

We claim:

1. A CAR-NK cell therapy product comprising NK cells genetically modified to express a CD19 CAR and an IL-15 formulated in a cryopreservation medium comprising PLASMA-LYTE A, trehalose, CS10 and human serum albumin (HSA).

2. The cell therapy product of claim 1, wherein the CD19 CAR comprises an anti-CD19 binding domain comprising a heavy chain variable region having at least 95% identity to SEQ ID NO: 2 and/or a light chain variable region having at least 95% identity to SEQ ID NO: 1.

3. The cell therapy product of any one of the preceding claims, wherein the CD19 CAR comprises a heavy chain variable region having the sequence of SEQ ID NO: 2 and/or a light chain variable region having the sequence of SEQ ID NO: 1; and/or

wherein the transmembrane domain is selected from the group consisting of alpha, beta or zeta chain of the T-cell receptor, CD28, CD3 epsilon, CD45, CD4, CD5, CD8, CD9, CD16, CD22, CD33, CD37, CD64, CD80, CD86, CD134, CD137 and CD154; and/or

wherein the intracellular signaling domain is selected from the group consisting of FcR gamma, FcR beta, CD3 gamma, CD3 delta, CD3-zeta, CD3 epsilon, CD5, CD22, CD79a, CD79b and CD66d.

4. The cell therapy product of any one of the preceding claims, wherein the CD-19 CAR comprises a CD28 transmembrane domain having at least 95% identity to SEQ ID NO: 3, optionally

wherein the CD19 CAR comprises a CD28 transmembrane domain of SEQ ID NO: 3; and/or

wherein the CD19 CAR comprises a CD3z signaling domain having at least 95% identity to SEQ ID NO: 4, optionally

wherein the CD19 CAR comprises a CD3z signaling domain of SEQ ID NO: 4.

5. The cell therapy product of any one of the preceding claims, wherein the cell therapy product further comprises a suicide switch, wherein the suicide switch is iCaspase9; and/or wherein the NK cells are derived from cord-blood, peripheral blood, T cells or iPS cells; and/or wherein the cryopreservation medium comprises 25% v/v to 50% v/v PLASMA-LYTE A; and/or wherein the trehalose is at a concentration of between about 10mM – 100 mM; and/or wherein the HSA is at a concentration of between about 1.25% v/v to 25% v/v; and/or wherein the cryopreservation medium comprises between about 40% v/v to 60% v/v CS10.
6. The cell therapy product of any one of the preceding claims, further comprising a cryoprotectant, wherein the cryoprotectant is DMSO.
7. A composition comprising the cell therapy product of any one of the preceding claims.
8. A cell therapy product comprising a CAR-NK cell population comprising NK cells genetically modified to express a CD-19 CAR and an IL-15 formulated in a cryopreservation medium comprising PLASMA-LYTE A, trehalose, CS10 and HSA, wherein the CD19 CAR comprises an anti-CD19 binding domain comprising a heavy chain variable region having at least 95% identity to SEQ ID NO: 2 and/or a light chain variable region having at least 95% identity to SEQ ID NO: 1, for use in treating cancer, such as a B-cell lymphoma.
9. A large-scale method of cryopreserving immune cells, the method comprising:
- (a) providing a container comprising a sample comprising immune cells suspended in a cryopreservation medium, wherein the sample volume is at least 5 percent less than the full capacity volume of the container, and wherein the sample volume is at least 10 ml;

- (b) cooling the container from a temperature above freezing temperature of the sample to a temperature of about or below -80°C in a multi-step process at a controlled rate to minimize latent heat of fusion; and
- (c) storing the cells in liquid nitrogen vapor phase, thereby cryopreserving the immune cells.

10. The method of claim 9, wherein the cells are stored for 1 week, 2 weeks, 1 month, 6 months, 1 year, 2 years, 5 years, 10 years or more; and/or

wherein thawing the cryopreserved cells comprises: (a) heating a water bath to a temperature ranging from 37°C and 90°C ; (b) transferring a container comprising cryopreserved cells to the pre-heated water bath; and (c) agitating the container at a speed of between about 100 and about 250 RPM for a suitable period of time, thereby thawing the cells; and/or

wherein the total viable cells post thawing is between about 200 million to about 800 million cells.

11. The method of claim 10, wherein the method comprises changing temperature of a sample containing immune cells from a first temperature above the freezing temperature of the sample to a final temperature of less than or equal to -80°C , thereby cryopreserving the sample at the final temperature, the method comprising the steps of:

- (a) placing the sample at a first temperature above the freezing temperature of the sample;
- (b) reducing the first temperature to a second temperature at a first controlled rate, where the second temperature is at least 2°C less than the first temperature;
- (c) reducing the second temperature to a third temperature at a second controlled rate, where the third temperature is at least 40°C less than the second temperature;
- (d) increasing the third temperature to a fourth temperature at a third controlled rate, where the fourth temperature is at least 20°C more than the third temperature;
- (e) reducing the fourth temperature to a fifth temperature at a fourth controlled rate, where the fifth temperature is at least 10°C less than the fourth temperature; and

(f) reducing the fifth temperature to the final temperature at a fifth controlled rate, where the final temperature is less than or equal to -80°C .

12. The method of claim 11, wherein the multi-step process comprises cooling the cells at the controlled rate of between 0.75°C per minute to 30°C per minute to a final temperature of -80°C or below, thereby cryopreserving the cells.

13. A cell therapy product comprising a CAR-NK cell population comprising NK cells genetically modified to express a B cell maturation antigen (BCMA) CAR and an IL-15 formulated in a cryopreservation medium comprising PLASMA-LYTE A, trehalose, CS10 and HSA.

14. The cell therapy product of any of claims 1-6 and 13, or the composition of claim 7, for use in treating cancer.

15. A cryopreservation medium comprising a cryoprotectant, an albumin, a disaccharide and a non-pyrogenic and isotonic crystalloid solution; such as a medium comprising: PLASMA-LYTE A, human serum albumin (HSA), trehalose and a cryoprotectant.