SUMMARY OF THE INVENTION

[0004a] In one aspect, provided herein is a cell or a population thereof, wherein: (i) the cell is (a) an induced pluripotent cell (iPSC); or (b) a derivative effector cell obtained from differentiating the iPSC; and (ii) the cell comprises: an exogenous polynucleotide encoding a CXCR2; and optionally a chimeric antigen receptor (CAR).

[0004b] In another aspect, provided herein is a method for improving T lineage cell migration and/or tumor cell control and clearance, the method comprising: obtaining a T lineage cell comprising an exogenous polynucleotide encoding a CXCR2, and expanding the T lineage cell, thereby producing a T lineage cell population having improved cell migration and/or tumor cell control and clearance as compared to counterpart cells without the exogenous polynucleotide encoding the CXCR2, wherein the T lineage cell: (i) is derived from an iPSC, or (ii) further comprises a chimeric antigen receptor (CAR).

[0004c] In another aspect, provided herein is a method of producing a clonal master engineered iPSC line using CRISPR, ZFN, or TALEN mediated editing of clonal iPSCs, wherein the editing comprises a knock-in of a polynucleotide encoding a CXCR2 and optionally a CAR, thereby producing the engineered iPSCs.

[0004d] In another aspect, provided herein is the composition as described herein for use in therapy.

[0004e] In another aspect, provided herein is use of the composition as described herein in the manufacture of a medicament for treating a tumor of a subject, wherein the composition is to be administered to the subject, and wherein the tumor comprises tumor cells preconditioned with a sensitizing agent.

[0005] There is a need for functionally improved effector cells that address issues ranging from response rate, cell exhaustion, loss of transfused cells (survival and/or persistence), tumor escape through target loss or lineage switch, tumor targeting precision, off-target toxicity, off-tumor effect, to efficacy against solid tumors, i.e., tumor microenvironment and related immune suppression, recruiting, trafficking and infiltration.

[0006] It is an object of embodiments of the present invention to provide methods and compositions to generate derivative non-pluripotent cells differentiated from a single cell derived iPSC (induced pluripotent stem cell) clonal line, which iPSC line comprises one or several genetic modifications in its genome. Said one or several genetic modifications include, in some embodiments, DNA insertion, deletion, and substitution, and which modifications are retained and remain functional in subsequently derived cells after differentiation, expansion, passaging and/or transplantation.

[0007] The iPSC-derived non-pluripotent cells of the present application include, but are not limited to, CD34 cells, hemogenic endothelium cells, HSCs (hematopoietic stem and progenitor cells), hematopoietic multipotent progenitor cells, T cell progenitors, NK cell progenitors, T cells, NKT cells, NK cells, and B cells. The iPSC-derived non-pluripotent cells of the present application comprise one or several genetic modifications in their genome through differentiation from an iPSC comprising the same genetic modifications. In some embodiments, the engineered clonal iPSC differentiation strategy for obtaining genetically engineered derivative cells benefits from the developmental potential of the iPSC in a directed differentiation that is not significantly impacted by the engineered modality in the iPSC, and also that the engineered modality functions as intended in the derivative cell. Further, this strategy overcomes the present barrier in engineering primary lymphocytes, such as T cells or NK cells obtained from peripheral blood, as such cells are difficult to engineer, with engineering of such cells often lacking reproducibility and uniformity, resulting in cells exhibiting poor cell persistence with high cell death and low cell expansion. Moreover, this strategy avoids production of a heterogenous effector cell population otherwise obtained using primary cell sources which are heterogenous to start with.

[0008] Some aspects of the present invention provide genome-engineered iPSCs obtained using a method comprising (I), (II) or (III), reflecting a strategy of genomic engineering subsequently to, simultaneously with, and prior to the reprogramming process, respectively:

(I): genetically engineering iPSCs by one or both of (i) and (ii), in any order: (i) introducing into iPSCs one or more construct(s) to allow targeted integration at selected site(s); (ii) (a) introducing into iPSCs one or more double stranded break(s) at selected site(s) using one