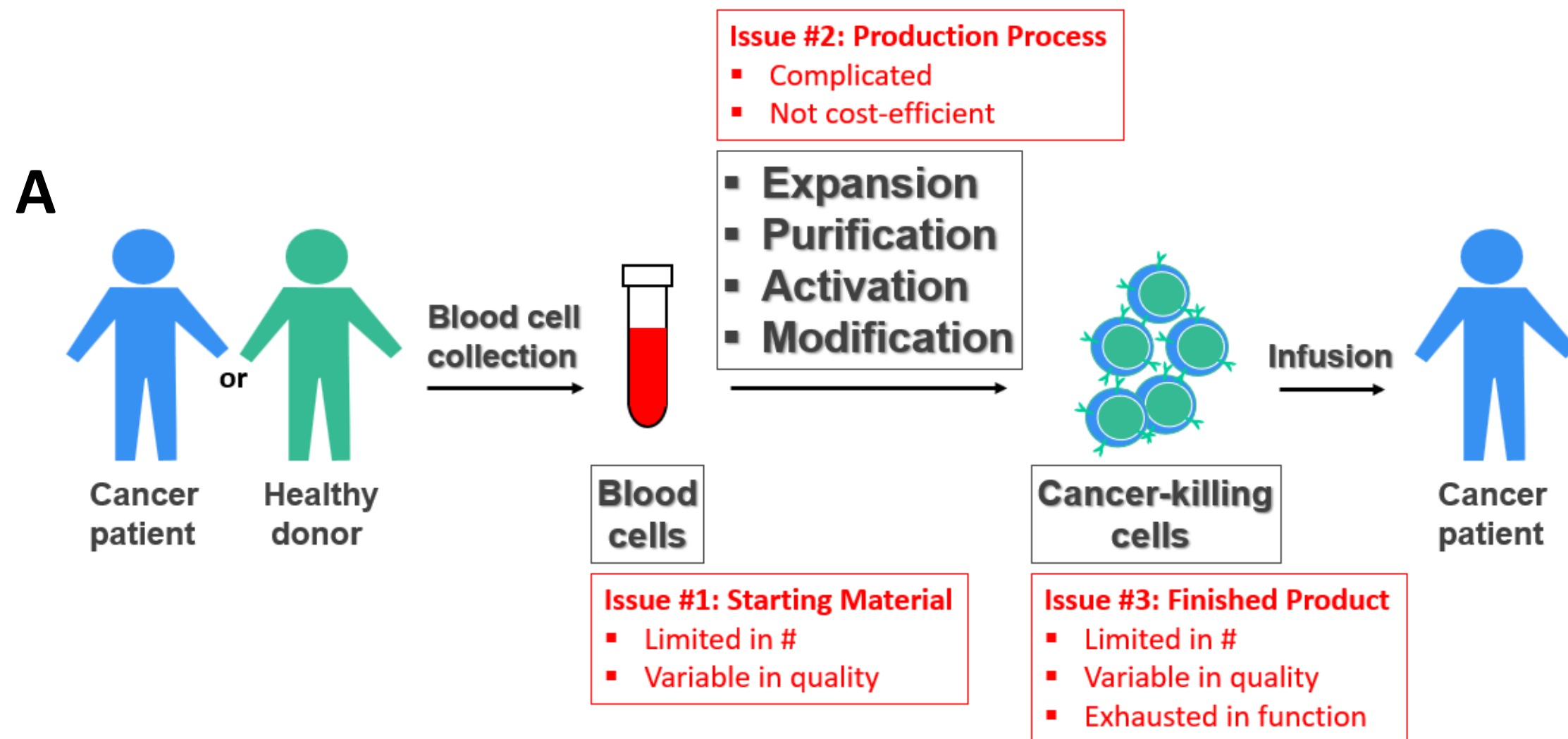


BEYOND $\alpha\beta$ T CELL: iPSC DERIVED $\gamma\delta$ NK T CELLS AS NEXT GENERATION "OFF-THE-SHELF" BROAD SPECTRUM CANCER IMMUNOTHERAPEUTICS

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Problem Statement: Lack of Ideal Starting Material in the Generation of CAR-T Therapy



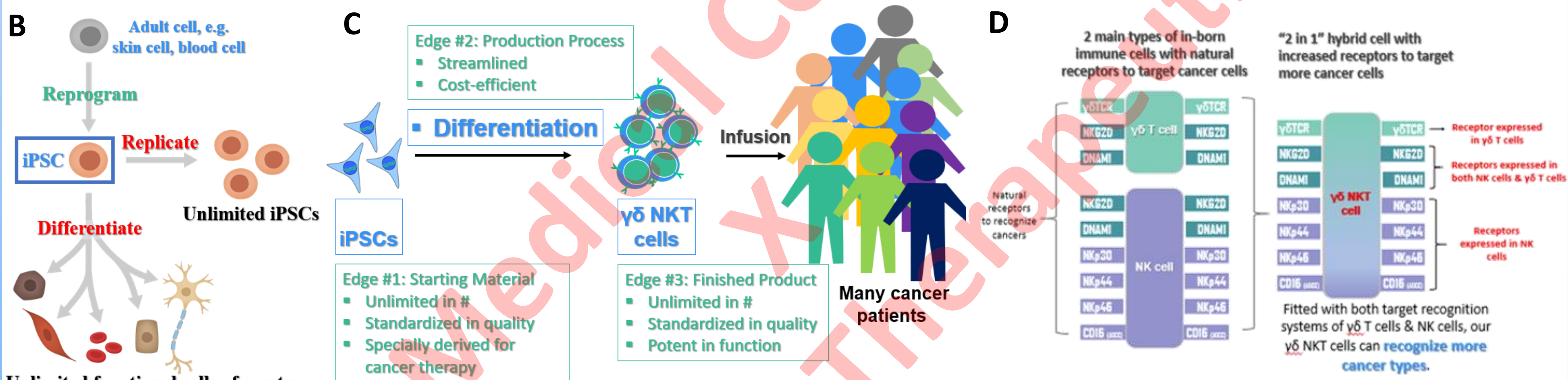
There are many pain point currently in the manufacturing process of CAR-T cells including manufacturing failure which reduces the number of patient who can benefit from this therapy.

What we want are:

1. Healthy donor blood cells as starting materials
2. Safer product!
3. Simpler manufacturing process
4. "Off-the-shelf" product for many patients
5. Accessible and affordable to many patients!
6. Broad spectrum cancer targeting therapy

Figure A: Schematic of a typical CAR-T manufacturing process

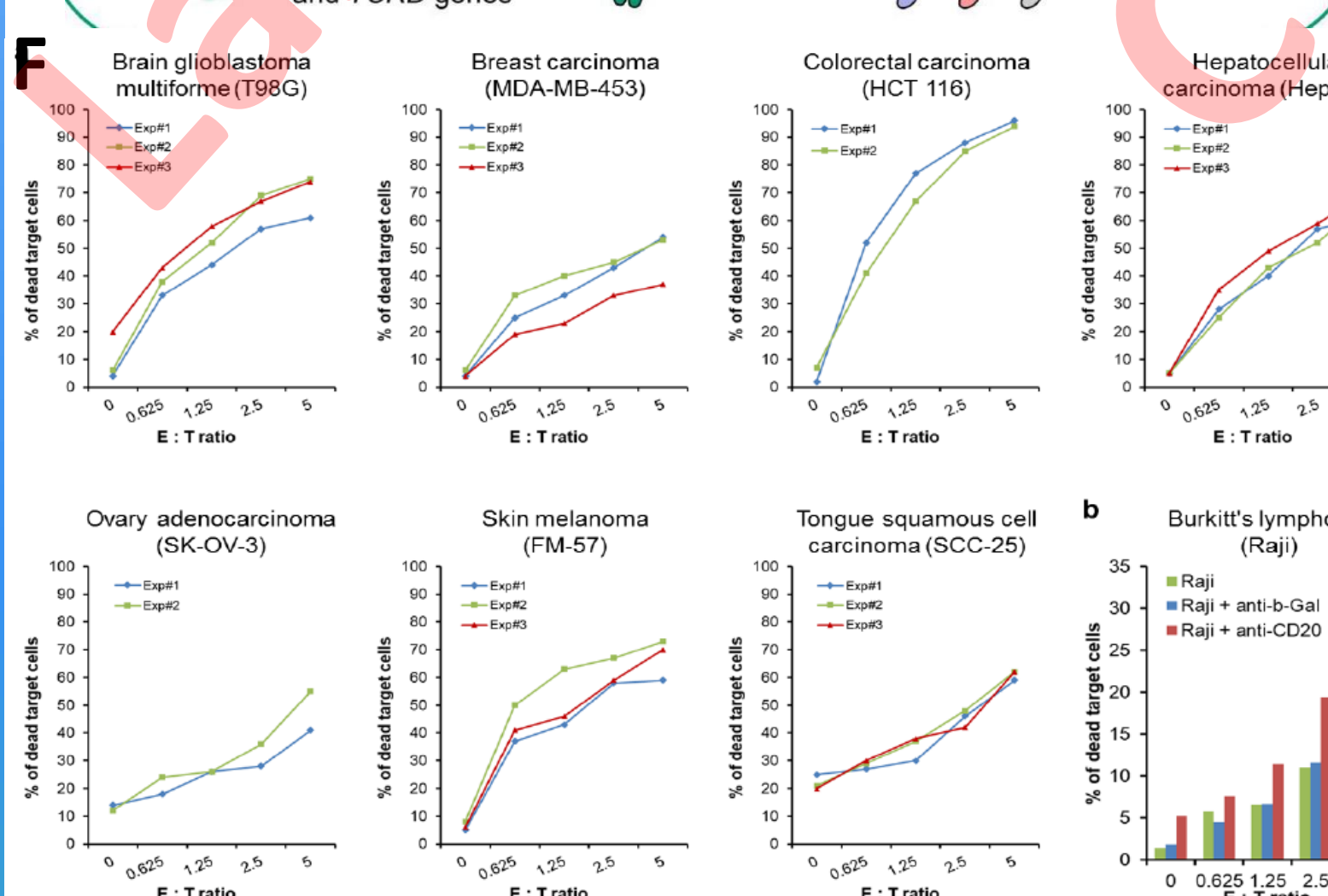
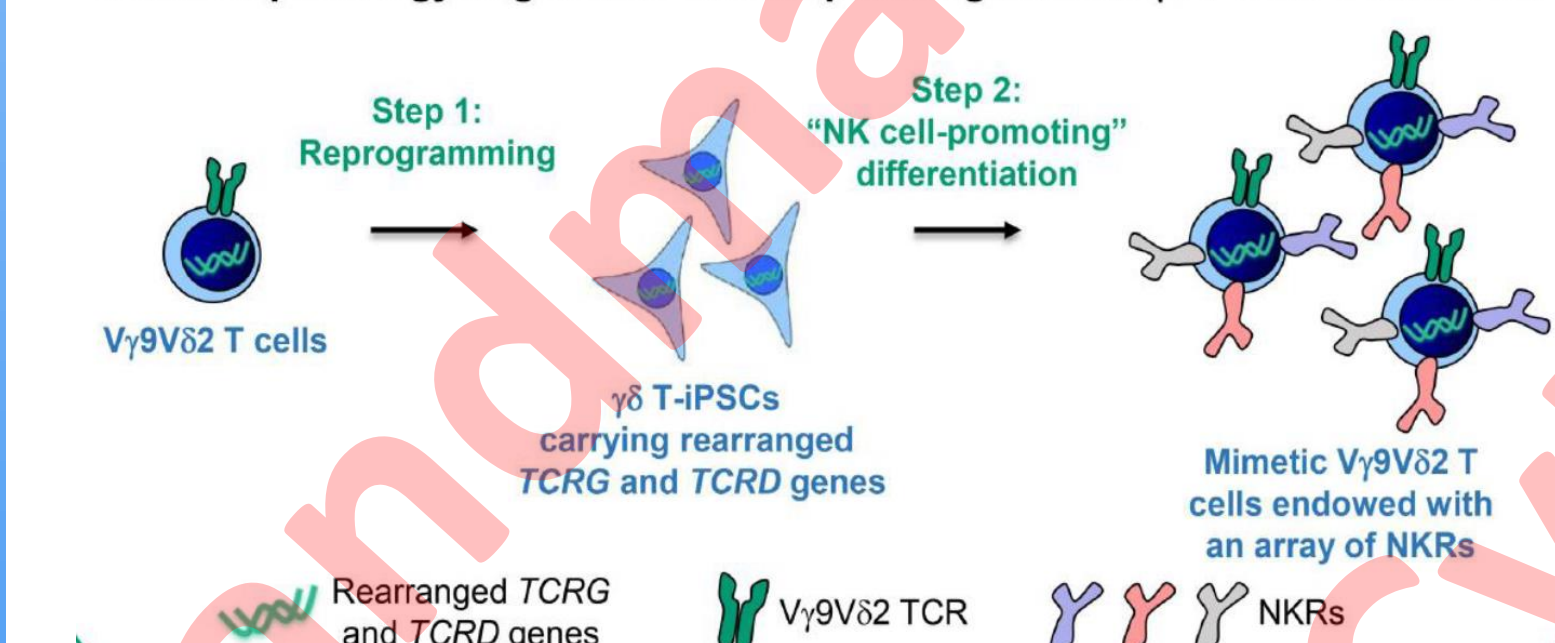
Solution: Induced Pluripotent Stem Cell as a infinite high quality starting material for the production of next-generation gamma delta natural killer ($\gamma\delta$ NK) T hybrid immune cells



Unlimited functional cells of any types

Figure B: Characteristic of iPSC. C: Schematic of iPSC - $\gamma\delta$ NK T cell. D: Receptors present on the surface of iPSC - $\gamma\delta$ NK T cell. iPSC - $\gamma\delta$ NK T cell retain characteristic of $\gamma\delta$ and NK cell, thus allowing this hybrid cell to be used in an allogeneic manner without causing graft versus host disease. The use of iPSC is an ideal starting material as it is infinite and can differentiate into any cell type of choice. By building a master cell line, one will be able to generate limitless amount of consistent, high quality cancer killing cells for "off-the-shelf" cancer immunotherapy.

E "From $\gamma\delta$ T cell to stem cells and back with more" – a two-step strategy to generate NK-expressing mimetic $\gamma\delta$ T cells from iPSCs



	Types of cancer	Cancer cell lines
1	Brain glioblastoma	T98G, U-87
2	Breast cancer	MCF7, BT-474, MDA-MB-453
3	Burkitt's lymphoma	Daudi, Raji
4	Colorectal cancer	HCT 116, SW480
5	Leukemia	K562, THP-1, MOLT-4
6	Liver cancer	Hep G2
7	Lung cancer	NCI-H460
8	Multiple myeloma	RPMI 8226
9	Ovarian cancer	SK-OV-3
10	Skin cancer	FM-57, Malme-3M
11	Tongue cancer	SCC-25
Total	11 types of cancer	19 cancer cell lines

H Color Code for Expression: Red – Positive; Blue – Negative

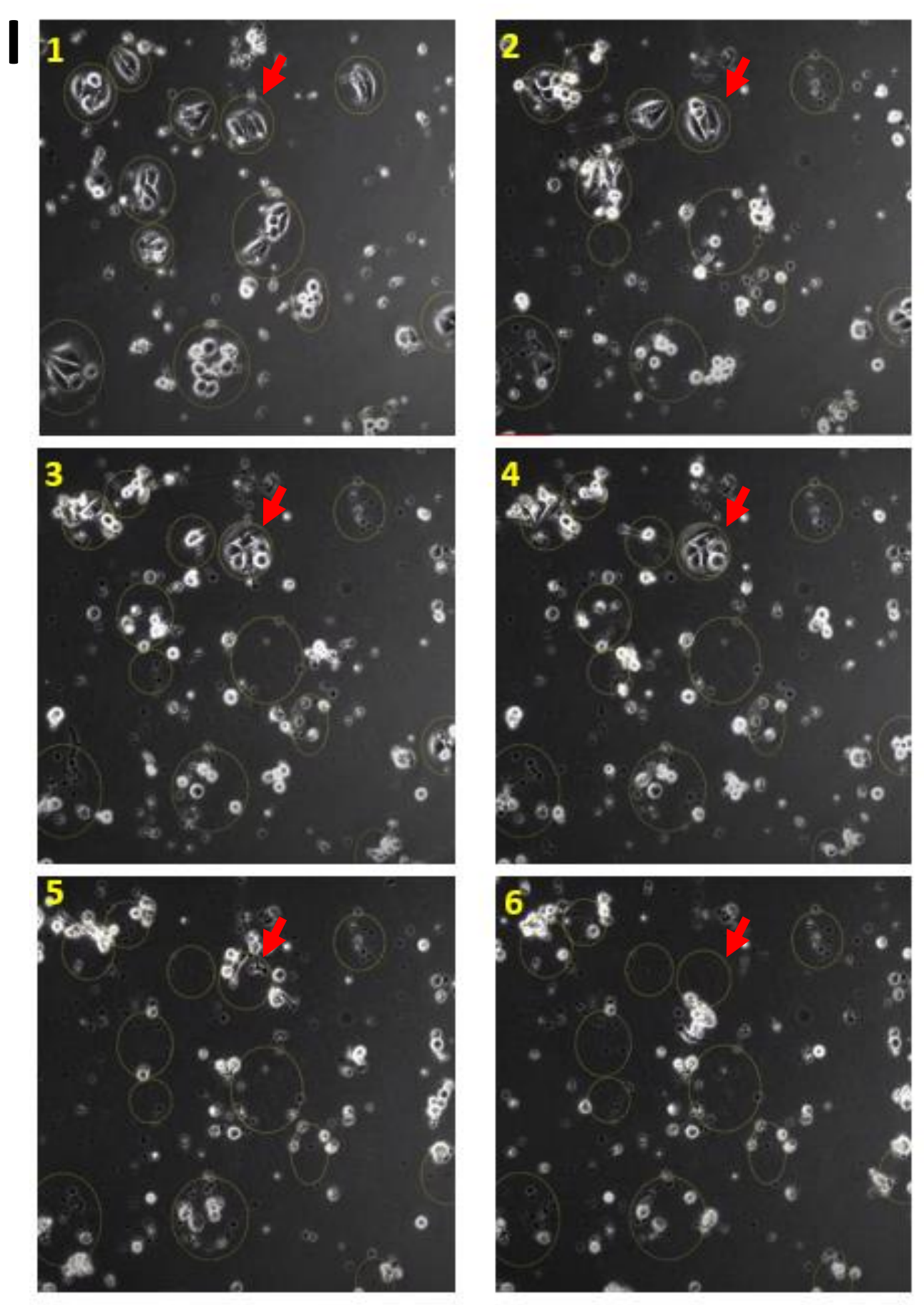
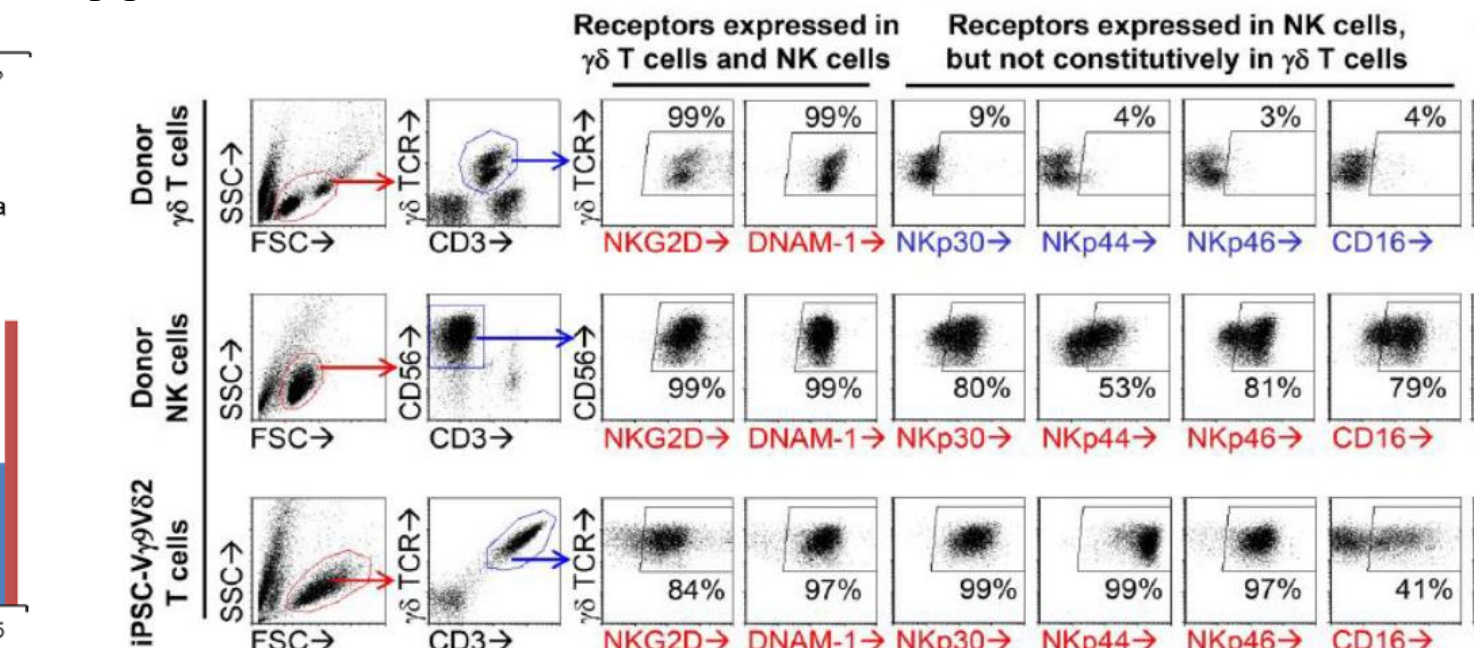


Figure E: Schematic of hybrid iPSC- $\gamma\delta$ NK T cell generation without gene editing. F & G: Cytotoxicity killing assay and the list of cancer cell lines that can be targeted by iPSC- $\gamma\delta$ NK T cell. H: Flow cytometry analysis of iPSC - $\gamma\delta$ NK T cell showing the expression of receptors unique to $\gamma\delta$ and NK cell. I: Photos of a timelapse video of iPSC - $\gamma\delta$ NK T cell killing a human colorectal cancer cell over 48 hours.

Conclusion: CytoMed Therapeutics possess a unique platform technology (worldwide exclusive patent) to produce a next generation iPSC - $\gamma\delta$ NK T cell, which is a ideal broad spectrum cancer immunotherapeutic. CytoMed is seeking collaborators to bring this technology to the clinical stage and beyond.