(2007)), on the other hand, are not physiologically-relevant, and/or are end-point tests that only focus on the bulk behavior of highly heterogeneous cellular populations.

SUMMARY

[0002a] In an aspect of the present disclosure, there is provided a method for producing a therapeutic stealth cell, comprising

(a) sorting tumor cells from a subject for a subpopulation of $CD11b^{+}Ly6C^{lo}Ly6G^{+}$ myeloid-derived suppressor cells; and

(b) engineering the subpopulation to contain anti-cancer agents, thereby producing a therapeutic stealth cell.

[0002b] In another aspect of the present disclosure, there is provided a composition, comprising a plurality of therapeutic stealth cell produced by the method disclosed herein.

[0002c] In a further aspect of the present disclosure, there is provided a use of a composition disclosed herein in the manufacture of a medicament for treating a tumor in a subject.

[0002d] In another aspect of the present disclosure, there is provided a composition disclosed herein for use in treating a tumor in a subject.

[0003] There is a subset of GSCs and MDSCs that exhibit high dissemination and therapy-resistance capacity. These findings suggest that GSCs and MDSCs are not monolithic populations, and that specific clonal subsets exhibit significantly more “aggressive” phenotypes, which could presumably be responsible for driving disease relapse.

[0004] Disclosed herein is a method of “reprogramming” highly motile cells found in tumors, such as these highly motile GSC and/or MDSC clones, into “auto-destructive” cell “missiles” (referred to herein as therapeutic stealth cells) that can seek and destroy new foci of recurrence within the body, such as the brain. Cells with enhanced motility can be sorted out from heterogeneous populations and then be rendered “auto-destructive” by deterministic delivery of an anti-cancer agent, such as an oncolytic virus plasmid cocktail.

[0005] The disclosed method can involve sorting cells from a subject to create the therapeutic stealth cells. In some examples, the cells are autologous, such as a blood cells or a tumor biopsy from the subject to be treated. However, in some cases, the cells are allogenic.

[0006] The disclosed method can involve sorting cells from a subject for a highly motile subpopulation and then reprogramming the subpopulation to deliver anti-cancer agents. In some examples, the subpopulation can be sorted in a migration assay using a chemoattractant gradient. In particular, the chemoattractant gradient can involve a chemokine produce by the tumor to be treated. For example, in some

WHAT IS CLAIMED IS:

1. A method for producing a therapeutic stealth cell, comprising

   (a) sorting tumor cells from a subject for a subpopulation of $CD11b^{+}Ly6C^{lo}Ly6G^{+}$ myeloid-derived suppressor cells; and

   (b) engineering the subpopulation to contain anti-cancer agents, thereby producing a therapeutic stealth cell.

2. The method of claim 1, wherein the subpopulation is sorted in a migration assay using a chemoattractant gradient.

3. The method of claim 1 or 2, wherein the subpopulation is sorted in a migration assay using a nanotextured and/or biomimetic surface.

4. The method of any one of claims 1 to 3, wherein the subpopulation is sorted in a transwell migration assay or Boyden chamber assay.

5. The method of any one of claims 1 to 4, wherein the subpopulation is engineered to heterologously express a transgene encoding an anti-tumor protein, oligonucleotide, or combination thereof.

6. The method of claim 5, wherein the transgene encodes tissue inhibitor of metalloproteinase-3 (TIMP-3).

7. The method of any one of claims 1 to 6, wherein the subpopulation is engineered with a kill switch system.

8. The method of any one of claims 1 to 7, wherein the subpopulation is sorted by flow cytometry.

9. A composition, comprising a plurality of therapeutic stealth cell produced by the method of any one of claims 1 to 8.

10. The composition of claim 9, further comprising a pharmaceutically acceptable excipient.

11. Use of a composition of claim 10 in the manufacture of a medicament for treating a tumor in a subject.

12. The use of claim 11, wherein the tumor is breast cancer.

13. A composition of claim 10 for use in treating a tumor in a subject.

14. The composition for use of claim 13, wherein the tumor is breast cancer.