CLAIMS

1. Use of a composition comprising a recombinant modified vaccinia Ankara (MVA) virus selected from the group consisting of: (i) MVA harboring a human Fms-like tyrosine kinase 3 ligand (hFlt3L) (MVA-hFlt3L); (ii) MVA with deletion of vaccinia virulence factor E3 (MVAΔE3L) harboring hFlt3L (MVAΔE3L-hFlt3L); and (iii) a combination thereof, in the manufacture of a medicament, for treating a malignant solid tumor in a subject in need thereof, wherein the recombinant MVA is to be administered by intratumoral injection.

2. The use of claim 1, wherein the composition is to be administered in an amount effective to: induce, in the subject, an immune response against the tumor or enhance or promote in the subject an ongoing immune response against the tumor; reduce the size of the tumor; eradicate the tumor; inhibit growth of the tumor; inhibit metastasis of the tumor; and/or reduce or eradicate metastatic tumor.

3. The use of claim 2, wherein to induce, enhance or promote the immune response comprises one or more of the following:

   proliferation and activation of $CD8^+$ cytotoxic T cells;

   proliferation and activation of $CD4^+$ effector T cells;

   increase of the ratio of $CD8^+$/Treg and of Tconv/Treg;

   recruitment of $CD45^+$ cells and $CD8^+$ T cells in injected and distant tumors;

   reduction of tumor-associated macrophages (TAM) in injected and distant tumors;

   influx of $Ly6C^{hi}CD11b^+$ inflammatory monocytes and $Ly6C^{hi}CD11b^-$ myeloid cells into injected and distant tumors;

   activation and mobilization of cross-presenting $CD103^+$ dendritic cells in injected and distant tumors via the production of type IFN and proinflammatory cytokines; and

   generation of anti-tumor $CD8^+$ T cells and cross-protection against heterologous tumor(s).

4. The use of claim 1 wherein the recombinant MVA is not harboring nucleic acid encoding or expressing a tumor antigen.

5. The use of claim 1 or 2, wherein the composition further comprises one or more pharmaceutically acceptable excipients, optionally or preferably wherein the one or more excipients is selected from the group consisting of solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic agents, absorption delaying agents and combinations of two or more of the foregoing.

6. The use of any one of claims 1-5, wherein the recombinant MVA comprises MVAΔE3L-hFlt3L.

7. The use of any one of claims 1-6, wherein the composition further comprises a second amount of a replication competent recombinant attenuated vaccinia virus with deletion of thymidine kinase encoding and expressing human Flt3L, wherein the second amount contributes to augmenting the induced or enhanced or promoted immune response; and/or

   the composition further comprises a third amount of inactivated MVA, wherein the third amount contributes to augmenting the induced or enhanced or promoted immune response.

8. The use of any one of the preceding claims, wherein the tumor is melanoma or colon carcinoma.

9. The use of any one of the preceding claims, wherein the recombinant MVA is to be administered for several weeks, months or years or indefinitely, as long as benefits persist or a maximum tolerated dose is reached.

10. The use of any one of the preceding claims, wherein the recombinant MVA is to be administered at a dosage per administration within a range of 10^6 - 10^{10} plaque-forming units (pfu), preferably within the range of 10^7 to 10^9 plaque-forming units (pfu); and/or

wherein the amount delivered is sufficient to infect all tumor cells; and/or

wherein the administration is intended to be repeated with a frequency within the range from once per month to two times per week, optionally or preferably repeated once weekly

11. The use of any one of the preceding claims, further comprising the conjoint use of a composition comprising an immune checkpoint blocking agent or an immune checkpoint agonist effective to block immune suppressive mechanisms within the tumor, wherein the immune checkpoint blocking agent or immune checkpoint blocking agonist is to be simultaneously or sequentially administered by systemic or intratumoral injection.

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12. The use of claim 11, wherein the immune checkpoint blocking agent is selected from the group consisting of PD-1 inhibitors, PD-L1 inhibitors, CTLA4 inhibitors, inhibitory antibodies against LAG- 3 (lymphocyte activation gene 3), TIM3 (T cell Immunoglobulin and Mucin-3), B7-H3, and TIGIT (T-cell immunoreceptor with Ig and ITIM domains); CD80, CD86, PDL2, B7-H4, II and DLBCL inhibitors, BTLA, or any combination thereof; and the immune checkpoint agonist is selected from the group consisting of anti-ICOS antibody, anti-OX40 antibody, agonist antibody against 4- IBB (CD 137) and against GITR; or

    wherein the immune checkpoint blocking agent comprises CTLA-4, CD80, CD86, PD-1, PDL1, PDL2, LAG3, B7-H3, B7-H4, TIM3, ICOS, II DLBCL inhibitors, BTLA, or any combination thereof; or

    wherein the immune checkpoint blocking agent comprises ipilimumab, nivolumab, pembrolizumab, pidilizumab, AMP-224, MPDL3280A, BMS-936559, MEDI4736, MSB 00107180, or any combination thereof.

13. A kit comprising:

    1) A first component comprising:
    (a) a recombinant modified vaccinia Ankara virus with deletion of vaccinia virulence factor E3 (MVAΔE3L) harboring human Fms-like tyrosine kinase 3 ligand (hFlt3L) (MVAΔE3L-hFlt3L); or
    (b) MVAΔE3L-hFlt3L and MVA harboring a human Fms-like tyrosine kinase 3 ligand (hFlt3L) (MVA-hFlt3L); and

2) a second component comprising one or both of a replication competent recombinant attenuated vaccinia virus with deletion of thymidine kinase encoding and expressing GM-CSF or human Flt3L, and inactivated MVA, respectively in a second and third amount, said second amount or third amount or both second and third amount contributing to augmenting the induced or enhanced or promoted immune response in a subject.

14. A recombinant modified vaccinia Ankara virus with deletion of vaccinia virulence factor E3 (MVAΔE3L) modified to express human Fms-like tyrosine kinase 3 ligand (hFlt3L), for use in treating a malignant solid tumor.