preference for intravenous or intratumoral route. In another aspect, the present disclosure refers to the oncolytic poxvirus as disclosed herein, or the oncolytic poxvirus prepared as disclosed herein, or the composition as disclosed herein, for use in the treatment of a disease or a pathologic condition in a subject in need thereof. In yet another aspect, the present disclosure refers to the use of the oncolytic poxvirus of the present disclosure, or the oncolytic poxvirus prepared according to the present disclosure, or the composition as disclosed herein, in the manufacture of a medicament for ~~the prophylaxis or~~ the treatment of ~~a proliferative disease~~cancers and/or tumors.

One example of the disclosure relates to an oncolytic virus comprising a nucleotide sequence encoding a cytidine deaminase (CDAse) polypeptide.

CLAIMS

1. An oncolytic poxvirus defective in the J2R locus comprising a nucleotide sequence encoding a cytidine deaminase (CDAse) polypeptide.

2. The oncolytic poxvirus of claim 1, wherein said CDAse polypeptide is selected from the group consisting of cytidine deaminase (CDA, CDD), EC 3.5.4.5, APOBEC, Activation-induced deaminase (AID) and cytidine deaminase-like proteins.

3. The oncolytic poxvirus of claim 2, wherein said APOBEC is selected from the group consisting of APOBEC1, APOBEC2, APOBEC3A, APOBEC3B, APOBEC3C, APOBEC3D, APOBEC3E, APOBEC3F, APOBEC3G, APOBEC3H and APOBEC4, and preferably wherein said APOBEC is APOBEC2.

4. The oncolytic poxvirus of claim 1 or 2, wherein said CDAse is a yeast cytidine deaminase (CDD1), preferably a CDD1 comprising an amino acid sequence having at least 80%, preferably greater than 90%, and more preferably greater than 95% identity with SEQ ID NO:1, or a human cytidine deaminase (hCD), preferably a hCD comprising an amino acid sequence having at least 80%, preferably greater than 90%, and more preferably greater than 95% identity with SEQ ID NO:2.

5. The oncolytic poxvirus of claim 3, wherein said APOBEC2 comprises an amino acid sequence having at least 80%, preferably greater than 90%, and more preferably greater than 95% identity with SEQ ID NO:3.

6. The oncolytic poxvirus of any of claims 1 to 5, wherein said CDAse polypeptide catalyses the deamination of cytidine-based components, preferably cytidine-based components that are free or complexed, to uridine-based components, like cytidine to uridine and deoxycytidine (dC) to deoxyuridine (dU).

7. The oncolytic poxvirus of any of claims 1 to 6, wherein said poxvirus is a poxvirus belonging to the Orthopoxvirus genus, wherein said poxvirus preferably belongs to the vaccinia virus (VV) species, preferably selected from the group consisting of Copenhagen, Wyeth and Western Reserve (WR), or to the cowpox virus species.

8. The oncolytic poxvirus of any of claims 1 to 7, wherein said virus is further defective in the I4L and/or F4L locus, wherein said virus is optionally a vaccinia virus defective in viral TK and RR encoded activities which encodes a human or yeast CDAse.

9. The oncolytic poxvirus of any of claims 1 to 8, wherein said virus further comprises one or more nucleic acid(s) of interest, said nucleic acid of interest preferably encoding an immunostimulatory polypeptide, an antigen or a permease.

10. The oncolytic poxvirus of any of claims 1 to 9, wherein said virus further comprises the elements necessary for the expression of said cytidine deaminase and said one or more nucleic acid(s) of interest.

11. A process for preparing an oncolytic poxvirus, in which process:

    (i) An oncolytic poxvirus according to anyone of claims 1 to 10 is introduced into a producer cell selected from the group consisting of HeLa, 293 cells, HER96, PER-C6, Vero, CV1, BSC1, BHK-21 and CEF cells;

    (ii) said producer cell is cultured under conditions which are appropriate for enabling said oncolytic poxvirus to be produced, and;

    (iii) said oncolytic poxvirus is recovered from the cell culture.

12. A composition comprising the oncolytic poxvirus of any one of claims 1 to 10, or the oncolytic poxvirus prepared according to claim 11, which further comprises a pharmaceutically acceptable vehicle, wherein said composition preferably comprises a dose of oncolytic virus comprised between 10^6 and $5x10^9$ PFU, and wherein said oncolytic virus is preferably formulated for parenteral route administration with a preference for intravenous or intratumoral route.

13. The oncolytic poxvirus of any one of claims 1 to 10, or the oncolytic poxvirus prepared according to claim 11, or the composition of claim 12, for use in the treatment of a disease or a pathologic condition in a subject in need thereof.

14. Use of the oncolytic poxvirus of any one of claims 1 to 10, or the oncolytic poxvirus prepared according to claim 11, or the composition of claim 12, in the manufacture of a medicament for ~~the prophylaxis or~~ the treatment of ~~a~~ cancers and/or tumors~~proliferative disease~~.

~~15. The use of claim 14, wherein the proliferative disease is selected from the group consisting of cancer, tumor and restenosis.~~

~~16.~~15. The use of claim ~~15~~14, wherein the cancer is a gastro-intestinal cancer, preferably comprising a cancer of oesophagus, gallbladder, liver, pancreas, stomach, small intestine, bowel (large intestine or colon and rectum), or anus.

~~17.~~16. The use of ~~any one of~~ claim~~s~~ 14 ~~to 16~~or 15, further comprising that one or more substances effective in anticancer therapy are to be administered.