

# Engineered T-cell Therapies at UCL

## UCL CAR T-cell Programme

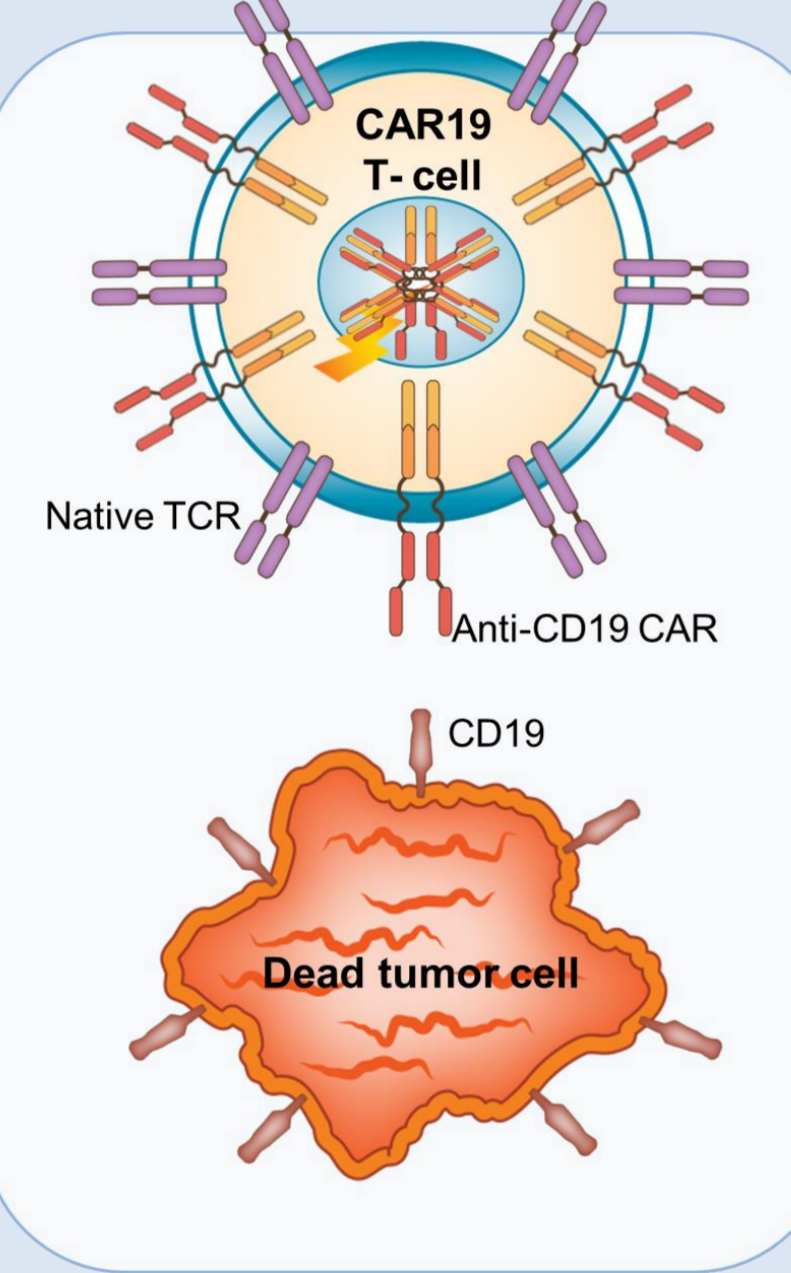
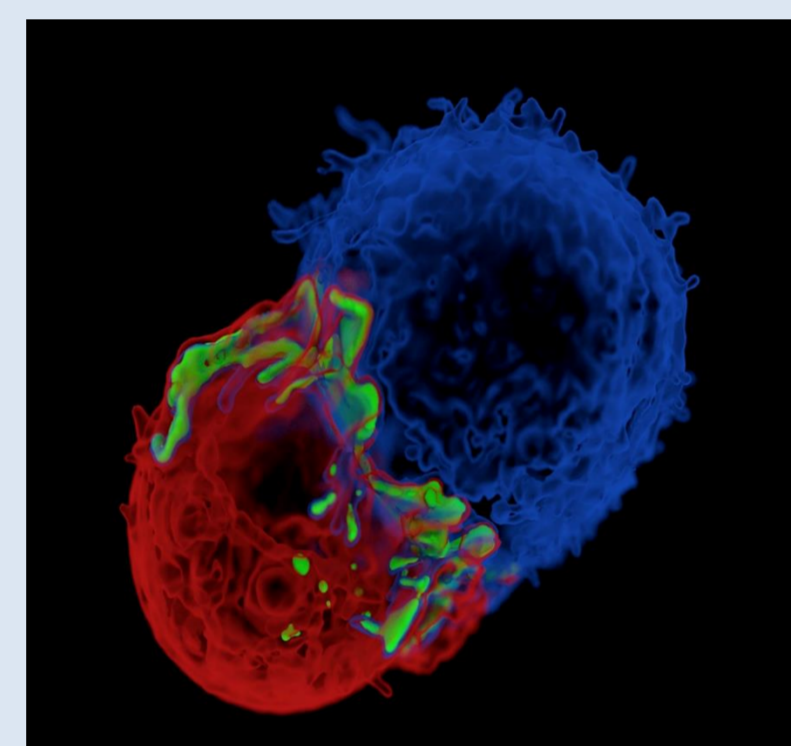
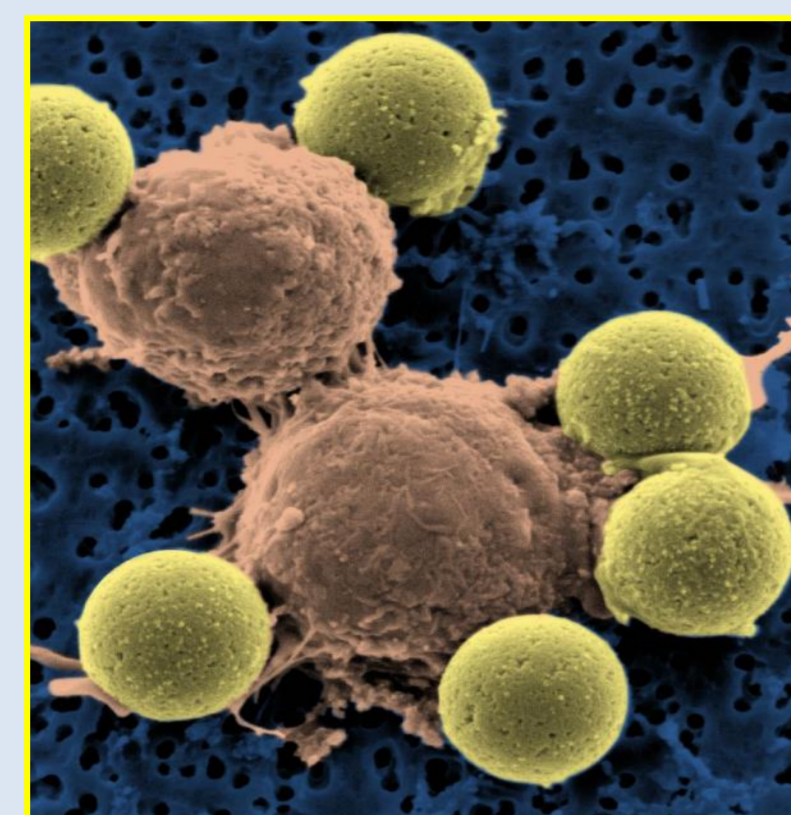
Claire Roddie<sup>1,2</sup>; Mahnaz Abbasian<sup>1</sup>; Maeve O'Reilly<sup>1,2</sup>; Juliana Pinto<sup>1</sup>; Ketki Vispute<sup>1</sup>; Harriet Roddy<sup>1</sup>; Lauren Nicolay<sup>3</sup>; Syed Fahetullah<sup>3</sup>; Waseem Qasim<sup>3</sup>; Kim Champion<sup>4</sup>; Alex Day<sup>4</sup>; Farzin Farzaneh<sup>5</sup>; Mark Lowdell<sup>1</sup>; Martin Pule<sup>1</sup>; Karl Peggs<sup>1,2</sup>.

<sup>1</sup> Cancer Institute, University College London; <sup>2</sup> Department of Haematology, University College London Hospitals NHS Trust; <sup>3</sup> Molecular and Cellular Immunology Section, UCL Great Ormond Street Institute of Child Health; <sup>4</sup> Cancer Research UK & UCL Cancer Trials Centre; <sup>5</sup> Department of Haematological Medicine, King's College London. Email contact: c.rodie@ucl.ac.uk



### The UCL CAR T-cell Programme

**C**himeric **A**ntigen **R**eceptor (CAR) T-cells are immune cells that have been genetically engineered or 'redirected' to recognise and kill cancer cells. The team have created a number of CAR constructs to target **CD19**, a cell-surface protein found on B-cell cancers such as leukaemia and lymphoma. The UCL CAR T-cell programme is the largest in Europe.

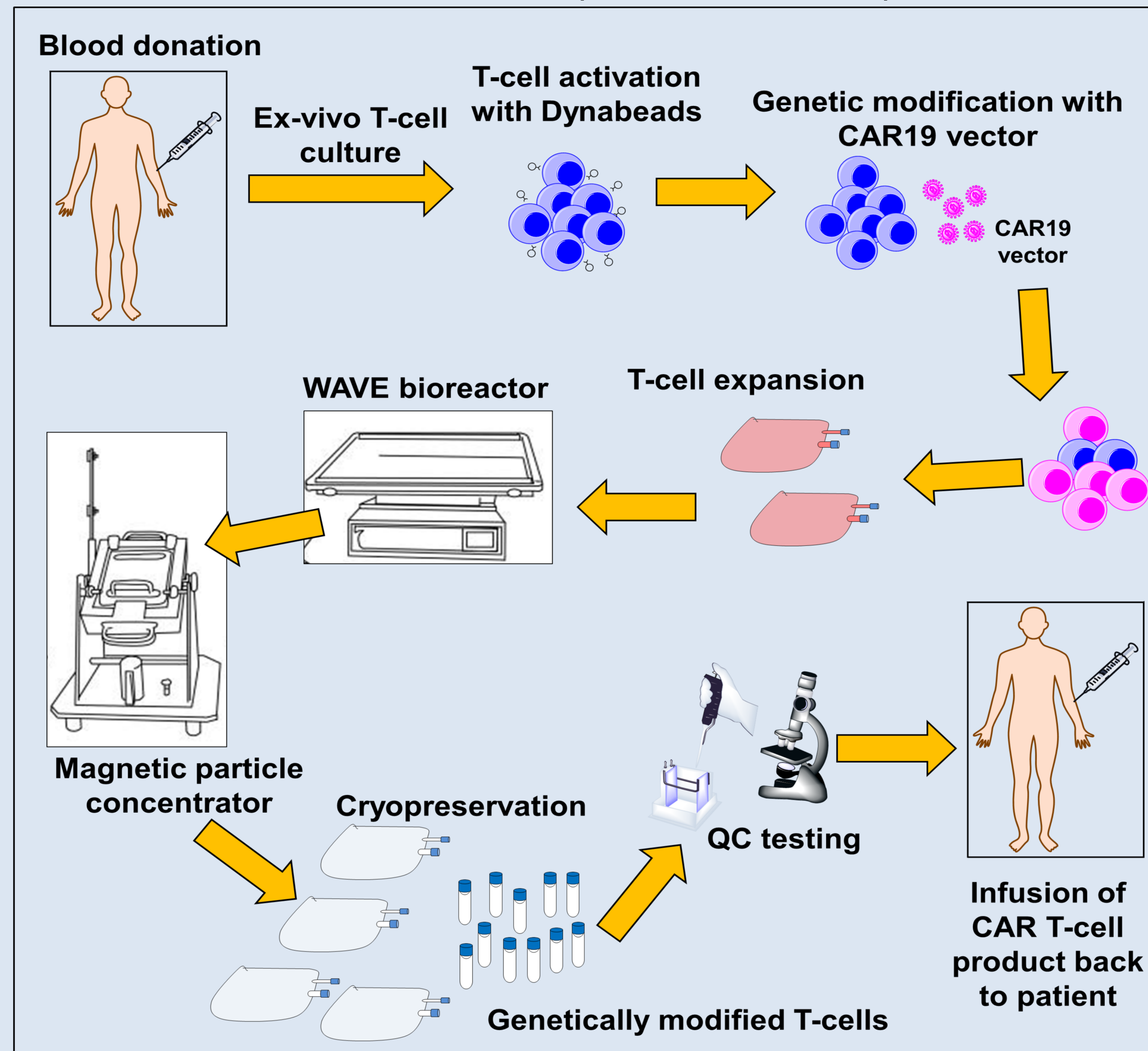


#### CAR structure

- Tumour binding domain**- this antibody-derived fragment permits binding of tumour-associated antigens
- Spacer domain**- this projects the tumour binding domain from the T-cell surface so it can easily bind to cancer cells
- Cell membrane**
- CAR T-cell activation domain**- this permits activation and cytotoxicity

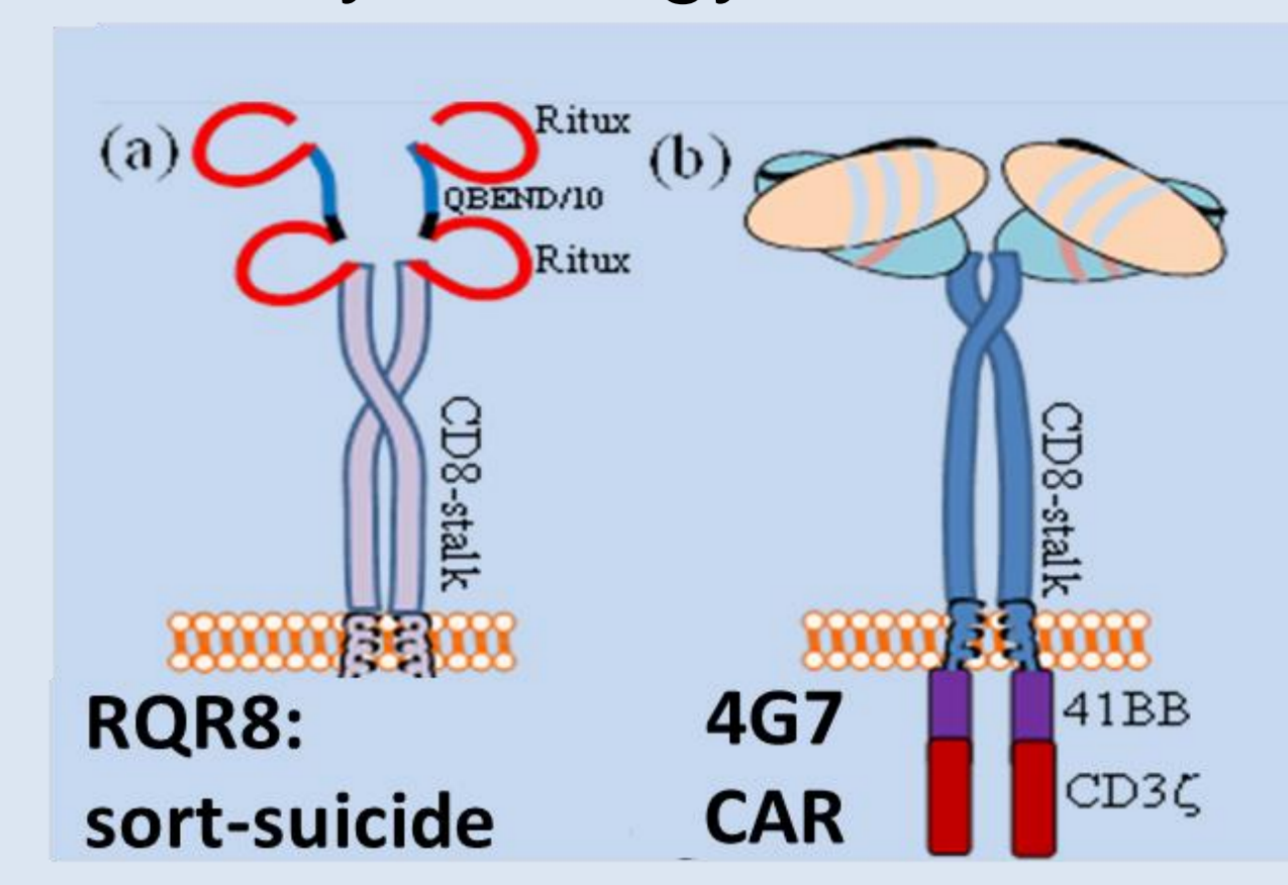
### CAR19 T-cell manufacture at UCL- challenges

CAR T-cell manufacture takes up to 2 weeks from blood donation → genetic modification → infusion of CAR T-cell product back to the patient.

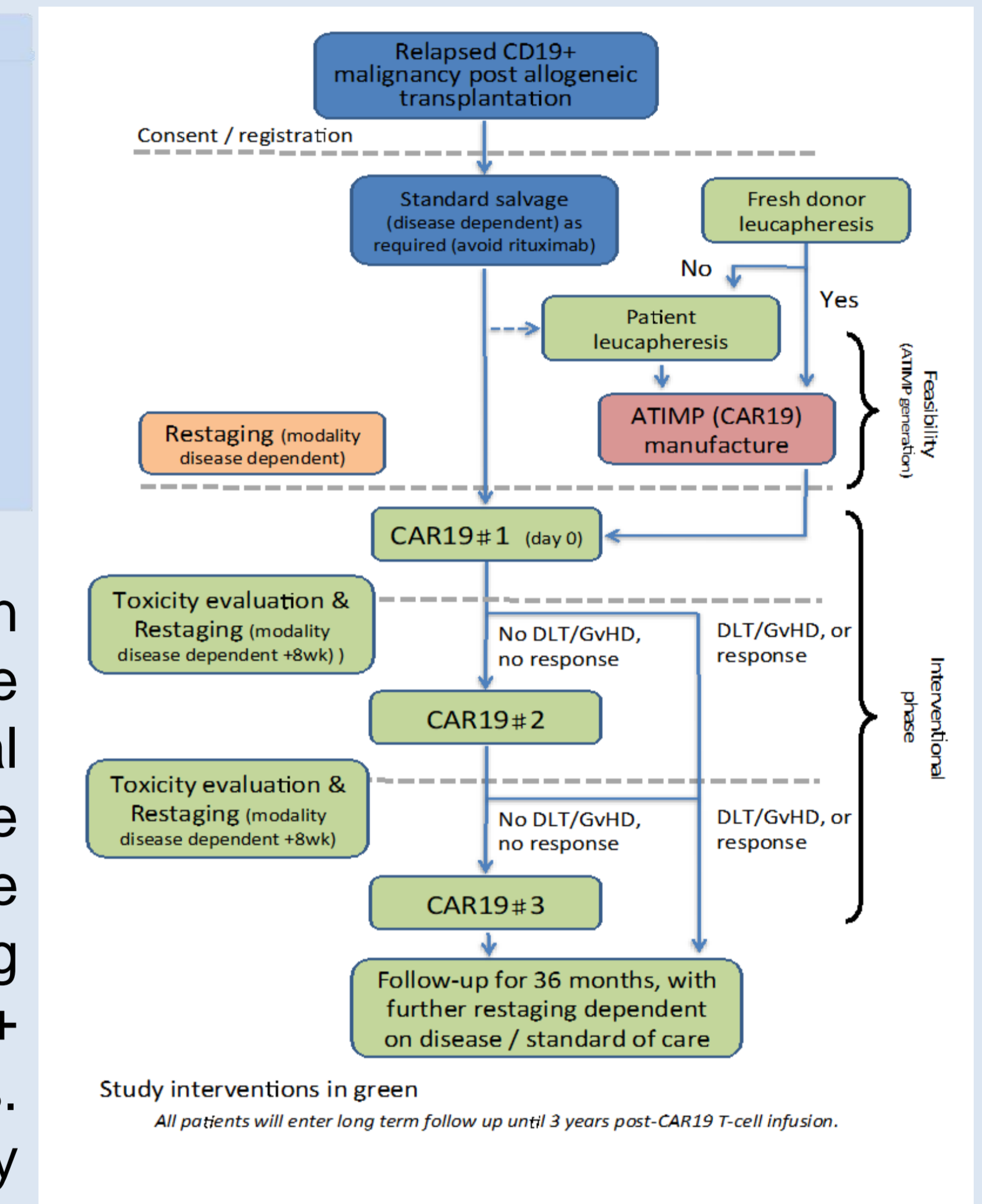


### State-of-the-art manufacture

On the UCL/H CARD Study (*CAR19 Donor Lymphocytes for relapsed CD19+ cancer post-allogeneic stem cell transplant*), the Miltenyi Prodigy has been used to manufacture CAR T-cells.



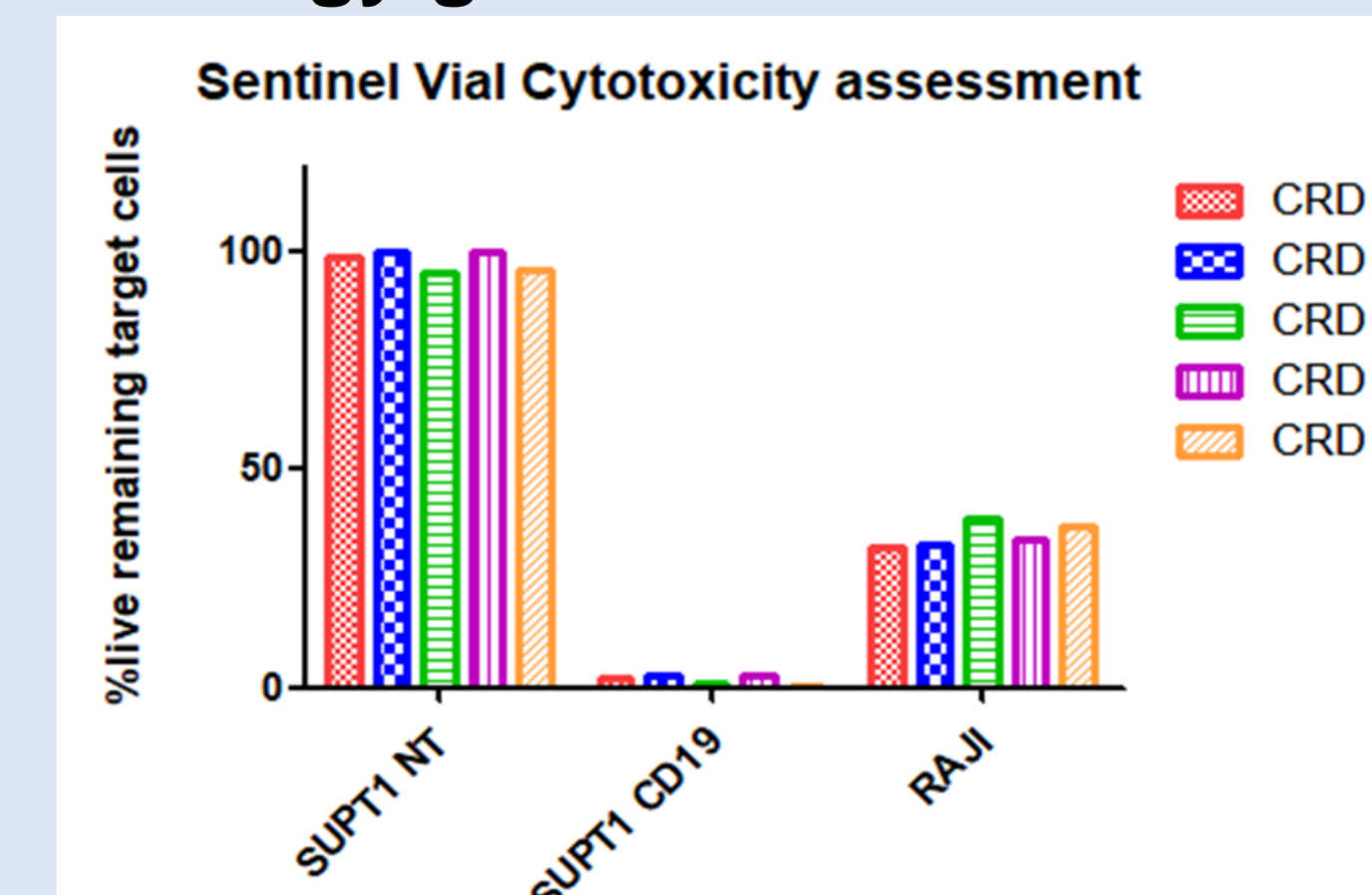
**CAR: 4G7 CD19 CAR**  
Using the Prodigy, we can make CAR T-cells at the numbers required for clinical trial, that are sterile and safe for use and that are functionally active, secreting cytokines and killing CD19+ targets in cytotoxicity assays. The clinical trial is now fully recruited (n=14 patients).



#### CARD study design

Run	Starting material	Yield Total lymph (x10 <sup>8</sup> )	% CAR19+ T cells	Yield CAR19 + T cells (x10 <sup>8</sup> )	Target met (≥ 3.5x10 <sup>8</sup> CAR19+ T cells)	Length of Process (Days)
15-01	Fresh	4.00	23.9	0.96	X	10
15-03	Fresh	8.08	44.3	3.6	✓	9
15-04	Frozen	23.2	27.5	6.4	✓	9
15-06	Frozen	18.5	50.2	9.3	✓	8
15-07	Frozen	17.1	56.7	9.7	✓	8
15-GMP-01	Frozen	20.0	66.4	13.3	✓	8
15-GMP-02	Frozen	18.6	57.4	10.7	✓	8
15-GMP-03	Fresh	17.1	54.0	9.2	✓	8
mean	n/a	15.8 ± 6.4 x10 <sup>8</sup>	47.6 ± 14.9%	7.9 ± 4.0 x10 <sup>8</sup>		

Prodigy generates CAR T # for trials; Qasim et al, Cytotherapy 2016



**Summary**  
Scalability of autologous CAR T-cell manufacture to meet patient need is enabled by the Prodigy. **ECMC funding supports the integration of new technologies into our manufacture space and ultimately allows us to bring more CAR T-cells to more patients.**

CARD products kill CD19+ target cells in Cytotoxicity assays in vitro

CAR T-cells manufactured at UCL are used in the Phase I/II clinical trials listed below. **ECMC support allows us to manufacture products for the COBALT, CARD, CARPALL and ALLCAR19 clinical studies**

Study	Indication	Status	Products made	Funder
COBALT	DLBCL	Open	8	Bloodwise
CARPALL	Paed. ALL	Open	6	Children with Cancer
CARD	Relapse post allo	Open	12	EU FP7 ATECT
ALLCAR19	Adult ALL	Open	14	NIHR

Due to the personalised nature of the products, CAR T-cell therapy is difficult to scale to patient need. The conventional manufacture process illustrated above is multi-step, multi-user, complex, costly and difficult to standardise. To address this, UCL collaborated with Miltenyi BioTech to trial a semi-automated, closed cell manufacturing platform (Miltenyi Prodigy, pictured right) in the CAR T-cell programme to facilitate scalability.

