PM21 PARTICLES TO IMPROVE BONE MARROW HOMING OF NK CELLS

This application claims the benefit of U.S. Provisional Application No. 62/464,747, filed on February 28, 2017, and which is incorporated herein by reference in its entirety.

I. BACKGROUND

Adoptive natural killer (NK) cell therapy is a promising novel intervention for oncology including for bone marrow malignancies. Therefore, the efficiency for trafficking of the NK cells to be used adoptively is of high importance. What are needed are methods that can efficiently traffic NK cells to the bone marrow.

II. SUMMARY

1. Disclosed are methods and compositions related to trafficking NK cells to the bone marrow comprising contacting NK cells with PM21 particles and/or FC21 feeder cells. In one example, the methods can further comprise stimulating the NK cells with IL-2, IL-12, IL-18, and/or IL-18.

2. Also disclosed are methods of treating a bone marrow malignancy or bone marrow born malignancy and/or treating a viral infection (such as a bone marrow associated viral infection including a bone marrow tropic viral infection or viral infection that adversely effects the bone marrow) comprising contacting NK cells with PM21 particles and/or FC21 feeder cells and adoptively transferring NK cells to the subject. In some examples, the contact of the PM21 particles and/or FC21 feeder cells with the NK cells can occur prior to transfer of the NK cells to a patient. In another example, the contact of the PM21 particles and/or FC21 feeder cells with the NK cells can occur in the patient.

In one aspect, the present disclosure refers to use of PM21 particles in the manufacture of a medicament for trafficking NK cells to the bone marrow said use comprising contacting NK cells with PM21 particles.

In another aspect, the present disclosure refers to use of NK cells with one or more of PM21 particles and FC21 feeder cells in the manufacture of a medicament for trafficking NK cells to the bone marrow, said use comprising contacting NK cells with one or more of PM21 particles and FC21 feeder cells prior to transfer of the NK cells to a patient.

In yet another aspect, the present disclosure refers to use of PM21 particles in the manufacture of a medicament for treating a bone marrow malignancy or bone marrow born malignancy in a subject wherein said use comprises contacting NK cells with PM21 particles and adoptively transferring the NK cells to the subject.

In yet another aspect, the present disclosure refers to use of NK cells with PM21 particles and/or FC21 feeder cells in the manufacture of a medicament for treating a bone marrow

malignancy or bone marrow born malignancy in a subject, wherein said use comprises contacting NK cells with PM21 particles and/or FC21 feeder cells and adoptively transferring the NK cells to the subject.

In yet another aspect, the present disclosure refers to use of PM21 particles in the manufacture of a medicament for treating a viral infection associated with the bone marrow in a subject wherein said use comprises contacting NK cells with PM21 particles and and adoptively transferring the NK cells to the subject.

In yet another aspect, the present disclosure refers to use of NK cells with one or more of PM21 particles and FC21 feeder cells in the manufacture of a medicament for treating a viral infection associated with the bone marrow in a subject, wherein said use comprises contacting NK cells with one or more of PM21 particles and FC21 feeder cells and adoptively transferring the NK cells to the subject.

III. BRIEF DESCRIPTION OF THE DRAWINGS

3. The accompanying drawings, which are incorporated in and constitute a part of this specification, illustrate several embodiments and together with the description illustrate the disclosed compositions and methods.

4. Figure 1 shows that PM-21 particles expand cytotoxic NK cells efficiently and selectively. Peripheral blood mononuclear cells (PBMCs) were isolated from leukocyte source and seeded at 0.1 x 10^6 NK cells/mL in SCGM supplemented with 10% FBS, 2 mM Glutamax and 50 U/mL IL-2. PBMCs were stimulated with PM15 (□, black) or PM21 (○, blue) particles at 200 µg/mL for 27 days, the cell content was tested every 2-3 days and shown are relative fold of NK cell expansion (A) and the percentage of suspension cells (B). PM21-particles (825 ± 188 fold, N=13, 4 donors) (blue) are more efficient for NK cell expansion compared to PM15-particles (425 ± 71, N=35, 9 donors) (black) based on cumulative analysis of day 14 data for NK cell expansion (C). PBMCs isolated from three AML patients in remission were cultured for 14

V. CLAIMS

What is claimed is:

1. Use of PM21 particles in the manufacture of a medicament for trafficking NK cells to the bone marrow said use comprising contacting NK cells with PM21 particles.

2. Use of NK cells with one or more of PM21 particles and FC21 feeder cells in the manufacture of a medicament for trafficking NK cells to the bone marrow, said use comprising contacting NK cells with one or more of PM21 particles and FC21 feeder cells prior to transfer of the NK cells to a patient.

3. The use of claim 1 or claim 2, wherein said use further comprise stimulating the NK cells with IL-2, IL-12, and/or IL-18.

4. The use of claim 1, wherein the contact of the PM21 particles with the NK cells occurs following transfer of the NK cells to a patient.

5. The use of any of claims 1, 2, or 4, wherein the use induces cellular mechanism within NK cells to induce the fucosylation of PSGL-1 on the NK cells surface.

6. The use of any of claims 1, 2, or 4, wherein the use induces expression of FUT7 within NK cells correlating to the fucosylation of PSGL-1 on the NK cells surface.

7. Use of PM21 particles in the manufacture of a medicament for treating a bone marrow malignancy or bone marrow born malignancy in a subject wherein said use comprises contacting NK cells with PM21 particles and adoptively transferring the NK cells to the subject.

8. Use of NK cells with PM21 particles and/or FC21 feeder cells in the manufacture of a medicament for treating a bone marrow malignancy or bone marrow born malignancy in a subject, wherein said use comprises contacting NK cells with PM21 particles and/or FC21 feeder cells and adoptively transferring the NK cells to the subject.

9. Use of PM21 particles in the manufacture of a medicament for treating a viral infection associated with the bone marrow in a subject wherein said use comprises contacting NK cells with PM21 particles and and adoptively transferring the NK cells to the subject.

10. Use of NK cells with one or more of PM21 particles and FC21 feeder cells in the manufacture of a medicament for treating a viral infection associated with the bone marrow in a subject, wherein said use comprises contacting NK cells with one or more of PM21 particles and FC21 feeder cells and adoptively transferring the NK cells to the subject.

11. The use of any of claims 7-10, wherein the contact of the PM21 particles and/or FC21 feeder cells with the NK cells occurs prior to transfer of the NK cells to a patient.

12. The use of any of claims 7 or 9, wherein the contact of the PM21 particles with the NK cells occurs following transfer of the NK cells to a patient.