FIGURE 1. A GNC protein comprising four antigen-specific binding domains in an antibody structure with targeting specificity to CD19 positive cells.

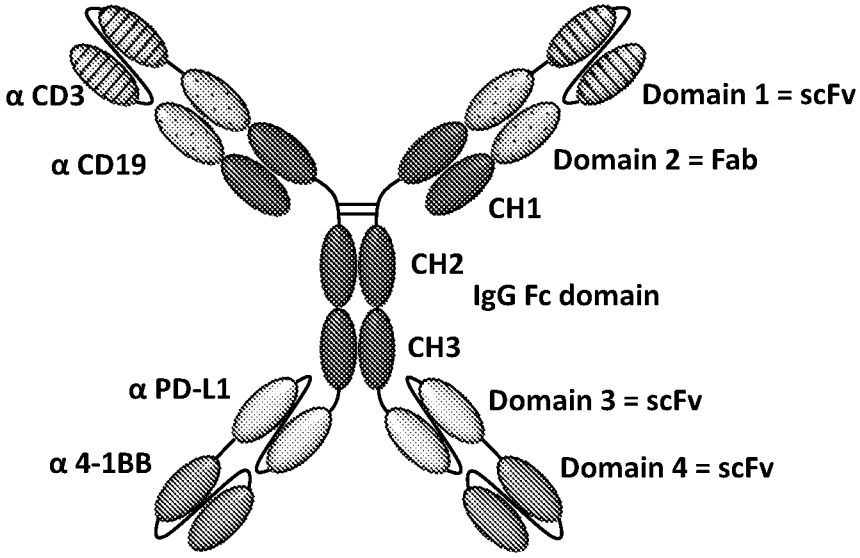


FIGURE 2. An illustration of multi-specific binding mediated by a tetra-specific GNC antibody between a T cell and a tumor cell.

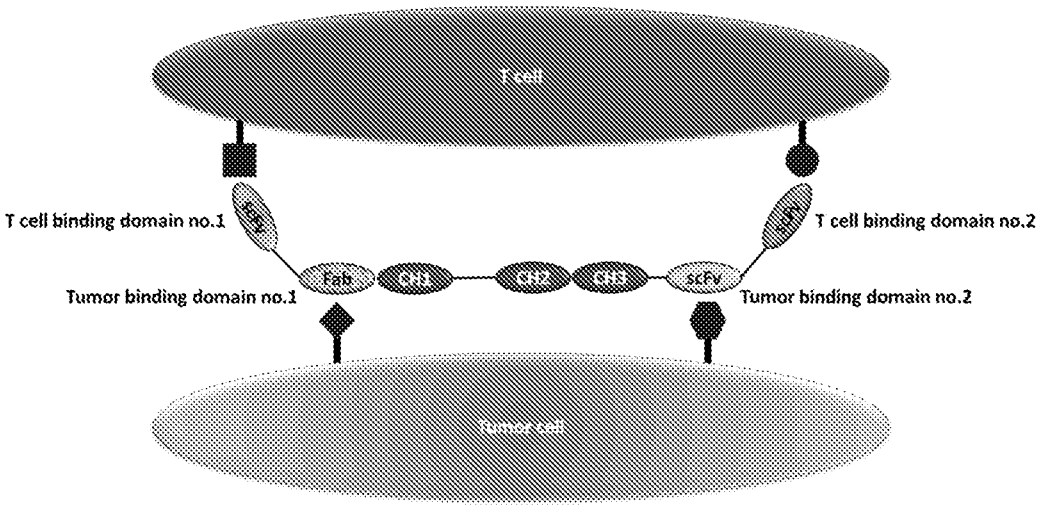


FIGURE 3. A flowchart of manufacturing processes for GNC-T cell therapy (left) and CAR-T cell therapy (right).

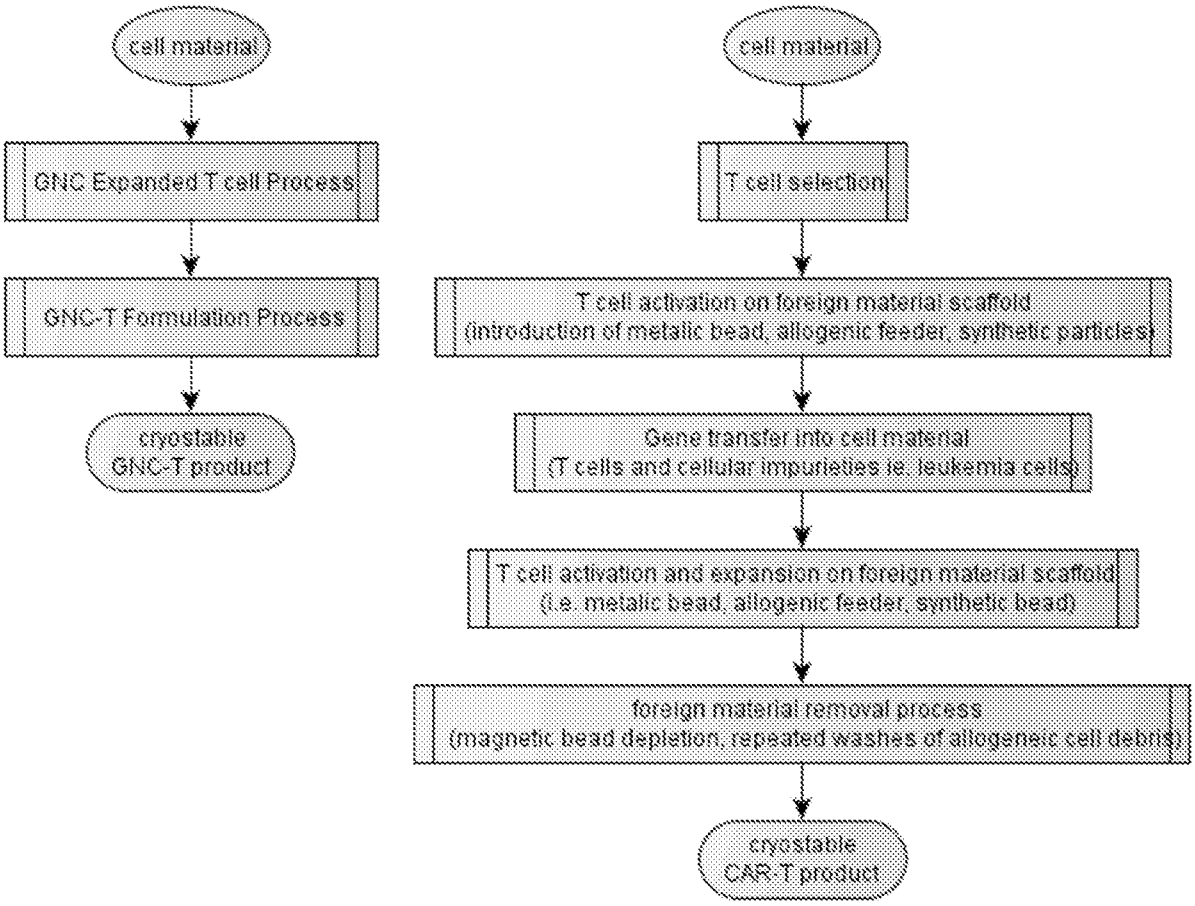


Figure 4. A diagram of sources of cell material for preparing GNC-activated therapeutic cell composition.

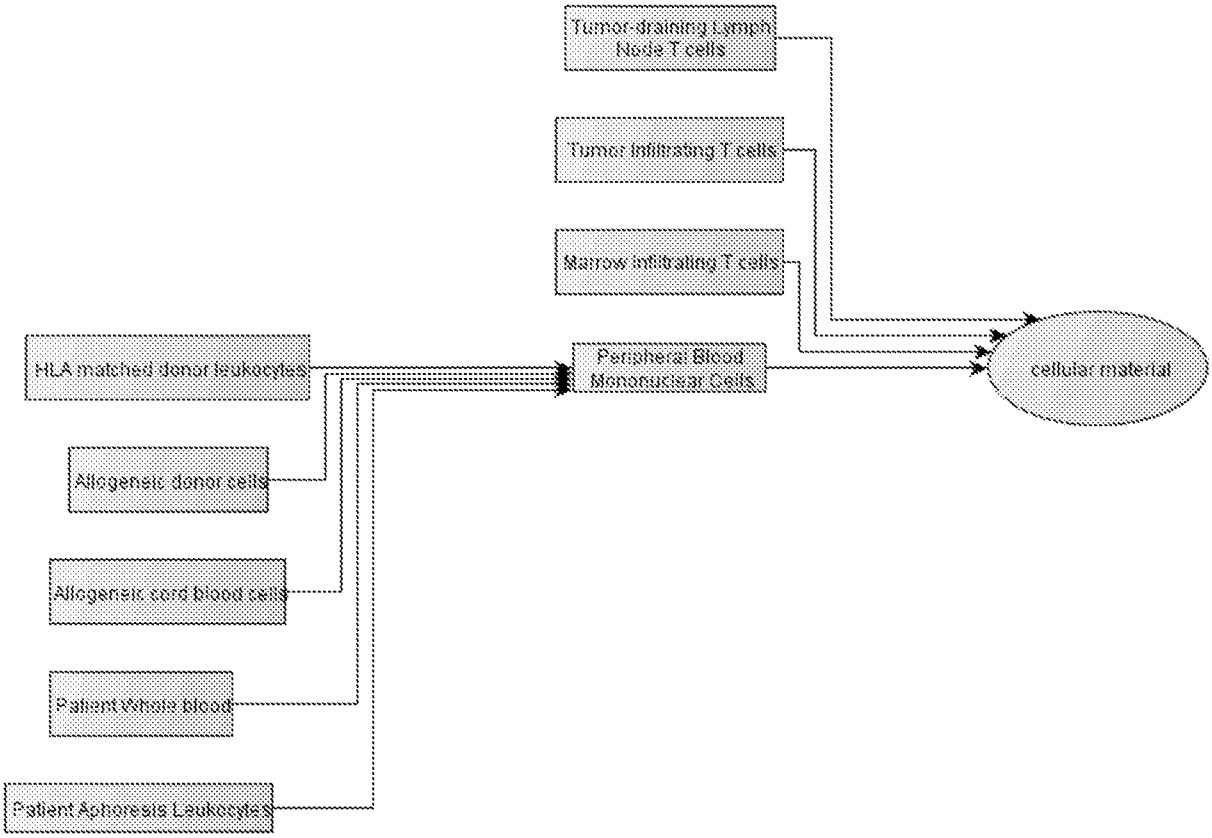


Figure 5. A diagram of sources of selected T cells for preparing GNC-activated therapeutic composition.

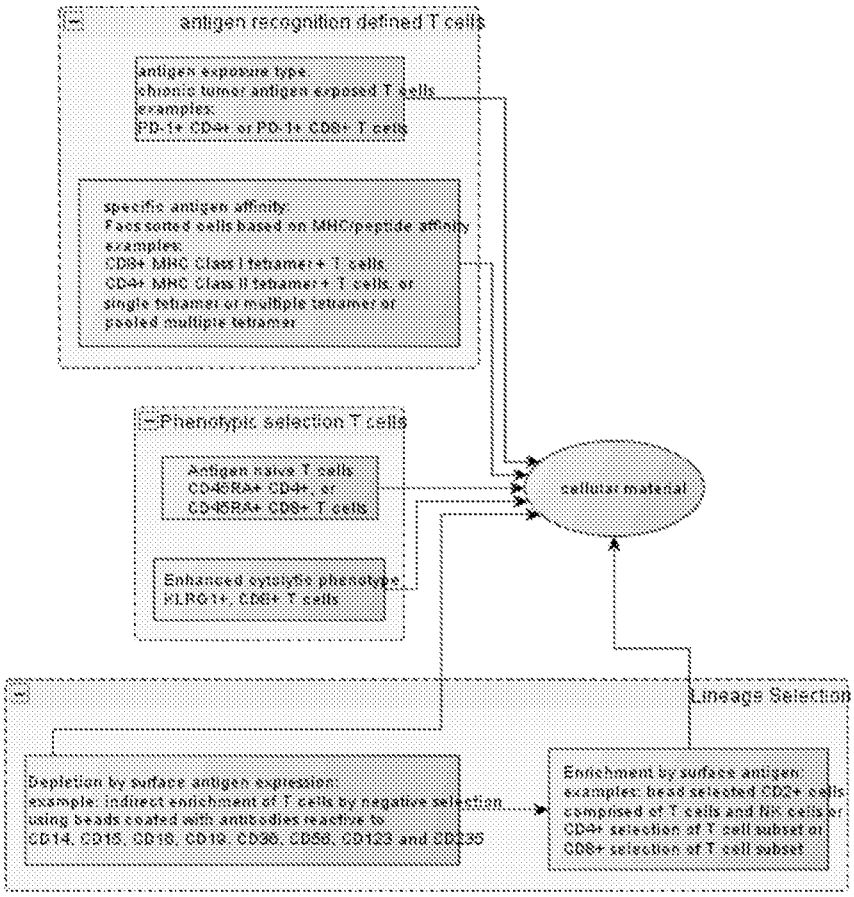


Figure 6. A diagram of preparing GNC-activated therapeutic T cell composition.

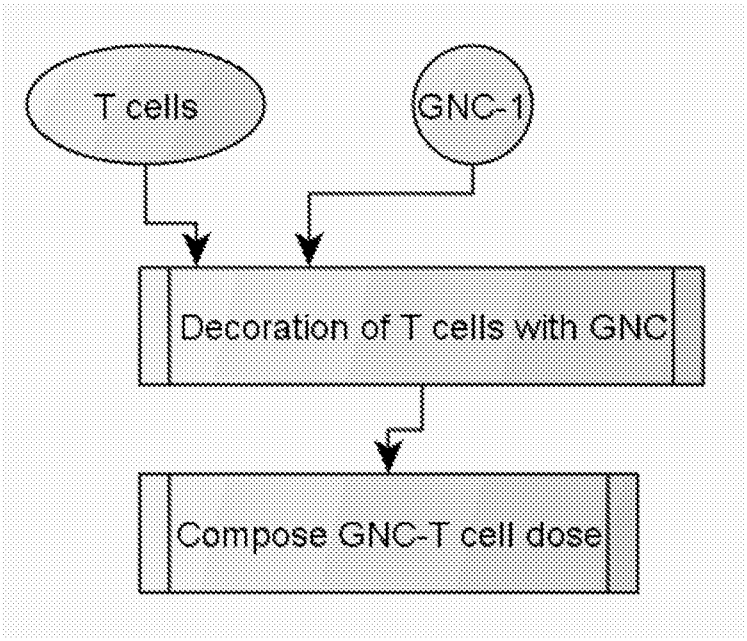


Figure 7. A diagram of incubating and formulating the first GNC-activated T cells for GNC-T cell therapy.

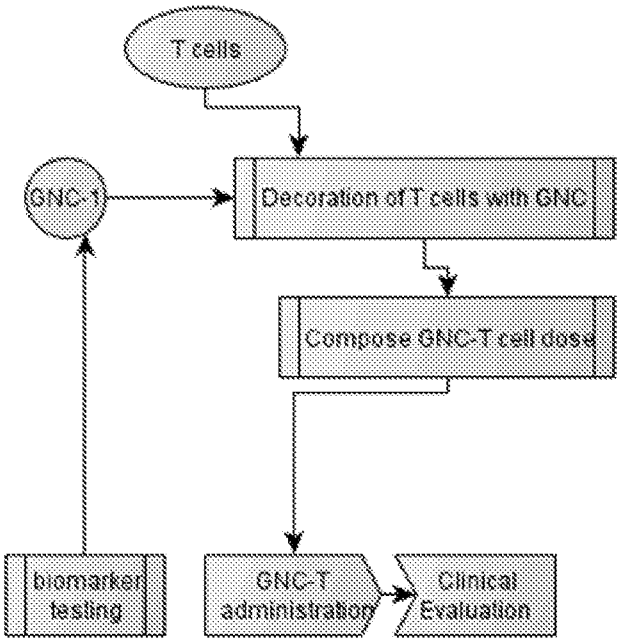


FIGURE 8. GNC proteins induce IL-2 secretion from PBMC.

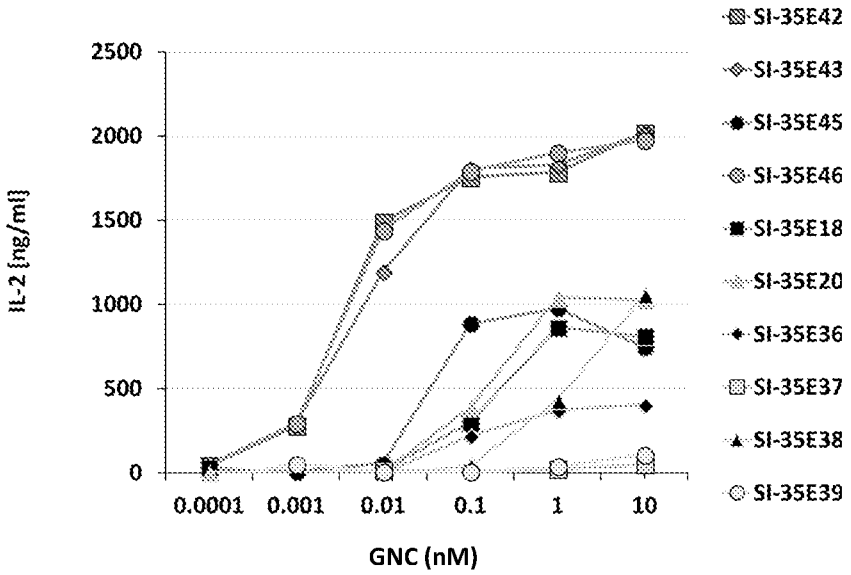


FIGURE 9. GNC proteins induce granzyme B secretion from PBMC.

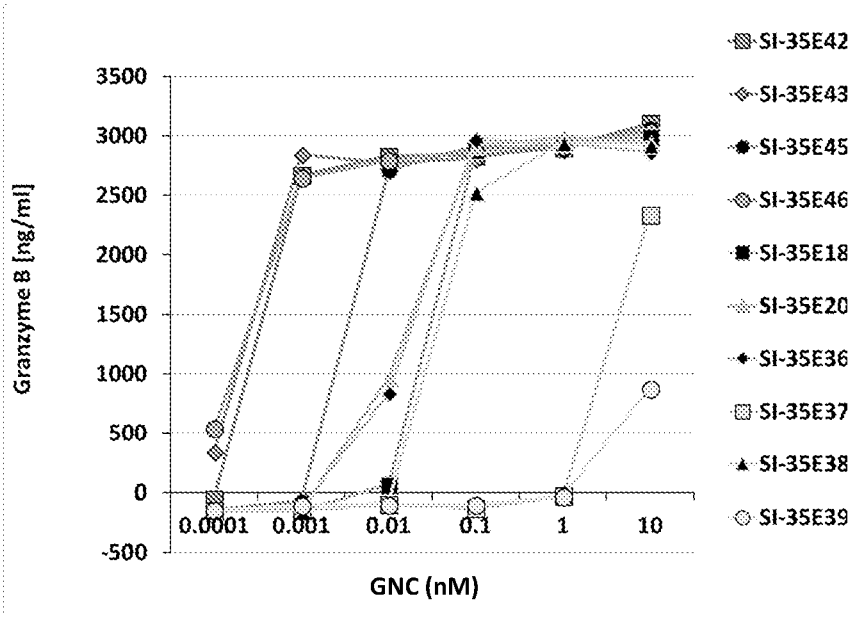


FIGURE 10. GNC proteins induce expression of the activation marker CD69 on CD4+ T cells.

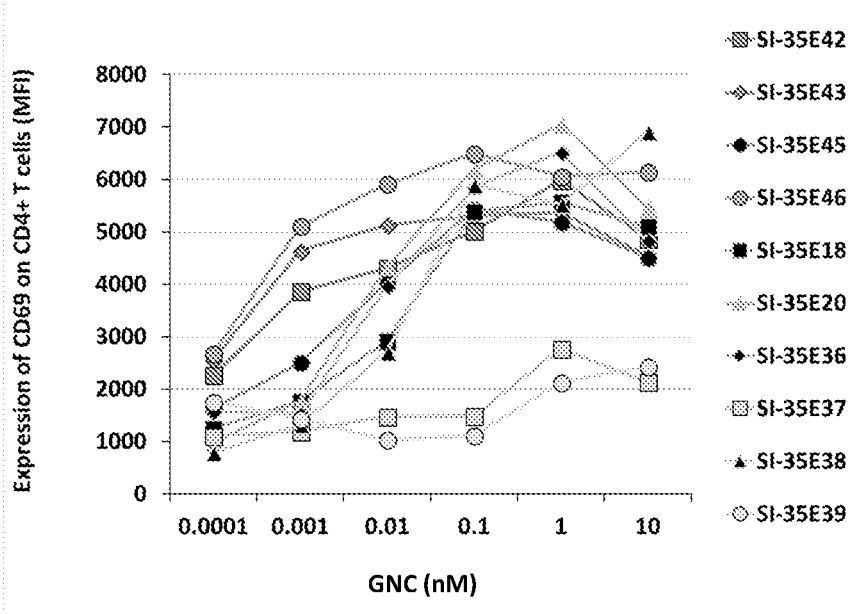


FIGURE 11. GNC proteins induce expression of the activation marker CD69 on CD8+ T cells.

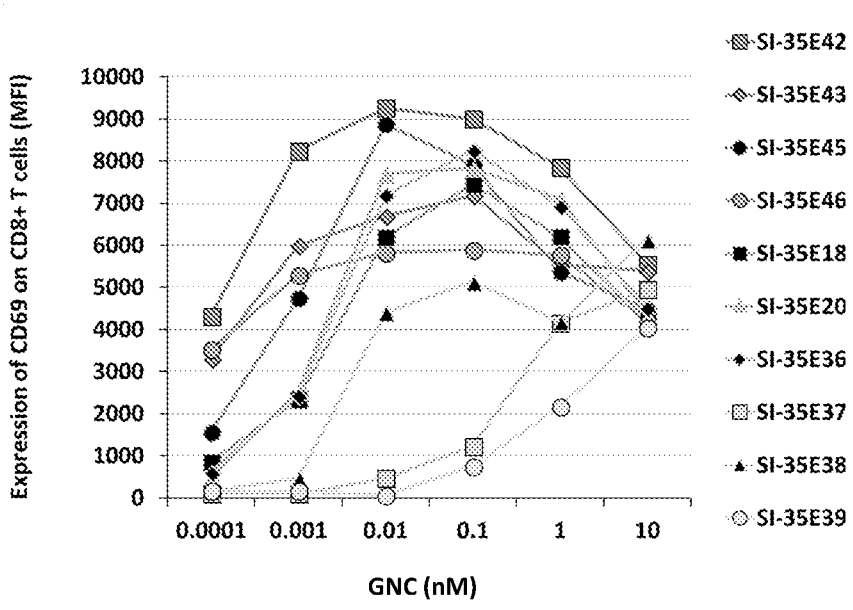


FIGURE 12. GNC proteins induce expression of the activation marker CD69 on CD56+ NK cells.

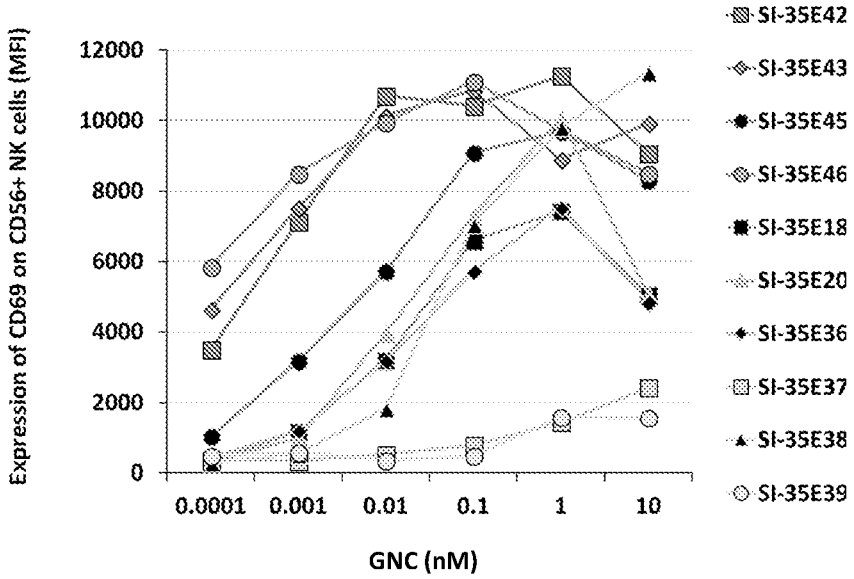


FIGURE 13. GNC proteins induce expression of the marker of cytotoxic degranulation CD107a on CD4+ T cells.

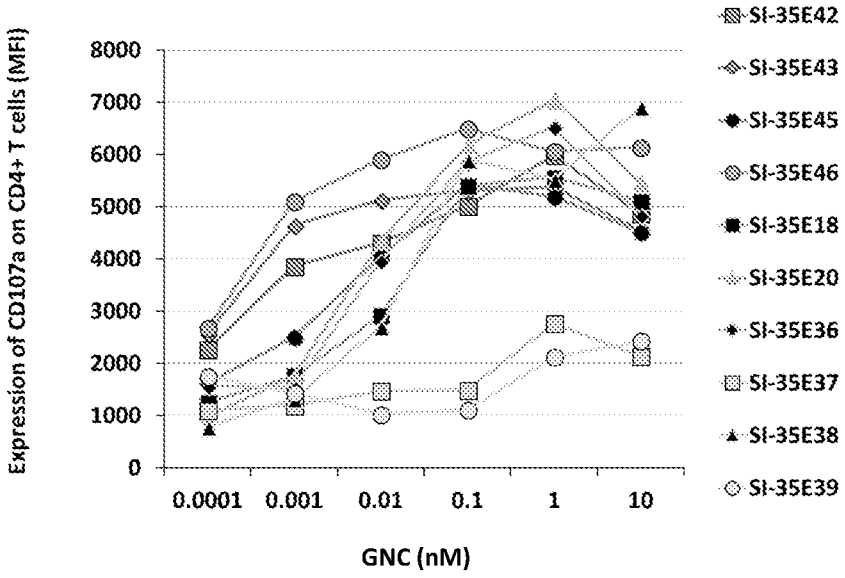


FIGURE 14. GNC proteins induce expression of the marker of cytotoxic degranulation CD107a on CD8+ T cells.

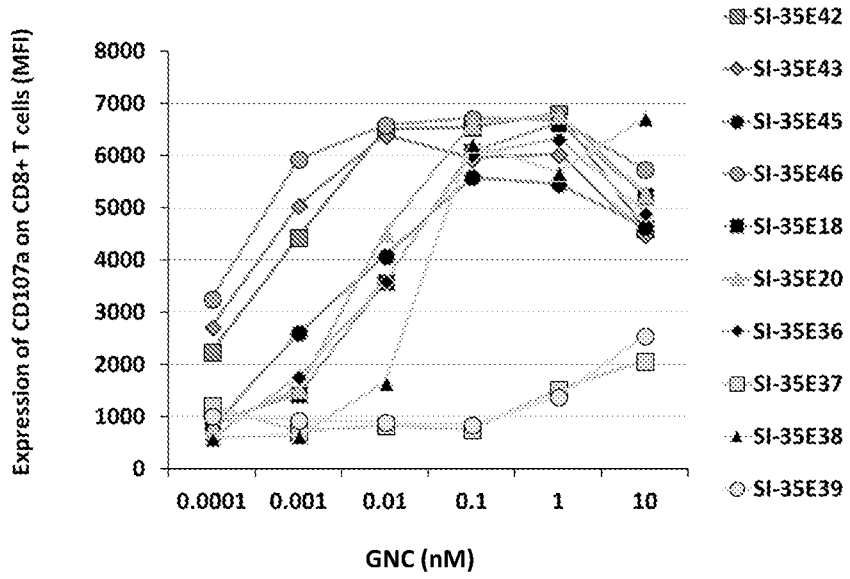


FIGURE 15. GNC proteins induce expression of the marker of cytotoxic degranulation CD107a on CD56+ NK cells.

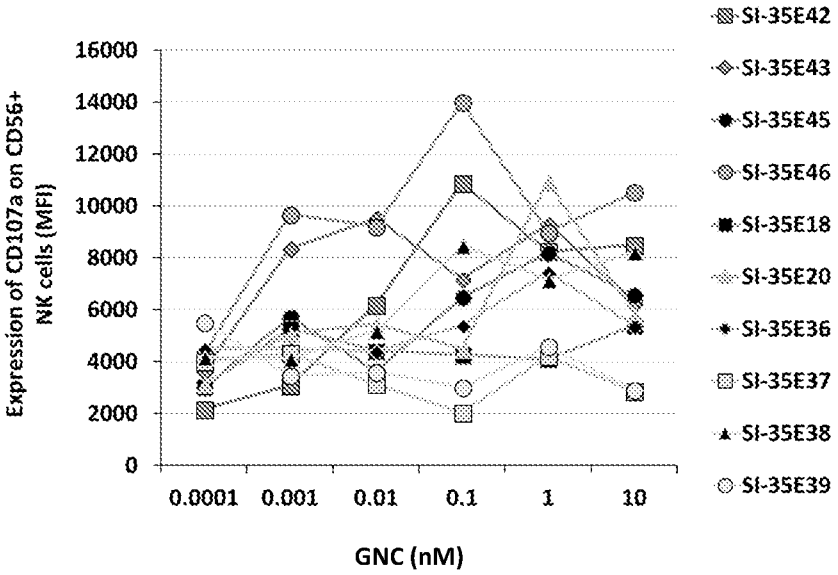


FIGURE 16. GNC proteins activate CD3+ T cells to proliferate.

GNC protein [nM]

| GNC protein | 10 | 3 | 1 | 0.3 | 0.1 | 0.03 | 0.01 | 0.003 | 0.001 | 0.0003 | 0 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| SI-35E18 460C3 x PL230C6 x 323H7 x 284A10 | 7.5 | 9.8 | 10.7 | 10.7 | 11.0 | 10.9 | 5.9 | 1.7 | 1.1 | 1.0 | 1.0 |
| SI-35E19 420H5 x PL230C6 x 323H7 x 284A10 | 7.6 | 9.7 | 9.7 | 9.4 | 9.5 | 10.3 | 7.6 | 2.2 | 1.0 | 1.0 | 1.0 |
| SI-35E20 466F6 x PL230C6 x 323H7 x 284A10 | 8.1 | 9.5 | 10.3 | 10.4 | 10.1 | 10.7 | 9.8 | 2.4 | 1.1 | 1.0 | 1.0 |
| SI-35E36 FITC x PL230C6 x 338H4 x 284A10 + 0.5nM 4-1BB mAb 420H5 | 4.5 | 10.2 | 11.4 | 10.4 | 11.5 | 12.2 | 10.7 | 6.0 | 1.8 | 1.1 | 1.0 |
| SI-35E36 FITC x PL230C6 x 338H4 x 284A10 | 8.0 | 8.8 | 9.1 | 10.0 | 10.4 | 10.3 | 10.8 | 4.6 | 1.5 | 1.0 | 1.0 |
| SI-35E37 460C3 x FITC x 338H4 x 284A10 | 6.2 | 9.8 | 9.9 | 10.1 | 10.4 | 10.3 | 9.6 | 3.1 | 1.4 | 1.1 | 1.0 |
| SI-35E38 460C3 x PL230C6 x FITC x 284A10 | 3.7 | 2.5 | 6.6 | 9.3 | 8.4 | 7.5 | 6.2 | 2.6 | 1.2 | 1.0 | 1.0 |
| SI-35E39 460C3 x PL230C6 x 338H4 x FITC | 1.1 | 1.0 | 1.2 | 1.0 | 1.1 | 1.0 | 1.0 | 1.0 | 1.2 | 1.0 | 1.0 |

Values are for fold-over background proliferation

FIGURE 17. GNC proteins activate CD3+ T cells to secrete gamma interferon.

GNC protein [nM]

| GNC protein | 10 | 5 | 2.5 | 1.25 | 0.63 | 0.31 | 0.16 | 0.078 | 0.04 | 0.02 | 0 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| SI-35E18 460C3 x PL230C6 x 323H7 x 284A10 | 1.66 | 1.83 | 2.12 | 2.14 | 2.16 | 1.91 | 0.65 | 0.15 | 0.06 | 0.06 | 0.05 |
| SI-35E19 420H5 x PL230C6 x 323H7 x 284A10 | 1.17 | 1.95 | 2.12 | 2.38 | 2.14 | 1.89 | 0.80 | 0.20 | 0.06 | 0.05 | 0.06 |
| SI-35E20 466F6 x PL230C6 x 323H7 x 284A10 | 1.18 | 2.26 | 2.20 | 2.29 | 2.11 | 1.90 | 1.19 | 0.25 | 0.06 | 0.05 | 0.05 |
| SI-35E36 FITC x PL230C6 x 338H4 x 284A10 + 0.5nM 4-1BB mAb 420H5 | 0.98 | 2.10 | 2.22 | 2.34 | 2.21 | 2.08 | 1.83 | 0.85 | 0.09 | 0.05 | 0.06 |
| SI-35E36 FITC x PL230C6 x 338H4 x 284A10 | 1.26 | 1.99 | 2.04 | 2.13 | 2.27 | 1.76 | 1.32 | 0.53 | 0.09 | 0.05 | 0.06 |
| SI-35E37 460C3 x FITC x 338H4 x 284A10 | 0.89 | 2.21 | 2.15 | 2.16 | 2.12 | 2.16 | 0.63 | 0.15 | 0.08 | 0.06 | 0.05 |
| SI-35E38 460C3 x PL230C6 x FITC x 284A10 | 0.50 | 0.33 | 0.73 | 1.65 | 0.55 | 0.76 | 0.60 | 0.23 | 0.07 | 0.05 | 0.06 |
| SI-35E39 460C3 x PL230C6 x 338H4 x FITC | 0.07 | 0.07 | 0.08 | 0.07 | 0.07 | 0.05 | 0.06 | 0.06 | 0.05 | 0.06 | 0.07 |

Values are for Gamma interferon $OD_{450}$

FIGURE 18. GNC proteins activate naïve CD8+/CD45RA+ T cells to proliferate.

GNC protein [nM]

| GNC protein | 10 | 5 | 2.5 | 1.25 | 0.63 | 0.31 | 0.16 | 0.08 | 0.04 | 0.02 | 0 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| SI-35E18 460C3 x PL230C6 x 323H7 x 284A10 | 3.9 | 7.8 | 8.7 | 9.0 | 9.8 | 6.9 | 1.8 | 1.0 | 1.0 | 1.0 | 1.0 |
| SI-35E19 420H5 x PL230C6 x 323H7 x 284A10 | 2.3 | 10.0 | 8.7 | 8.5 | 9.5 | 9.1 | 1.3 | 1.0 | 1.0 | 1.0 | 1.0 |
| SI-35E20 466F6 x PL230C6 x 323H7 x 284A10 | 3.1 | 8.7 | 8.8 | 10.0 | 9.2 | 10.3 | 2.3 | 1.1 | 1.0 | 1.0 | 1.0 |
| SI-35E36 FITC x PL230C6 x 338H4 x 284A10 + 0.5nM 4-1BB mAb 420H5 | 1.6 | 8.0 | 8.5 | 10.3 | 11.2 | 9.5 | 4.9 | 1.6 | 1.1 | 1.0 | 1.0 |
| SI-35E36 FITC x PL230C6 x 338H4 x 284A10 | 1.2 | 3.6 | 5.0 | 6.6 | 5.0 | 4.1 | 1.2 | 1.1 | 1.1 | 1.0 | 1.0 |
| SI-35E37 460C3 x FITC x 338H4 x 284A10 | 2.3 | 7.0 | 6.7 | 9.1 | 10.2 | 8.1 | 2.7 | 1.2 | 1.0 | 1.0 | 1.0 |
| SI-35E38 460C3 x PL230C6 x FITC x 284A10 | 1.8 | 2.0 | 2.6 | 2.3 | 3.1 | 2.2 | 2.6 | 1.0 | 1.0 | 1.0 | 1.0 |
| SI-35E39 460C3 x PL230C6 x 338H4 x FITC | 0.8 | 0.9 | 1.1 | 1.1 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 | 1.0 |

Values are for fold-over background proliferation

FIGURE 19. GNC proteins activate naïve CD8+/CD45RA+ T cells to secrete gamma interferon.

GNC protein [nM]

| GNC protein | 10 | 5 | 2.5 | 1.25 | 0.63 | 0.31 | 0.16 | 0.08 | 0.04 | 0.02 | 0 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| SI-35E18 460C3 x PL230C6 x 323H7 x 284A10 | 0.66 | 1.66 | 2.08 | 2.12 | 1.69 | 0.94 | 0.09 | 0.06 | 0.06 | 0.06 | 0.05 |
| SI-35E19 420H5 x PL230C6 x 323H7 x 284A10 | 0.35 | 1.88 | 1.97 | 1.91 | 1.85 | 1.28 | 0.05 | 0.06 | 0.05 | 0.05 | 0.06 |
| SI-35E20 466F6 x PL230C6 x 323H7 x 284A10 | 0.30 | 1.64 | 1.76 | 1.74 | 1.77 | 1.06 | 0.08 | 0.05 | 0.06 | 0.05 | 0.05 |
| SI-35E36 FITC x PL230C6 x 338H4 x 284A10 + 0.5nM 4-1BB mAb 420H5 | 0.08 | 2.23 | 2.06 | 2.12 | 1.79 | 1.41 | 0.27 | 0.06 | 0.05 | 0.05 | 0.05 |
| SI-35E36 FITC x PL230C6 x 338H4 x 284A10 | 0.06 | 1.12 | 1.02 | 1.77 | 1.30 | 0.56 | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 |
| SI-35E37 460C3 x FITC x 338H4 x 284A10 | 0.22 | 1.47 | 1.09 | 1.33 | 1.91 | 1.32 | 0.13 | 0.05 | 0.05 | 0.05 | 0.05 |
| SI-35E38 460C3 x PL230C6 x FITC x 284A10 | 0.09 | 0.06 | 0.10 | 0.09 | 0.11 | 0.08 | 0.13 | 0.05 | 0.05 | 0.05 | 0.05 |
| SI-35E39 460C3 x PL230C6 x 338H4 x FITC | 0.05 | 0.06 | 0.09 | 0.09 | 0.06 | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 | 0.07 |

Values are for Gamma interferon $OD_{450}$

Figure 20. Images of GET cell growth in 6-well G-Rex plates over time

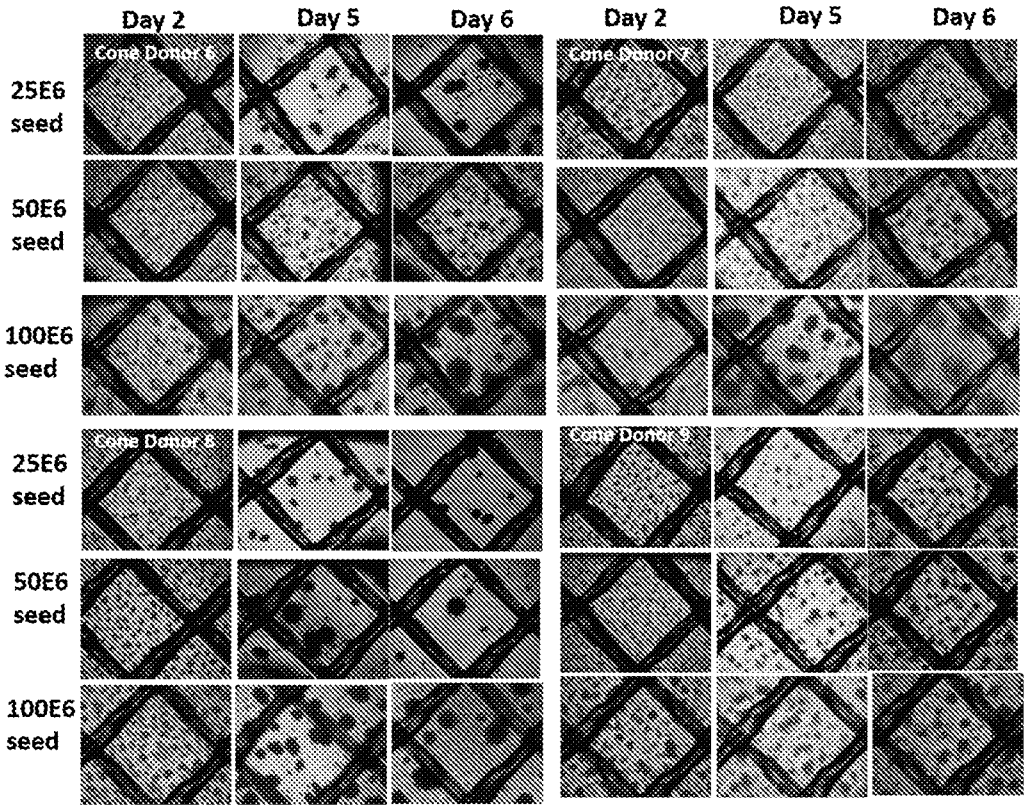
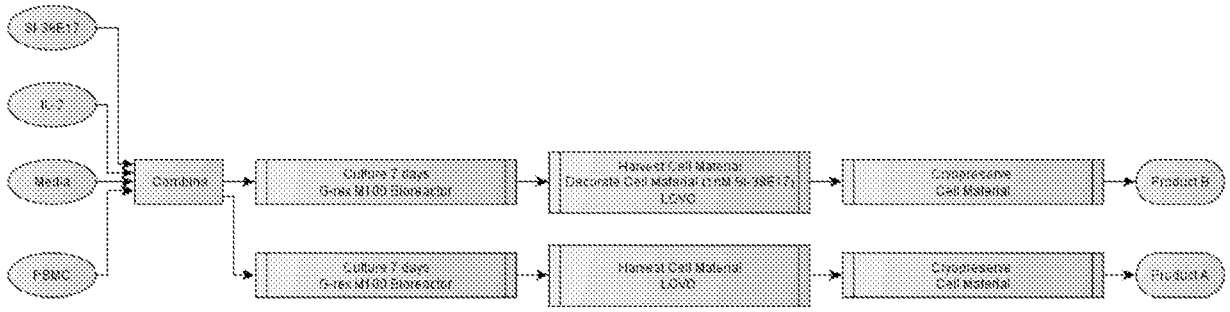


FIGURE 21. A, an example process of making the therapeutic composition as disclosed thereof, and B, cell viability of PBMC, GET, and GNC-T cells after thawing.

A.




B.

| Sample ID | Avg. Viability (%) | Avg. Average Diameter (microns) |
|---|---|---|
| Donor12 post-thaw PBMC A | 86.35 | 8.55 |
| Donor12 post-thaw PBMC B | 88.52 | 8.60 |
| Donor12 post-thaw GET A | 78.43 | 9.03 |
| Donor12 post-thaw GNC-T B | 77.74 | 9.00 |

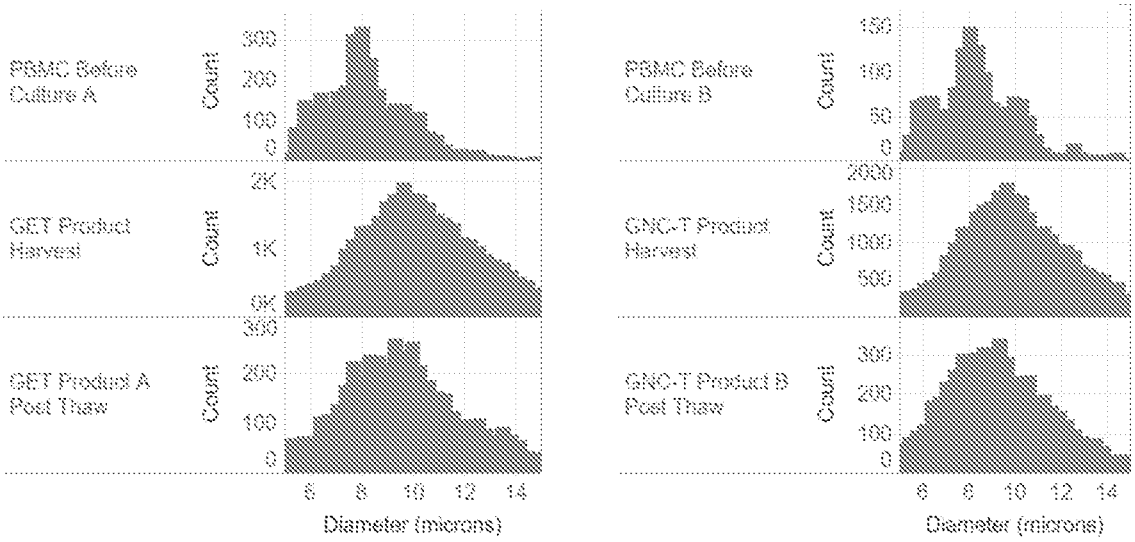


FIGURE 22. A. Flow cytometry analysis of PBMC-derived, the first GNC (SI-38E17)-activated therapeutic cell composition (Product A).

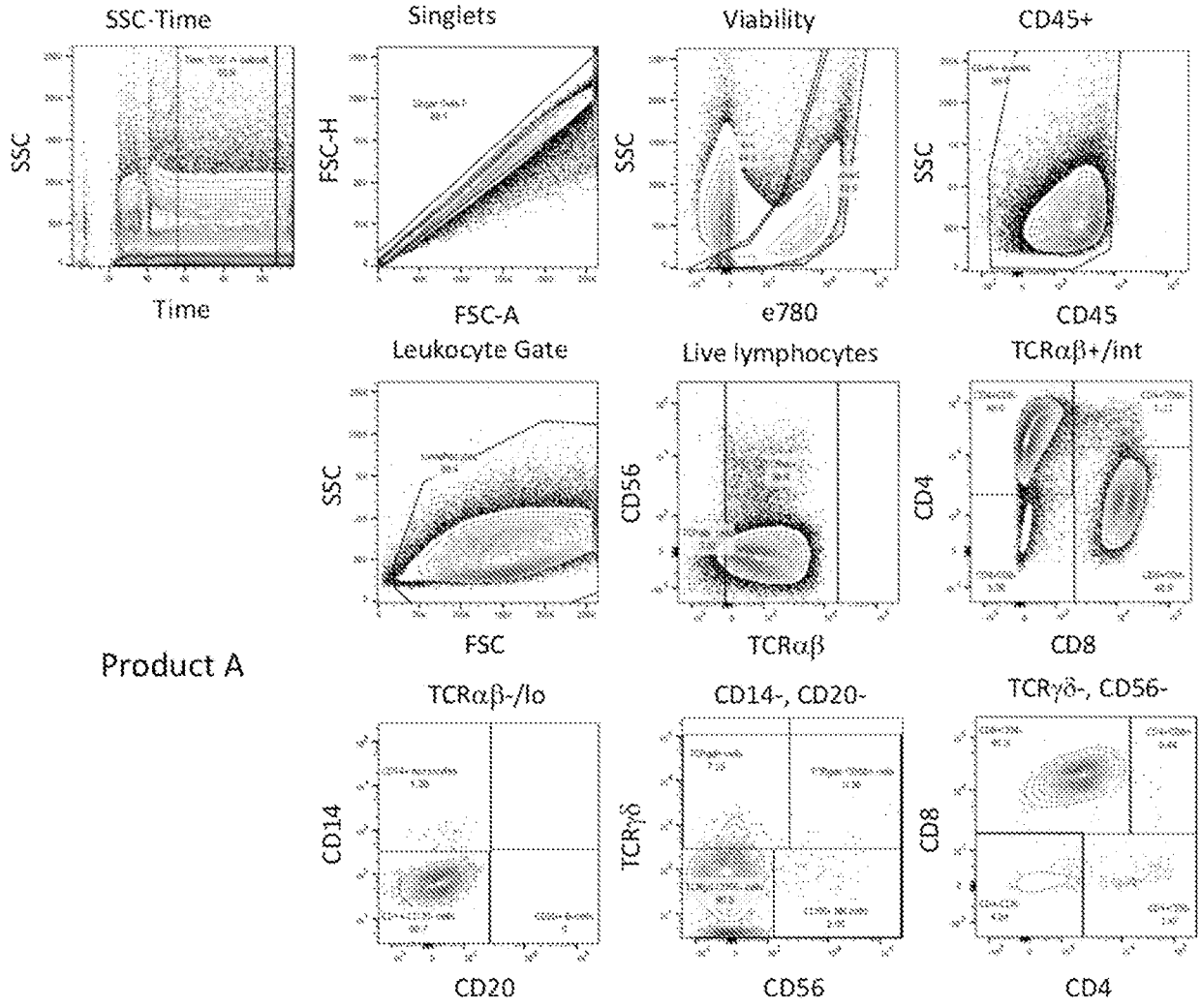


FIGURE 22. B. Flow cytometry analysis of PBMC-derived, the second GNC (SI-38E17)-decorated therapeutic cell composition (Product B).

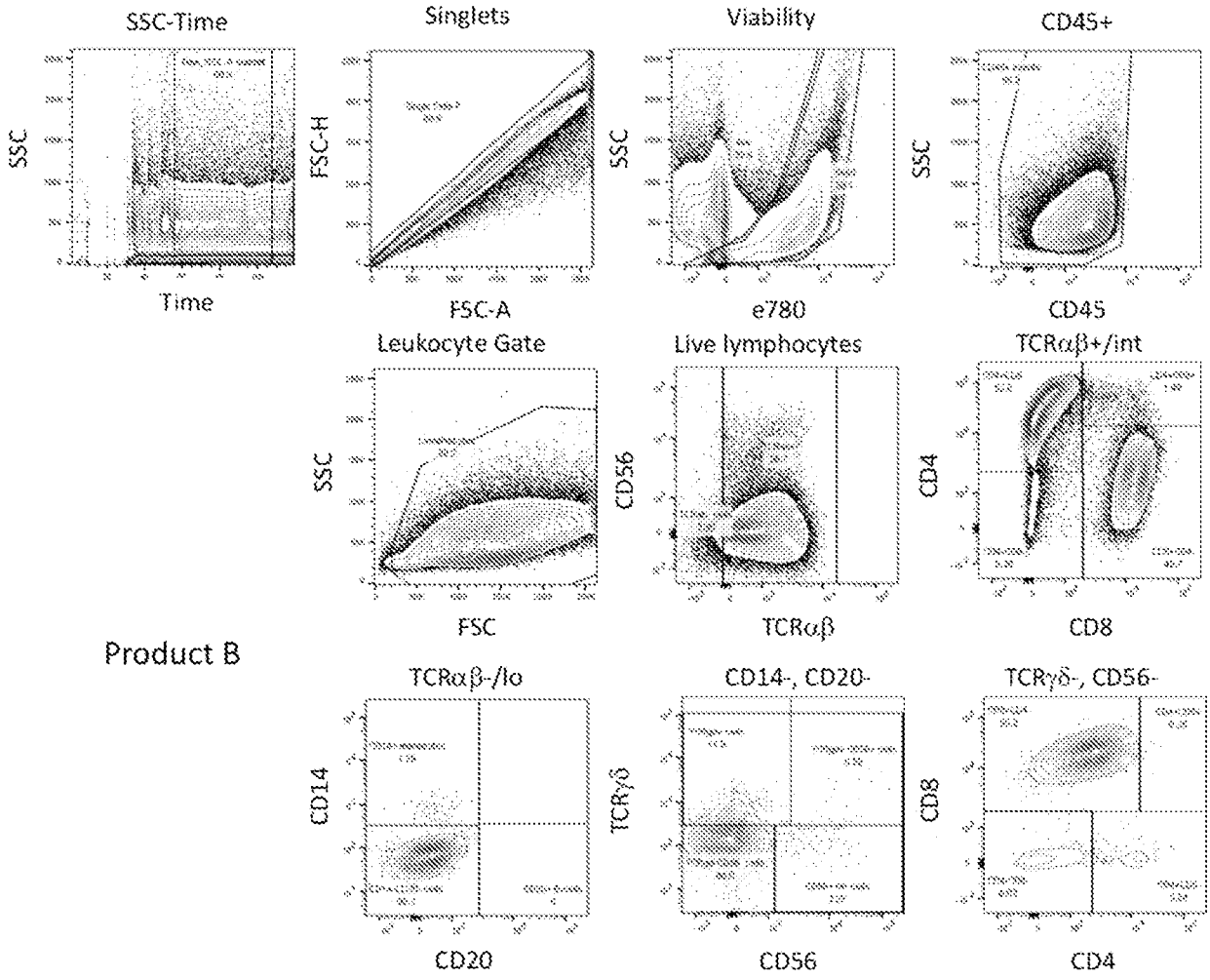


FIGURE 22. C. Flow cytometry analysis of input PBMC cell material.

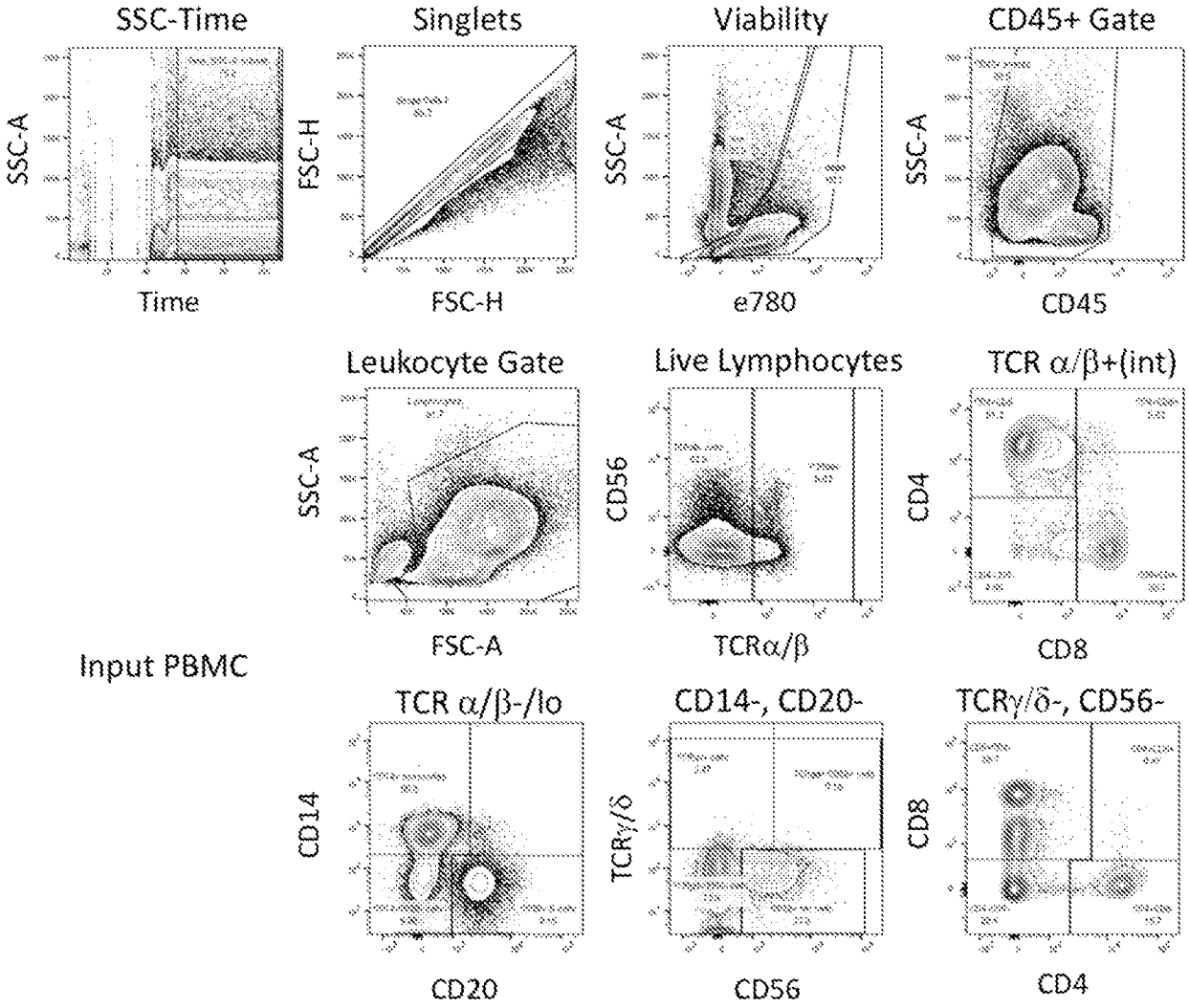


Figure 23. GNC-T therapeutic cell composition of GET cells and formulated GNC-T cells from G-Rex 100M bioreactor after thawing.

| Cell Composition | PBMC as input cell material<br>Number of Cells (%) | GNC-activated therapeutic composition-A<br>Number of Cells (%) | GNC-activated therapeutic composition-B<br>Number of Cells (%) |
|---|---|---|---|
| Leukocyte | 250,000,000 (100) | 1,000,000,000 (100) | 1,000,000,000 (100) |
| TCR $\alpha/\beta$ T cells | 17,375,000 (7) | 964,000,000 (96.4) | 959,000,000 (95.9) |
| CD4+ TCR $\alpha/\beta$+ T cells | 10,225,000 (4.1) | 468,000,000 (46.8) | 504,000,000 (50.4) |
| CD8+ TCR $\alpha/\beta$+ T cells | 5,725,000 (2.3) | 451,000,000 (45.1) | 409,000,000 (40.9) |
| TCR $\alpha/\beta$-/lo T cells | 224,500,000 (89.8) | 30,500,000 (3.1) | 32,800,000 (3.3) |
| CD14+ monocytes | 179,250,000 (71.7) | 380,000 (0) | 610,000 (0.1) |
| CD56+ NK cells | 4,825,000 (1.9) | 620,000 (0.1) | 730,000 (0.1) |
| TCR $\gamma/\delta$ T cells | 450,000 (0.2) | 2,200,000 (0.2) | 3,800,000 (0.4) |
| CD20+ B cells | 20,350,000 (8.1) | 0 (0) | 0 (0) |

FIGURE 24. RTCC of CHO-ROR1 cells by using GNC (SI-35E class)-treated PBMC cells.

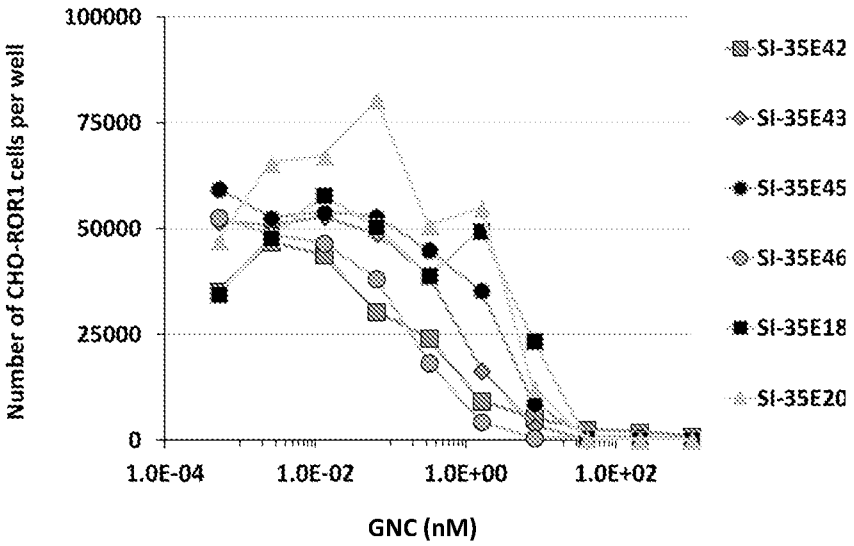


FIGURE 25. Kinetics of PBMC-derived, SI-38E17 GNC-activated therapeutic cells on killing precursor B cell leukemia Kasumi over time.

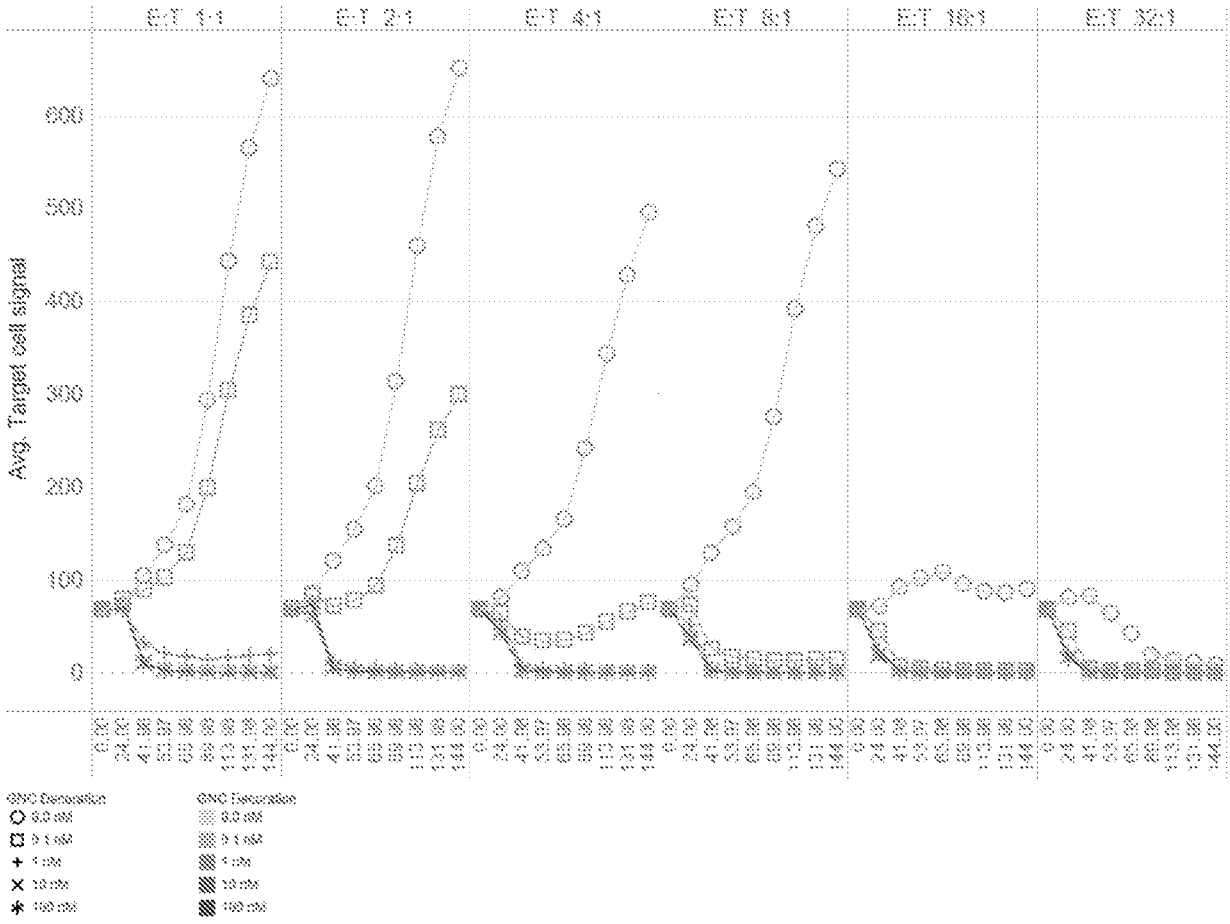


FIGURE 26. Efficacy of killing Nalm-6, MEC-1, Daudi, and Jurkat cells by using PMBC-derived, SI-38E17 GNC-activated therapeutic cells.

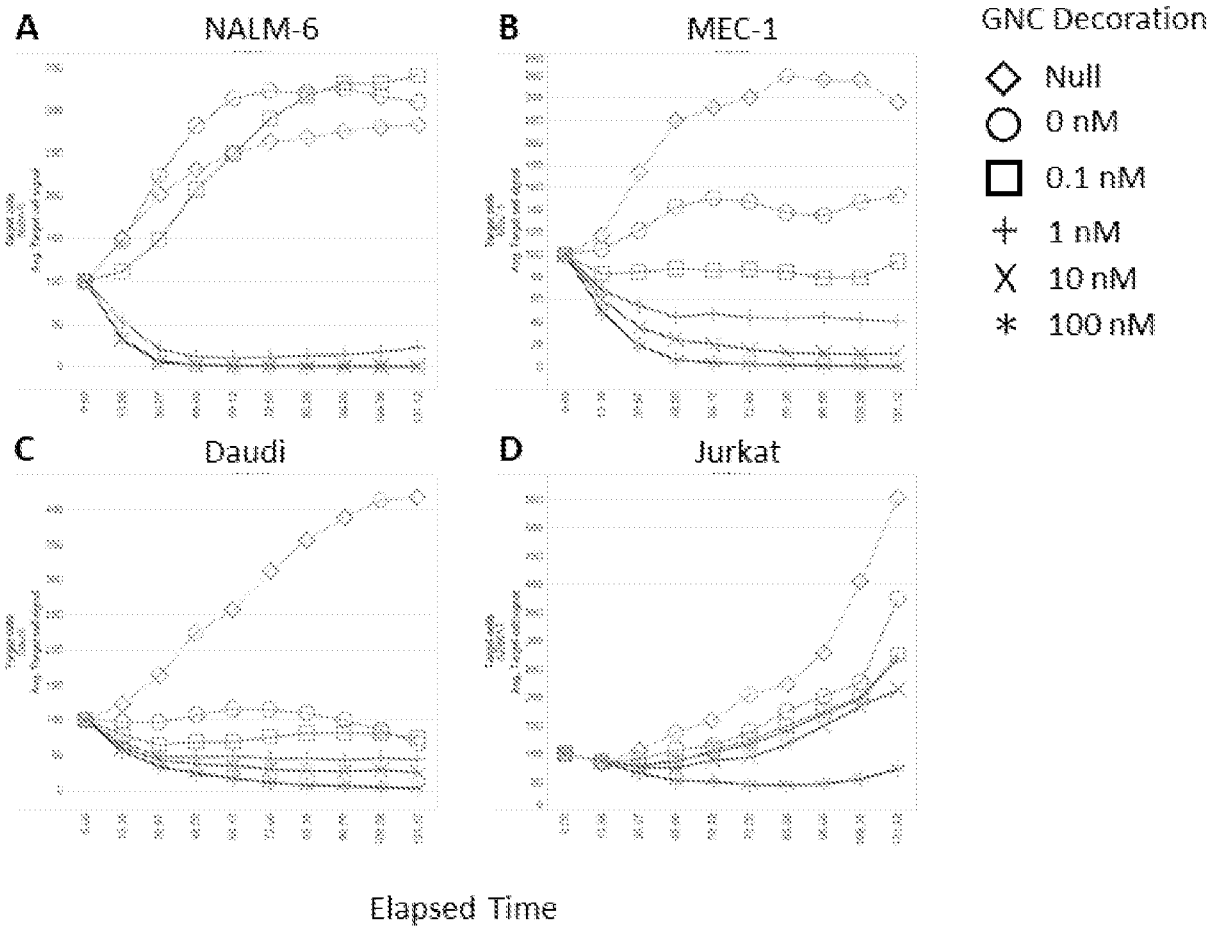
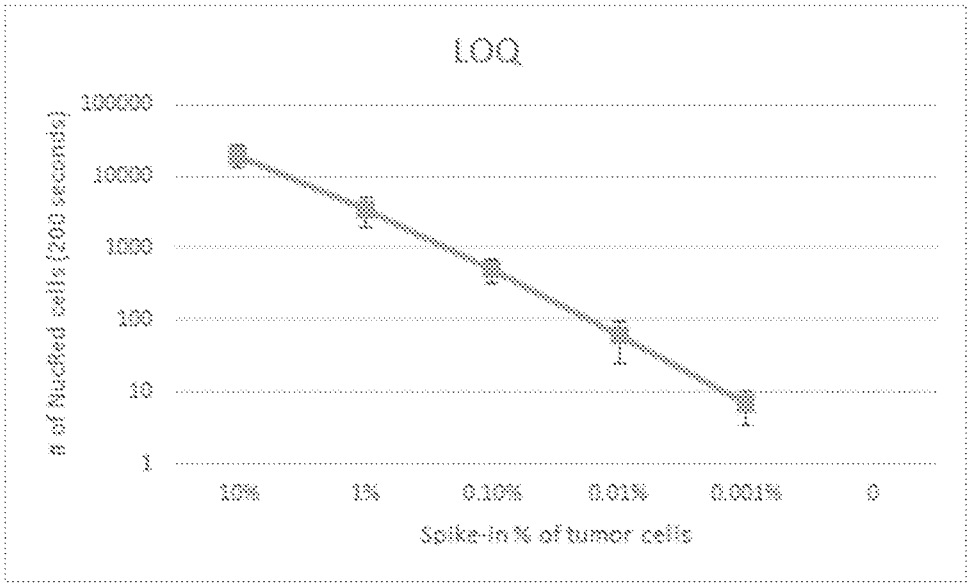


FIGURE 27. Killing of Nalm-6, MEC-1, Daudi, and Jurkat leukemic cells by PBMC-derived, SI-38E17 GNC-activated therapeutic cells in a spike-in model.




| Spike-in | Nalm-6 | Mec-1 | Jurkat | Daudi |
|---|---|---|---|---|
| 10% | 1 | 44 | 0 | 0 |
| 1% | 0 | 0 | 0 | 0 |
| 0.10% | 1 | 0 | 0 | 0 |