EXTRACELLULAR VESICLES FOR TARGETED THERAPIES AGAINST MYELOID-DERIVED SUPPRESSOR CELLS

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims benefit of U.S. Provisional Application No. 62/747,982, filed October 19, 2018, which is hereby incorporated herein by reference in its entirety.

SEQUENCE LISTING

[0002] This application contains a sequence listing filed in electronic form as an ASCII.txt file entitled “321501-2360 Sequence Listing_ST25” created on October 16, 2019. The content of the sequence listing is incorporated herein in its entirety.

BACKGROUND

[0003] Myeloid-derived suppressor cells (MDSCs) play a fundamental role in a number of physiological and pathological processes, including cancer, wound healing and tissue repair. MDSCs, for example, enable tumor/cancer progression by shielding tumor cells from the host's immune system and/or anti-cancer therapies, and by promoting tumor cell dissemination/spreading. As such, therapeutic approaches need to be developed to selectively target MDSCs and modulate their activity.

SUMMARY

[0003a] In an aspect of the present disclosure, there is provided a fusion protein comprising ICAM1 and ~~an~~ a heterologous exosomal or lysosomal transmembrane protein.

[0003b] In another aspect of the present disclosure, there is provided a cell comprising a nucleic acid encoding the fusion protein disclosed herein.

[0003c] In a further aspect of the present disclosure, there is provided a method of producing an extracellular vesicle, comprising culturing the cell disclosed herein under conditions suitable for vesicle secretion, and isolating extracellular vesicles secreted by the cell.

[0003d] In another aspect of the present disclosure, there is provided a use of an extracellular vesicle disclosed herein in the manufacture of a medicament for treating cancer in a subject.

[0003e] In a further aspect of the present disclosure, there is provided an extracellular vesicle disclosed herein for use in treating cancer in a subject.

[0004] Disclosed herein is a nanocarrier system to effectively target MDSCs and deliver therapeutic cargo. These nanocarriers are based on designer extracellular vesicles

WHAT IS CLAIMED IS:

1. A fusion protein comprising ICAM1 and a~~n~~ heterologous exosomal or lysosomal transmembrane protein.
2. The extracellular vesicle comprising the fusion protein of claim 1.
3. The extracellular vesicle of claim 2, further comprising a therapeutic cargo.
4. The extracellular vesicle of claim 3, wherein the therapeutic cargo comprises miR146a.
5. The extracellular vesicle of claim 3 or 4, wherein the therapeutic cargo comprises Ibrutinib.
6. A cell comprising a nucleic acid encoding the fusion protein of claim 1.
7. The cell of claim 6, further comprising a nucleic acid encoding a therapeutic RNA.
8. A method of producing an extracellular vesicle, comprising culturing the cell of claim 6 or 7 under conditions suitable for vesicle secretion, and isolating extracellular vesicles secreted by the cell.
9. The method of claim 8, further comprising loading the extracellular vesicle with a therapeutic drug.
10. Use of an extracellular vesicle of any one of claims 3 to 5 in the manufacture of a medicament for treating cancer in a subject.
11. The use of claim 10, wherein the subject has circulating myeloid-derived suppressor cells (MDSCs).
12. An extracellular vesicle of any one of claims 3 to 5 for use in treating cancer in a subject.
13. The extracellular vesicle for use of claim 12, wherein the subject has circulating myeloid-derived suppressor cells (MDSCs).