

Transforming patients' lives through
cellular immunotherapy

Karen Hodgkin, COO

Novel Approaches for the Treatment of Solid
Tumours

Overview of Cell Medica

Our mission: Transform the treatment of cancer with cellular immunotherapy

- Founded 2007
- Treating patients since 2008
- 55 staff
- London, Zurich, Houston

Shareholders



Two oncology platforms with leading research partners, targeting solid tumours

CAR-NKT Cells

NKT cells modified with chimeric antigen receptors

Planned Phase I by Q1 2018



THE UNIVERSITY
of NORTH CAROLINA
at CHAPEL HILL

Engineered TCRs

T cells modified to express Dominant TCRs

Planned Phase I by Q1 2019



The Challenge in Oncology



Haematological Malignancies



Solid Tumours

??

Haematological malignancies: Efficacy comparison to other treatments

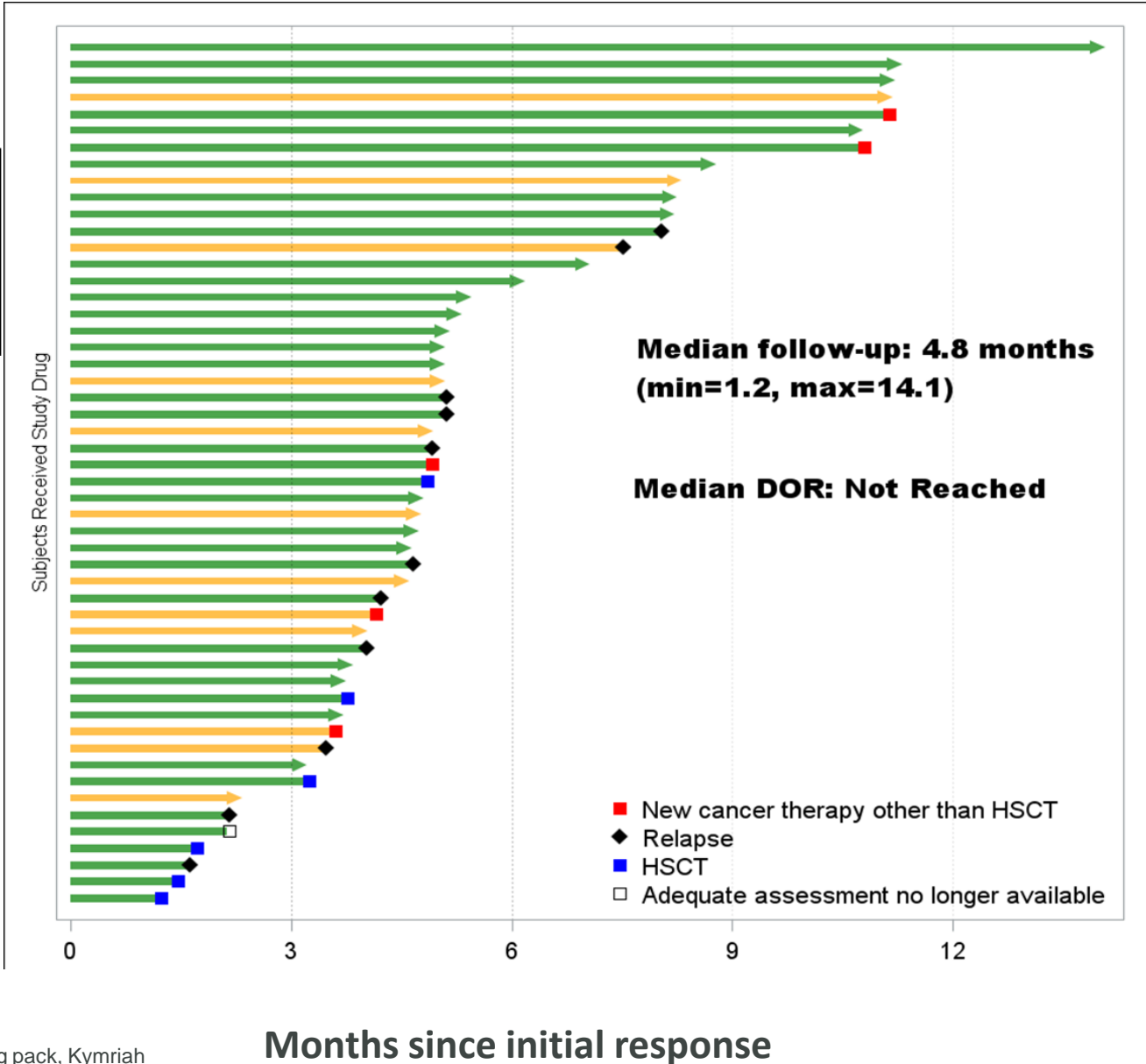
	Clofarabine mono	Blinatumomab	Kymriah (B2202)
Patients (N)	61	70	68
≥3 prior regimens	62%	7%	60%
ORR (CR+CRi)	20%	39%	83%
MRD negative	NA	20%	83%
Median OS	3 months	7.5 months	16.6 months
12 months OS	20%	40%	79%
Early mortality (within 30 days)	25%	7%	3%

Disclaimer: Cross-trial comparisons cannot be made based upon differences in study designs, patient populations, and other factors.
Source: FDA Briefing pack, Kymriah

Kymriah: Duration of Response

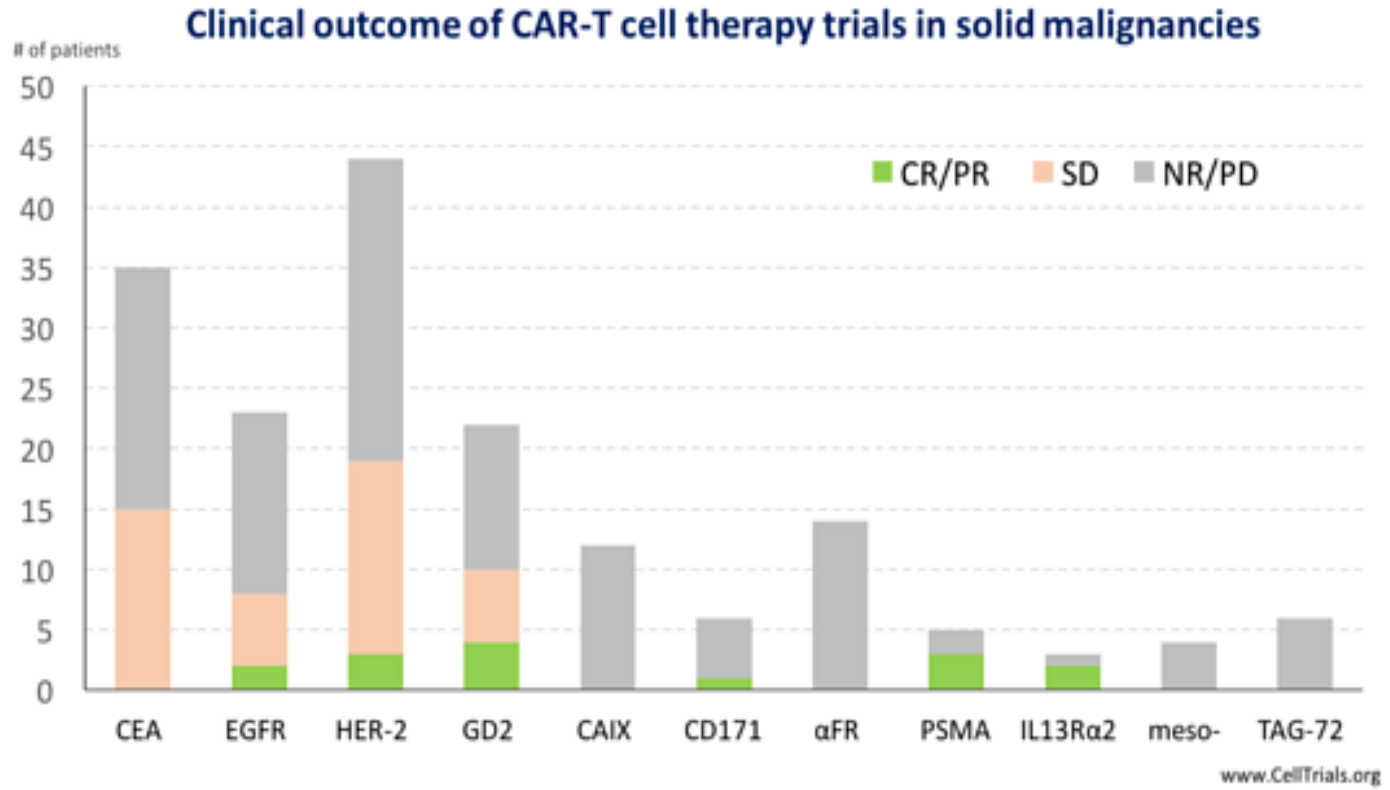
Response

- CR
- CRi



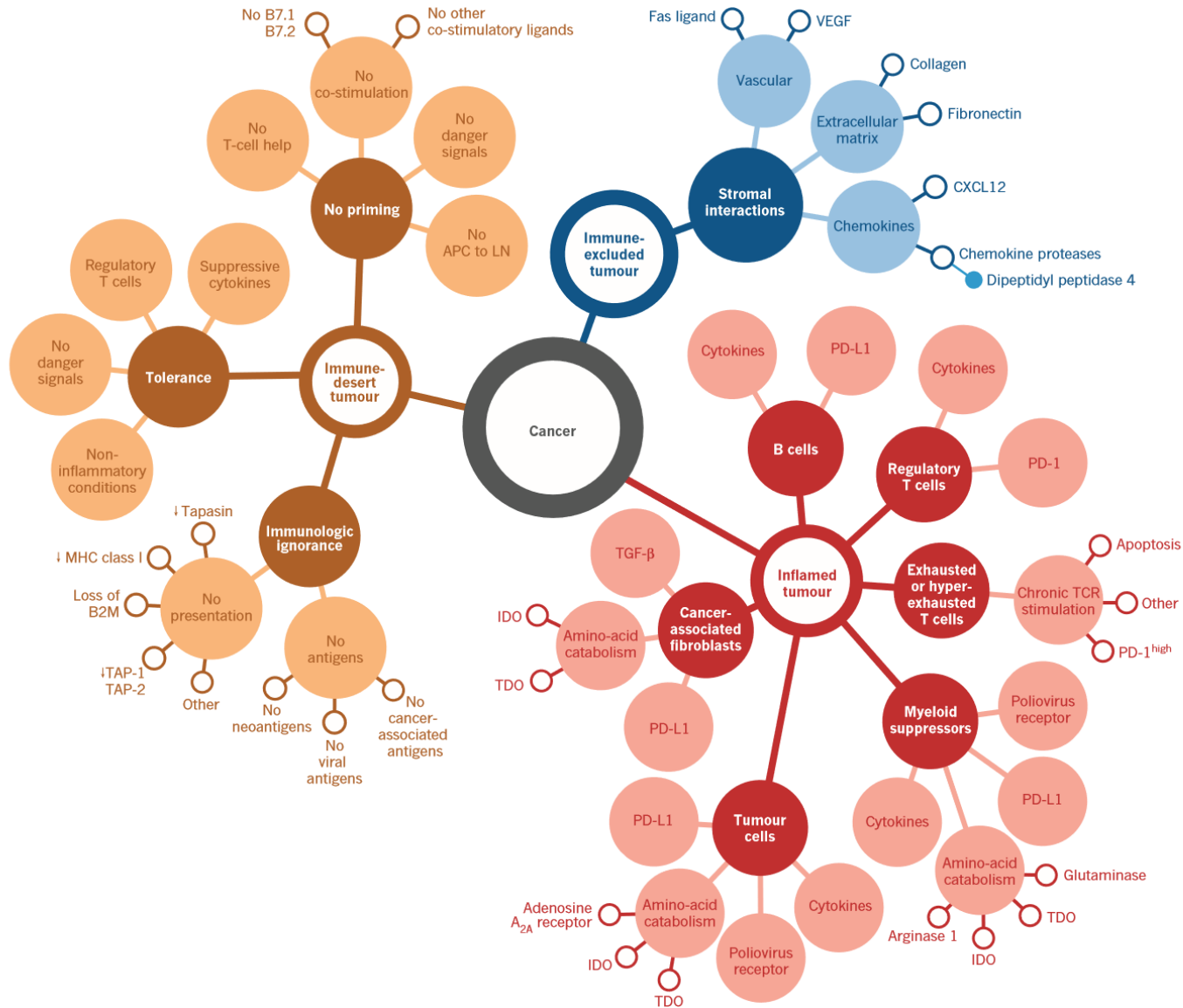
Source: FDA Briefing pack, Kymriah

In Contrast: Data with CARs in solid tumours



Source: Cell Trials Data by Couto, Verter, Bersenev 2017

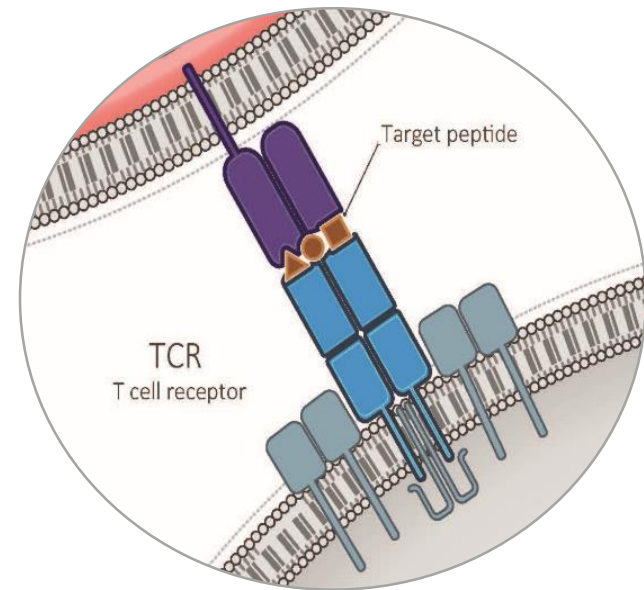
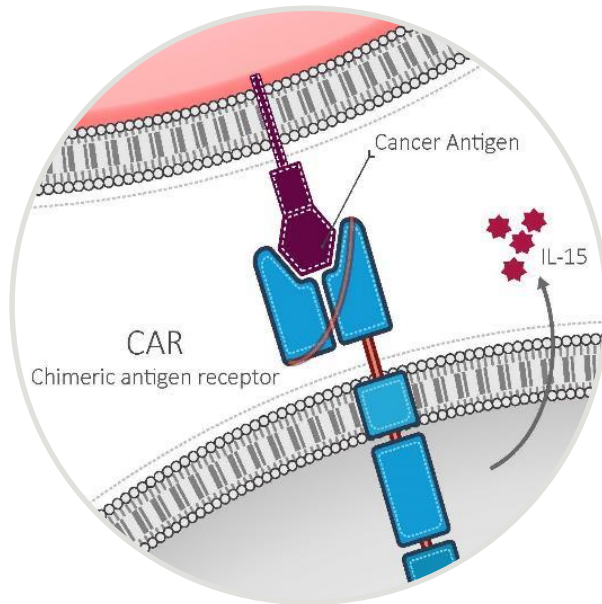
Cancer Immunity/Phenotype



Source: Daniel S. Chen & Ira Mellman,
19 JANUARY 2017 | VOL 541 | NATURE



Cell Medica's Approaches for CAR/TCR Cell Therapies for Solid Tumors



1

NKT Cell (subset of T cells)
Powerful cytolytic activity
No GvHD in allo setting

2

Humanised scFvs
Improves persistence by preventing
immune rejection

3

Activating Cytokines
Helps to overcome tumor
microenvironment

4

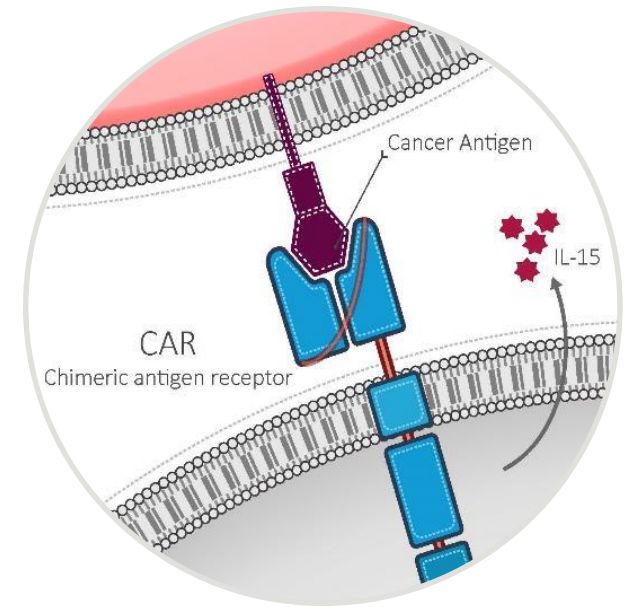
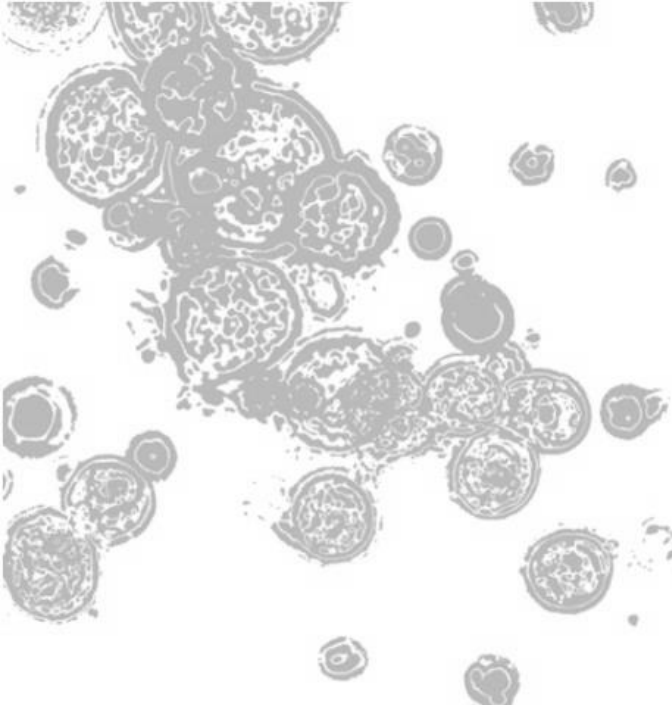
**Localised anti-PDL1 and other engineered
immuno-modulators**
Creates a more favourable TME

5

Dominant TCR technology
Improves TCR expression and efficacy

6

Panel of CAR/TCR High Value Cancer Targets
Targeting large patient populations solid and liquid
tumours



Next Generation CAR NKTs for Solid Tumours

Autologous

- CMD 501-CAR-IL15-NKT cells for Neuroblastoma, Small Cell Lung Cancer/Melanoma
- CMD 504-CAR-IL15-NKT cells for Triple Negative Breast, Glioblastoma, Colorectal Cancer
- CMD-503-CAR-IL15-NKT cells for Hepatocellular Cancer

Allogeneic

- CD19-CAR-IL15-NKT cells for CD19+ Lymphomas (off-the-shelf)



Next Generation CAR-NKTs for Solid Tumours

Homing to Sites of Tumour

- NKT Cell (subset of T cells) navigate to sites of solid tumor

Engineered to overcome the suppressive tumour microenvironment

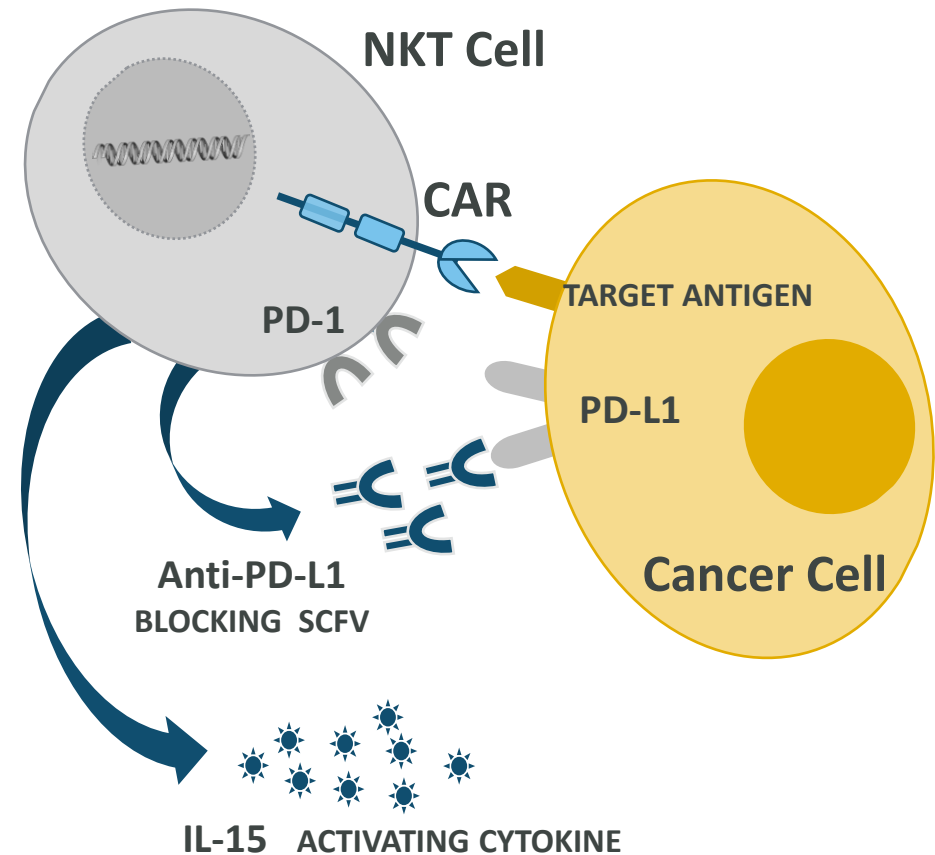
- CAR-NKTs kill cancer cells through CAR
- Alter tumour microenvironment through modulating suppressive tumour-associated macrophages
- IL15 is an activating cytokine associated with T cell memory and long-term activation
- Localized checkpoint inhibitor can be delivered in CAR construct

Humanised scFvs

- Humanized scFvs improve persistence by minimizing rejection

Optimal Targets for Tumor Antigens

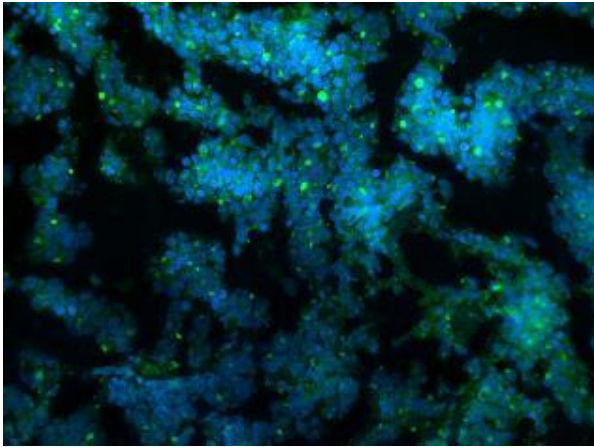
- High differential expression of tumor antigen on malignant cells relative to healthy tissue



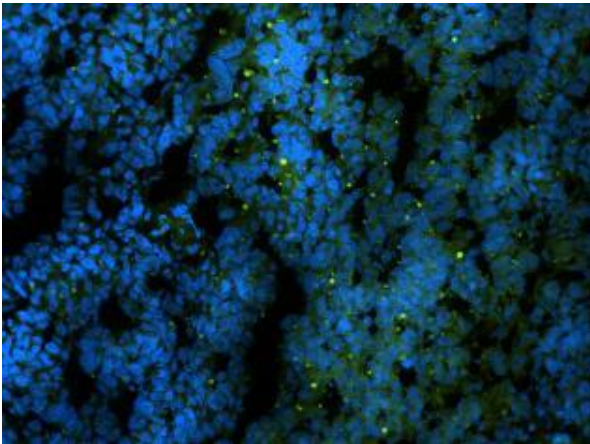


CAR-NKTs Homing to Tumour Superior to CAR-Ts

GD2- CAR- NKT Cells

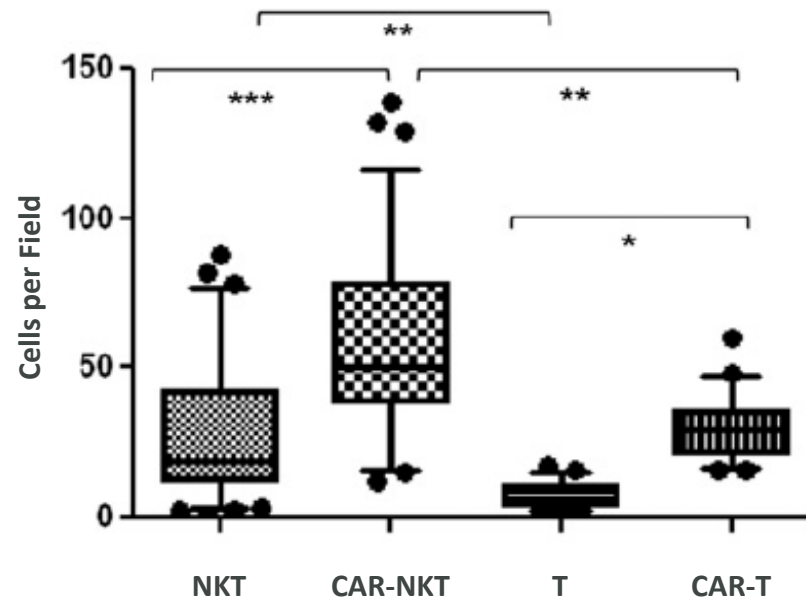


GD2-CAR-T Cells



- Significantly more intra-tumoral CAR-NKT cells compared to CAR-T cells in mouse neuroblastoma model

Source: Heczey et al. (2014), Blood 124:2824.



* $p < 0.05$; ** $p < 0.01$; **** $p < 0.001$

CMD-502- Off the Shelf Product

NKT Cells recognize a specific glycolipid antigen which is not associated with Graft vs Host Disease – safety is increased

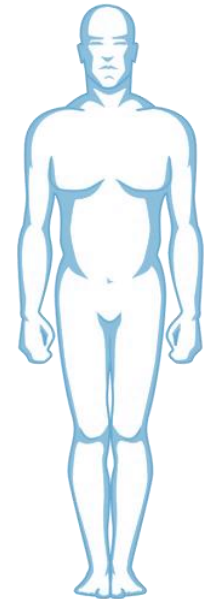
▶ **Reduces complexity of manufacturing product by avoiding need to gene-edit the endogenous T cell receptor**



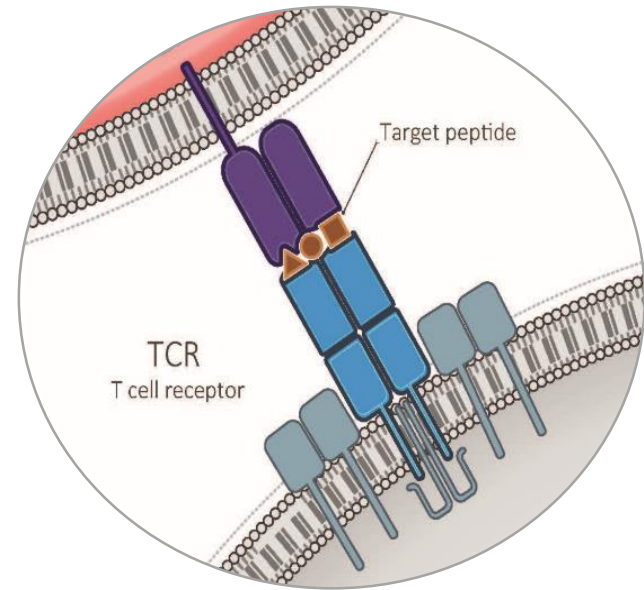
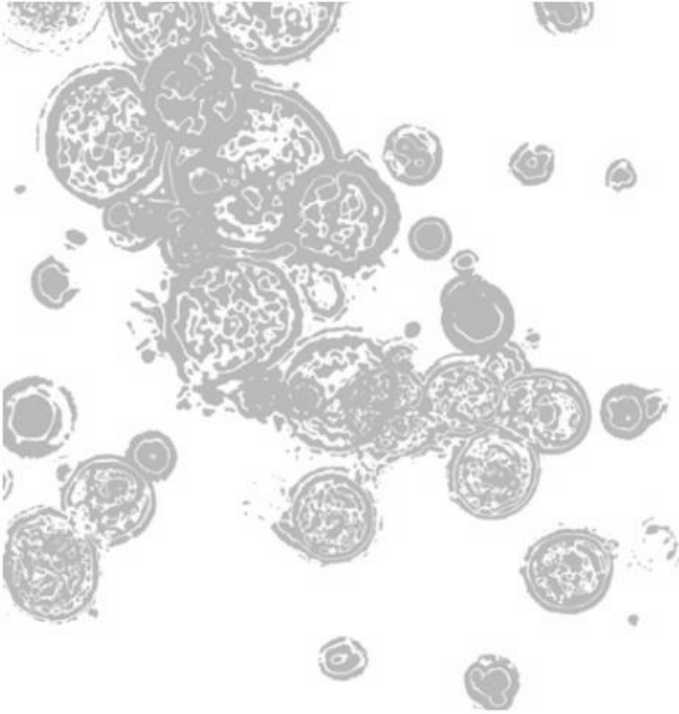
Off the shelf product (allogeneic cells) will be mass produced from healthy donors who are “non-self” to patient

T cell off-the-shelf product may attack patient’s body as “non-self” relative to donor.

NKT cells do not and are advantageous for this application



Cell Medica is currently developing off-the-shelf CAR NKT products with Baylor College of Medicine



Next Generation Engineered T Cell Receptors

For treatment of

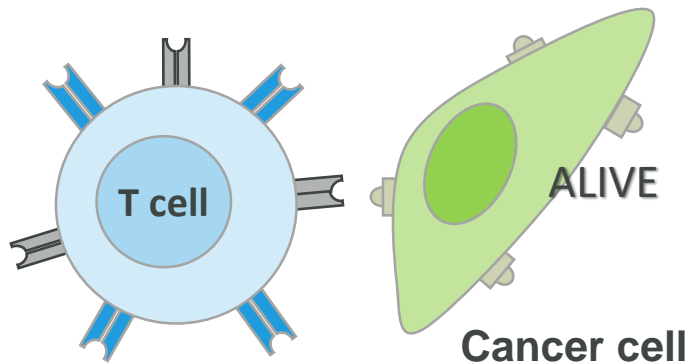
- CMD-601 (Survivin-Dominant TCR) for Ovarian and Pancreatic Cancer
- CMD-602 (WT1-Dominant TCR) for multiple cancers






Exclusive License to UCL Dominant TCR Platform

High TCR expression levels enhance antigen-specific activation

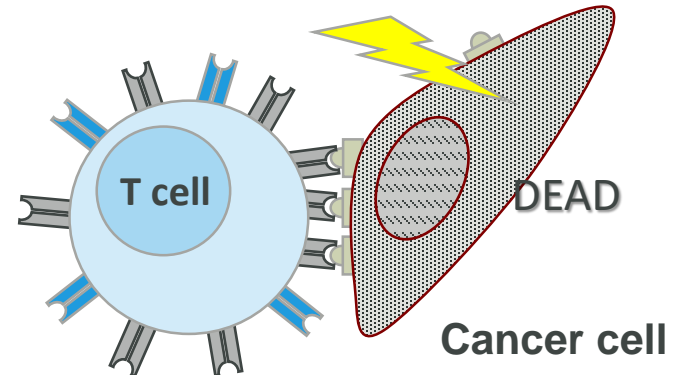
Genetically modified TCRs often do not express well relative to endogenous TCRs



T cells with modified TCRs are usually expressed at too low levels to achieve activation and are therefore ineffective

- Key:**
-  Endogenous TCR
 -  Genetically engineered TCR
 -  MHC/Target Complex

Dominant TCR technology increases number of T cells expressing TCR and expression level on each T cell



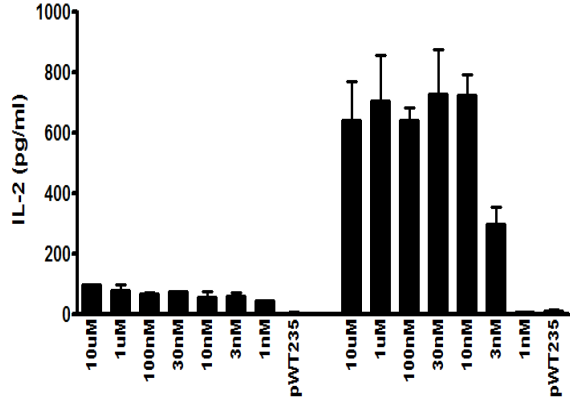
- ✓ Recognition of cancer targets expressed at low levels, or rare mutations, even when levels of HLA presentation are reduced (common in tumours)
- ✓ Reduced mispairing with endogenous TCR
- ✓ Validated with multiple TCRs



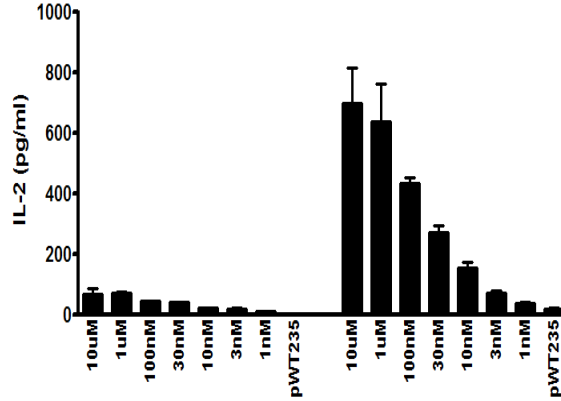
UCL Dominant TCR Platform

High expression levels lead to improved effector function

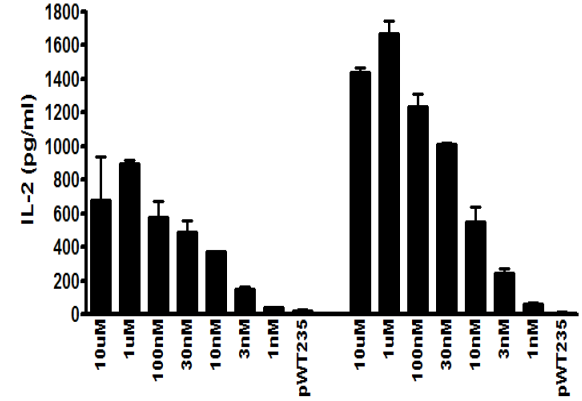
TCR 1



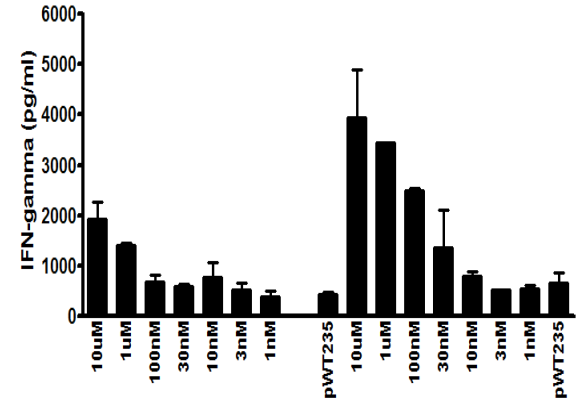
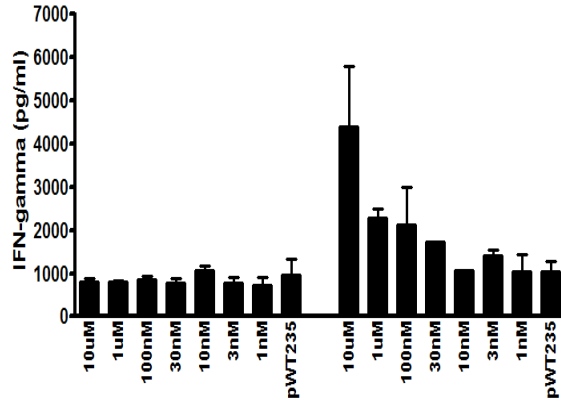
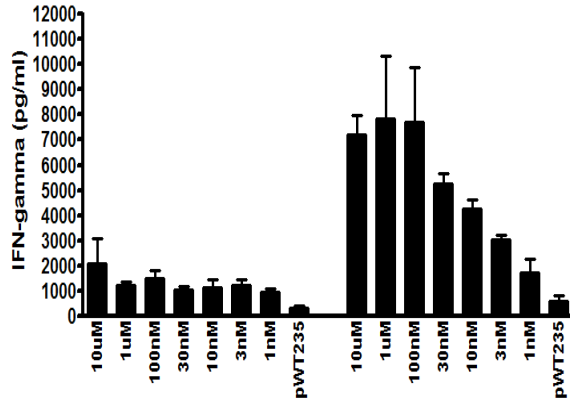
TCR 2



TCR 3



IL-2



IFN-γ

Wild type

Dominant

Wild type

Dominant

Wild type

Dominant



Pipeline: Five New Programs progressing towards the Clinic

		2017				2018				2019				2020			
		Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2		
CAR-NKT		CMD - 501 - Development				IND	Phase 1										
	US	CMD - 504 - Development						IND	Phase 1								
		CMD - 502 (Off the shelf) - Development								IND	Phase 1						
TCRs		CMD - 602 (Dominant WT1-TCR)						IND	Phase 1								
	EU	CMD - 601 (Dominant Survivin-TCR)								IND	Phase 1						

○ Conclusions: ATMPs as Cures – for solid tumours

- We are not there yet!
- But... many attempts to scale the summit!
- Thank you

