



Reimagined
2020 
NOVEMBER 9-14



Society for Immunotherapy of Cancer



Difficulties and Opportunities in developing Cellular therapy trials for Cancer :

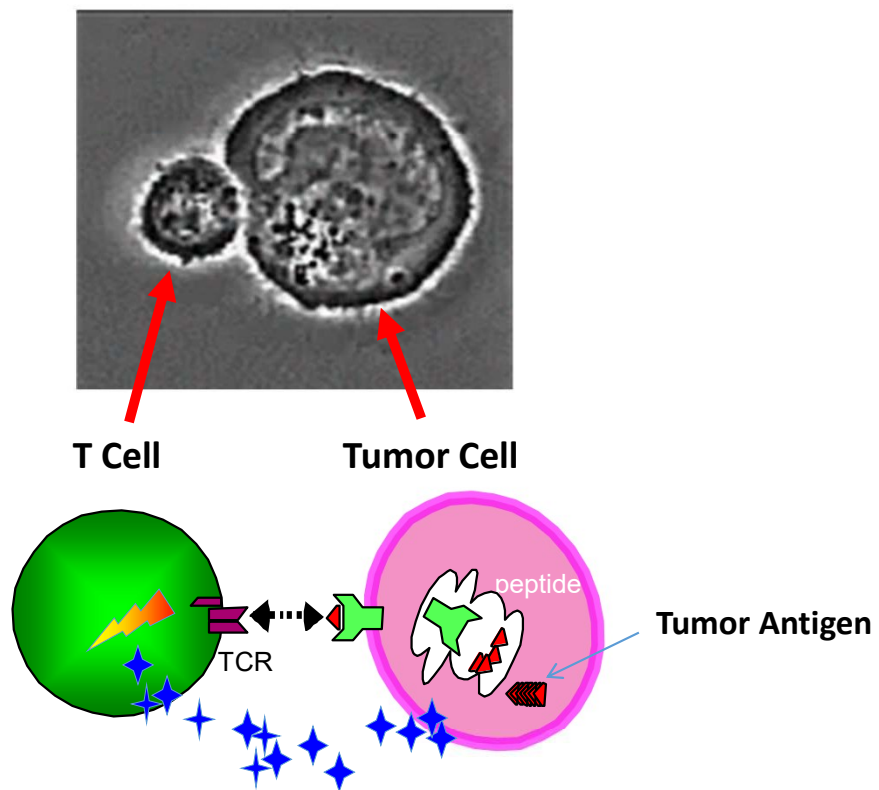
The Power of ONE



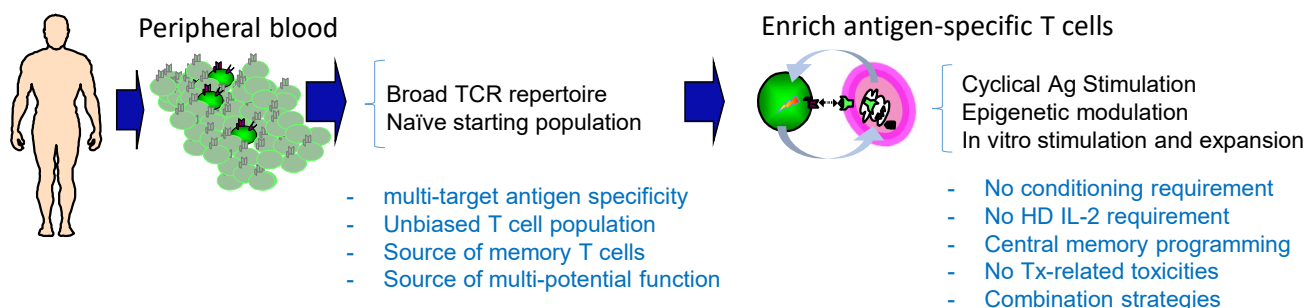
Society for Immunotherapy of Cancer

#SITC2020

T Cell Recognition and Killing of Tumor Target

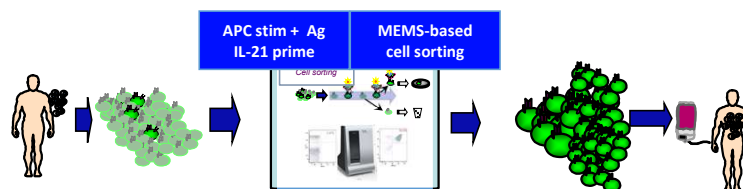


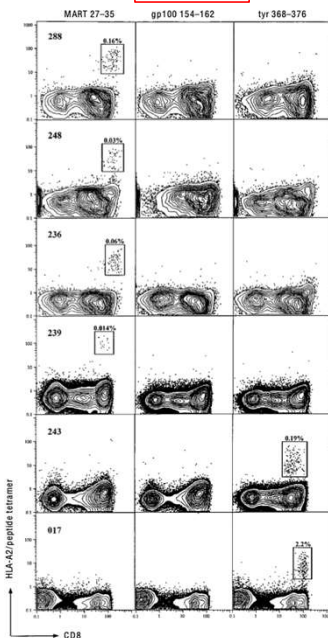
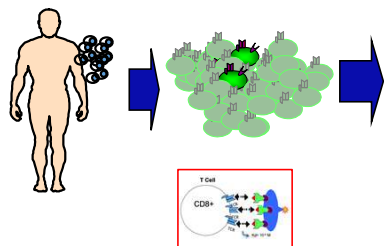
Endogenous T Cell (ETC) Therapy:



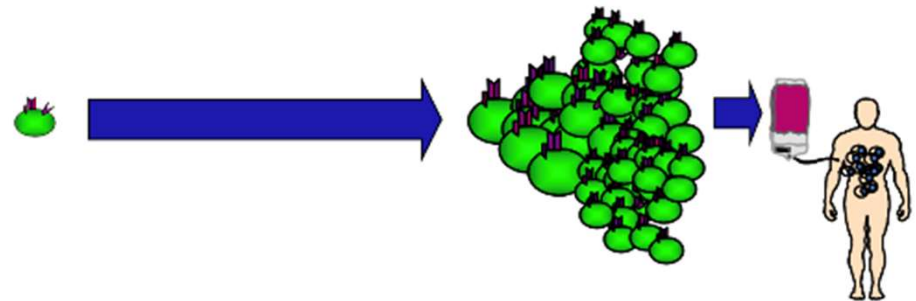
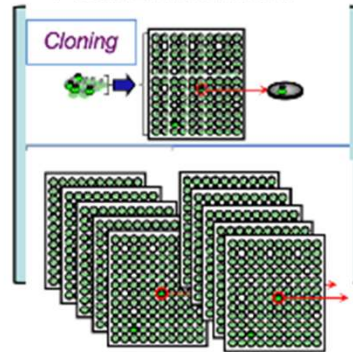
Why has this not be done before?

< 1:1,000,000 Tumor antigen-specific T_{CM} cells > 80 % 10^{10}

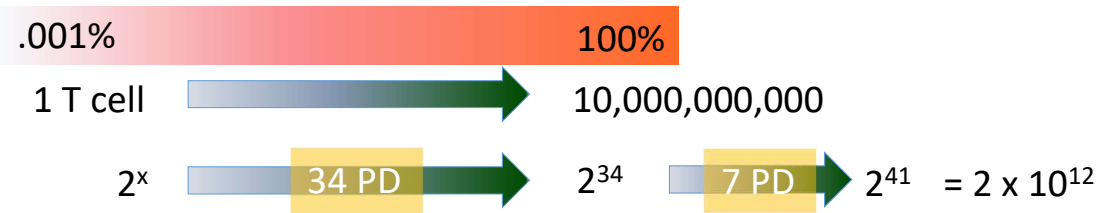
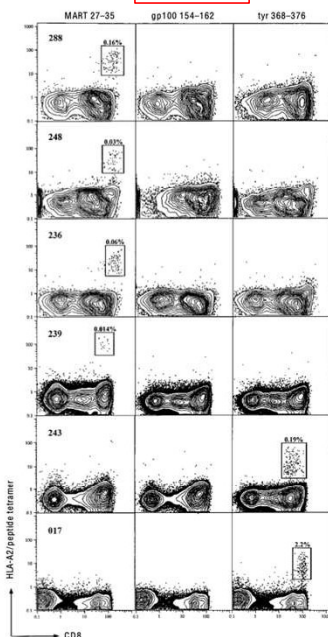
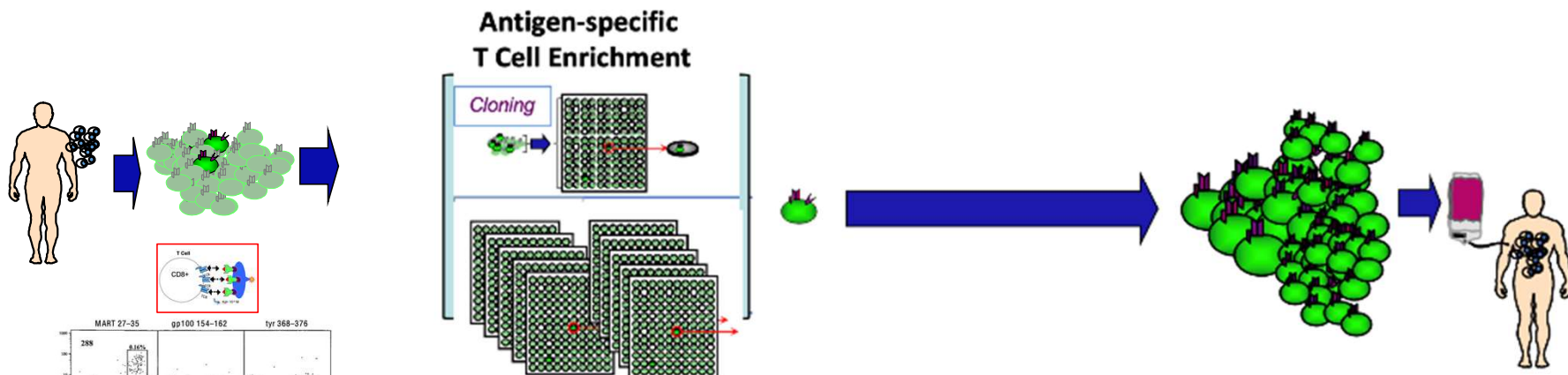




Antigen-specific T Cell Enrichment



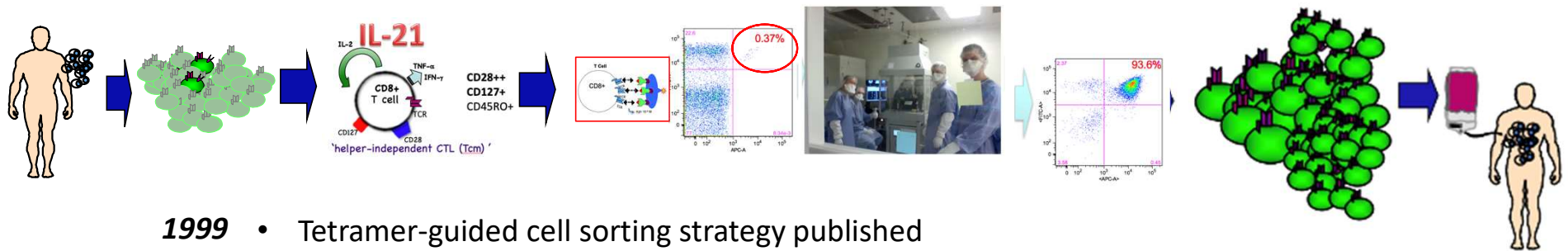
⁷ Lee and Yee et al, Nat Med 1999



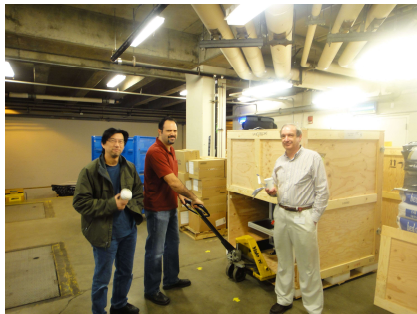
Naïve "50-70 PD in T cell lifetime" Minimal vector

Pawełec et al 1995

⁷ Lee and Yee et al, Nat Med 1999



- 1999** • Tetramer-guided cell sorting strategy published
- 2005** • IL-21 induction of central memory T cells published
- 2010** • September: received call from Toni Ribas about patient LZ with metastatic breast cancer failing 8+ lines of therapy including ASCT.
 - Meet with SP and LZ at Stand Up 2 Cancer Telethon
 - October: LZ has NY-ESO-1+ tumor, HLA-24. Leukapheresis -> brute-force cloning
 - November: check arrives to purchase clinical grade cell sorter



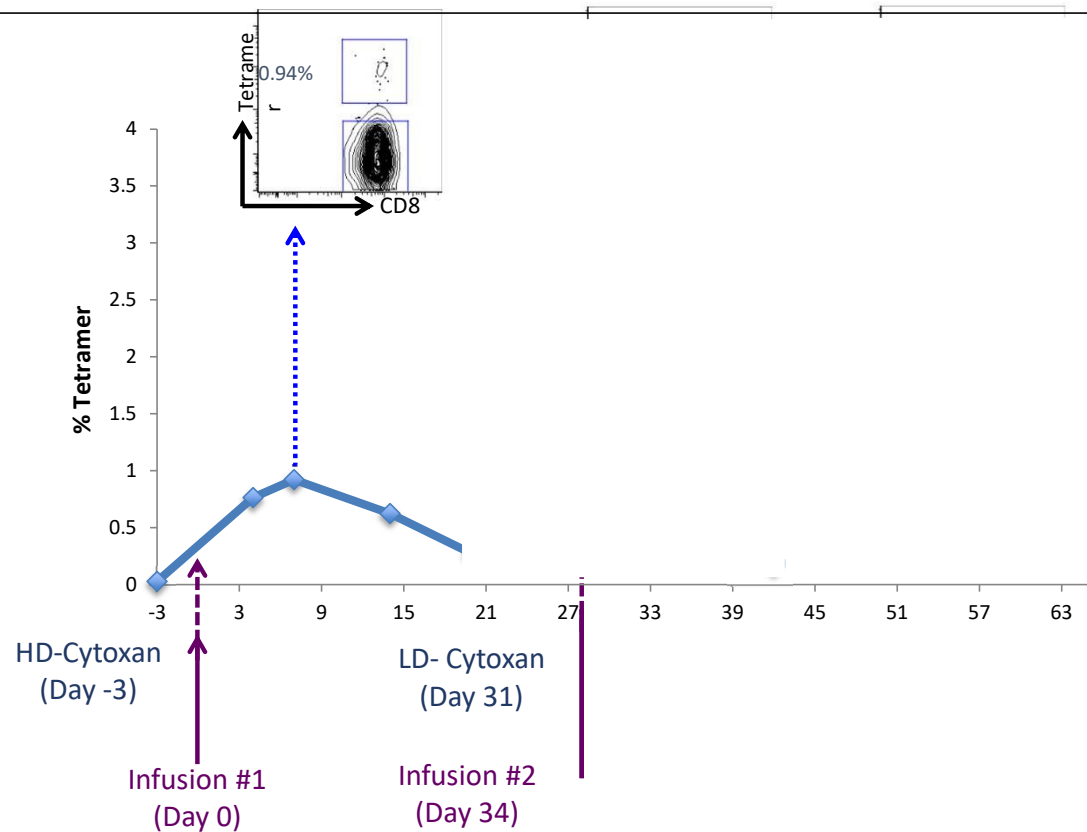


- 1999** • Tetramer-guided cell sorting strategy published
- 2005** • IL-21 induction of central memory T cells published
- 2010** • September: received call from Toni Ribas about patient YY with metastatic breast cancer failing 8+ lines of therapy including ASCT.
 - Meet with XX and YY at Stand Up 2 Cancer Telethon
 - October: YY has NY-ESO-1+ tumor, HLA-24. Leukapheresis -> brute-force cloning
 - November: check arrives to purchase clinical grade cell sorter
 - December: Single patient CIND submitted to FDA for first-in-class use of clinical grade cell sorter, first-in-human use of IL-21 primed, Tetramer guided sorting of antigen-specific T cells for treatment of cancer.
 - January 4, 2011: sorter arrives -> sorter does not work
 - January 20, 2011: visit Stanford to learn how to fit 99 cent spigot into sheath tank
 - Feb 4, 2011: FDA grants **CIND**
 - Feb 5, 2011: First use of tetramer guided cell sorting on patient NY-ESO-1-specific CTL

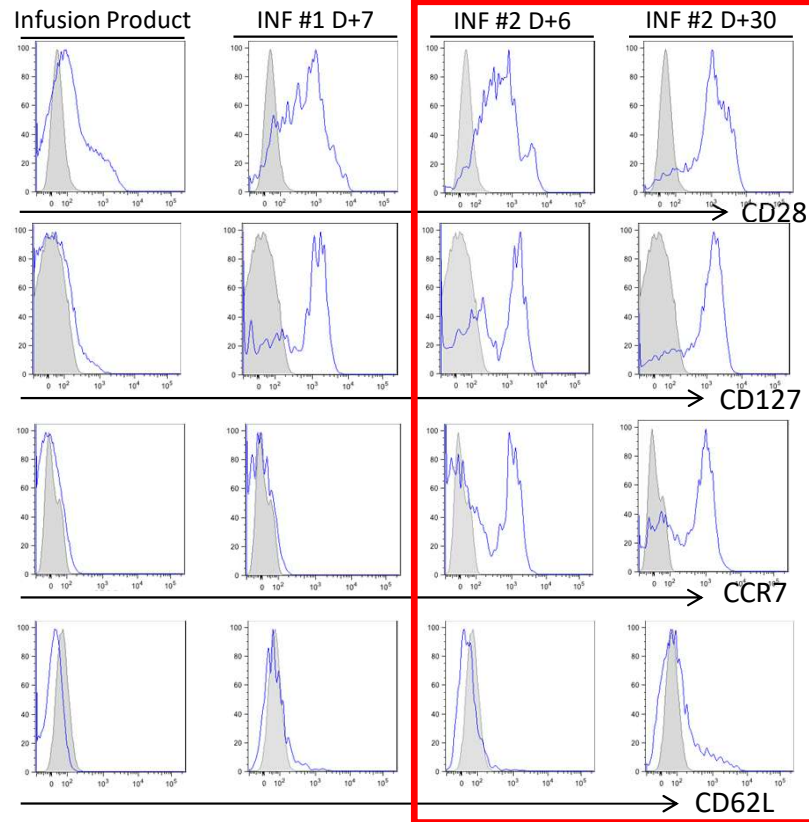
Expanded Access (Compassionate Use) IND

	Action	Supporting Documentation	IRL
Day 0-1	Contact sponsor/manufacture to obtain their agreement to provide expanded access to the investigational drug	Letter of authorization from sponsor/manufacture granting a right of reference to the information contained in their existing IND	<ul style="list-style-type: none"> Modified CMC cross-reference existing IND NEW IND
Day 1	Call FDA to obtain FDA authorization for the expanded access use	Information will be requested by the FDA representative and can be provided via phone, fax, or e-mail	<ul style="list-style-type: none"> Provide supporting information for manufacturing C of A, SOP documentation, Release criteria, GMP runs if applicable Supporting literature Clinical course, unmet need and urgency
Day 1	Obtain informed consent from patient or their legally authorized representative prior to administering treatment		Obtain informed consent from patient or their legally authorized representative prior to administering treatment For cell therapy – at time of T cell collection and manufacturing
Post-treatment by Day 5	Notify Institutional Review Board (IRB) of the emergency expanded access use	Supporting documentation as required by the respective applicable IRB	Contemporaneous review by IRB BEFORE TREATMENT
By Day 15	Submit the expanded access IND application to the appropriate Review Division in the Center for Drug Evaluation and Research (CDER) at FDA	Form FDA 3926 ¹ Letter of Authorization ² from sponsor/manufacture	Post-infusion follow-up for safety, toxicity and efficacy if applicable

Metastatic breast cancer, NY-ESO-1+,
T-cells targeting HLA A*2402/NY-ESO-1

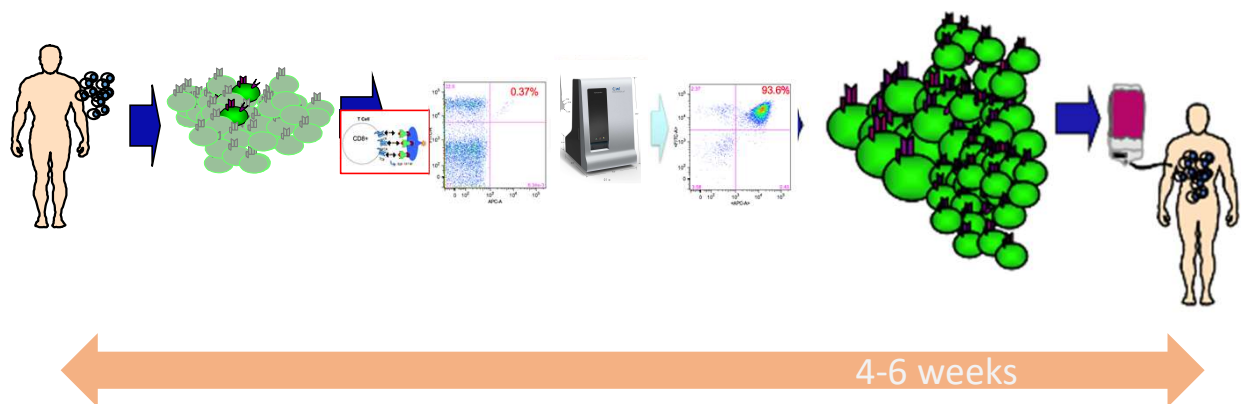
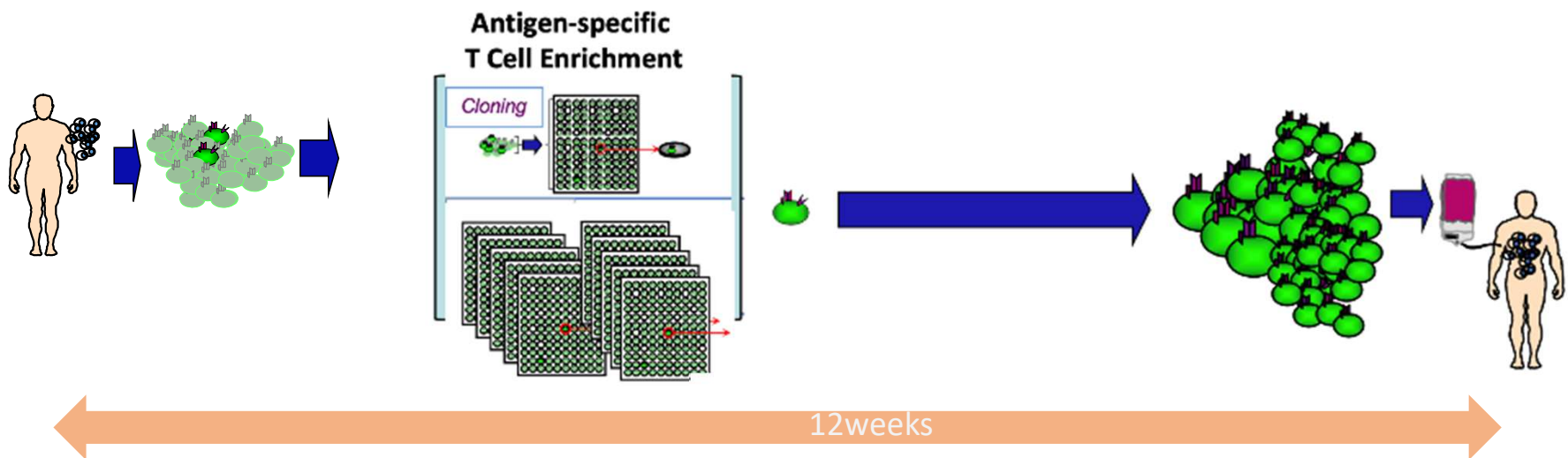


Surface phenotype of infused T-cells



With
Anti-CTLA4
(Tremelimumab)

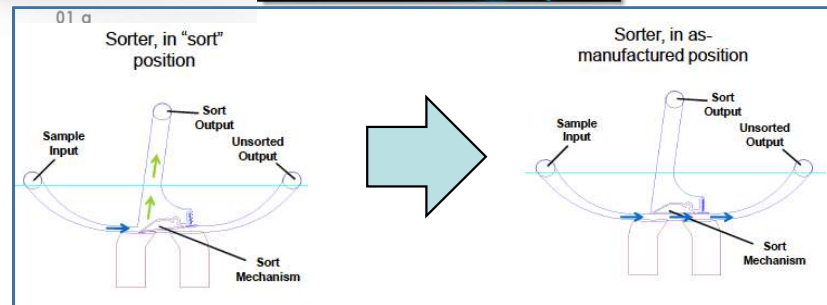
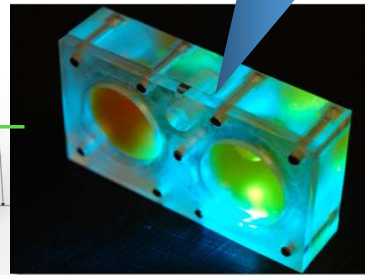
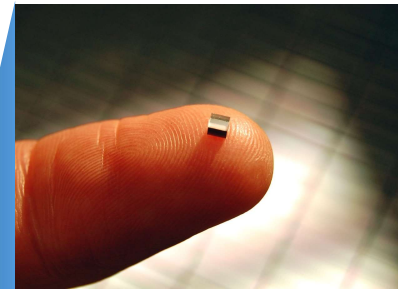
Why we do this?



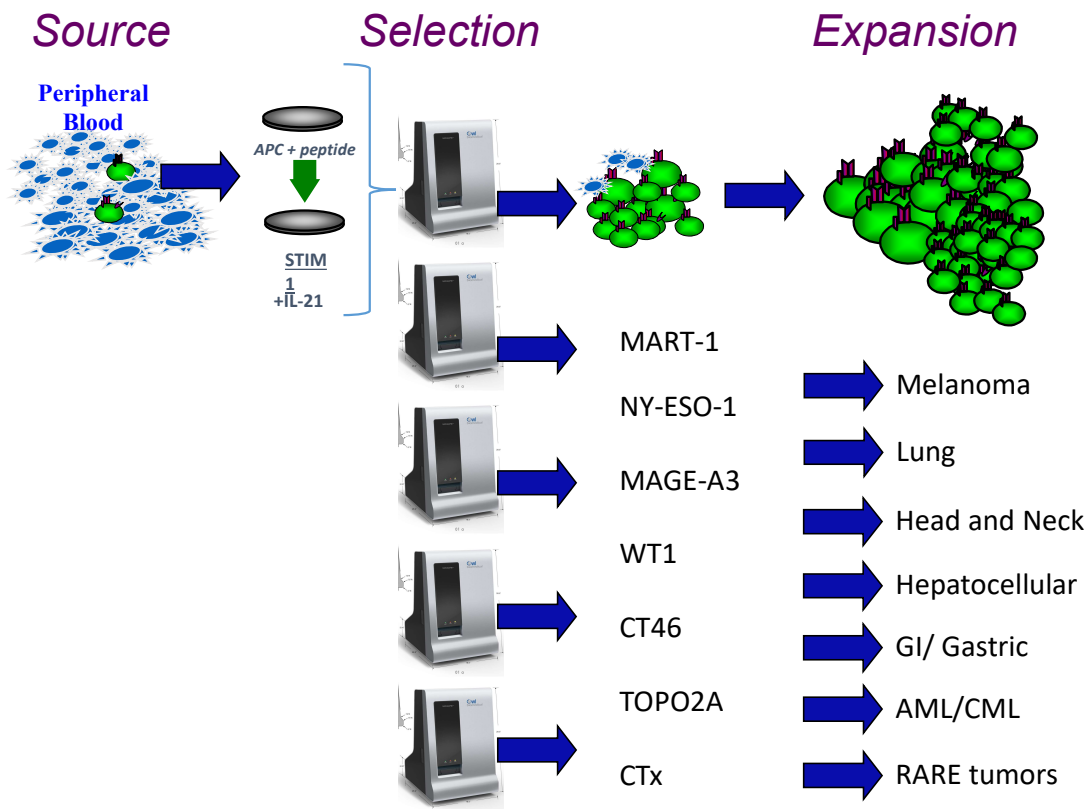
MEMS-Based Nanosorter™

Nanosorter Chip

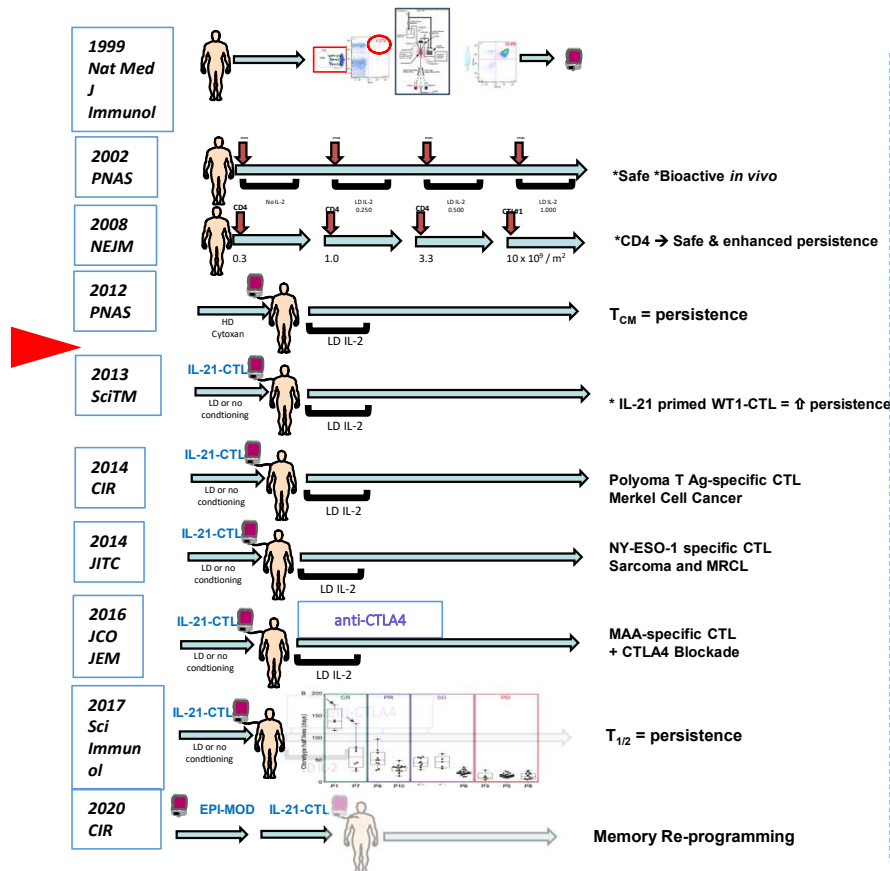
Instrument



T Cell Therapy: Enabling Technologies Turnkey Operation



Endogenous T Cell Therapy



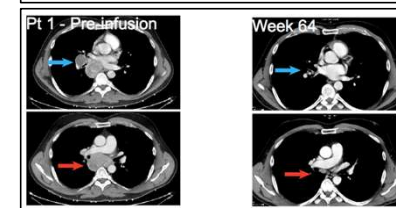
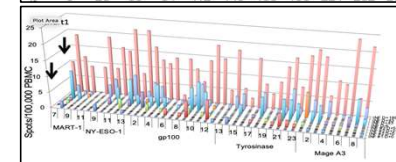
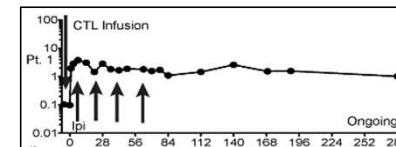
Persistence

Ag Spreading

Durable Responses

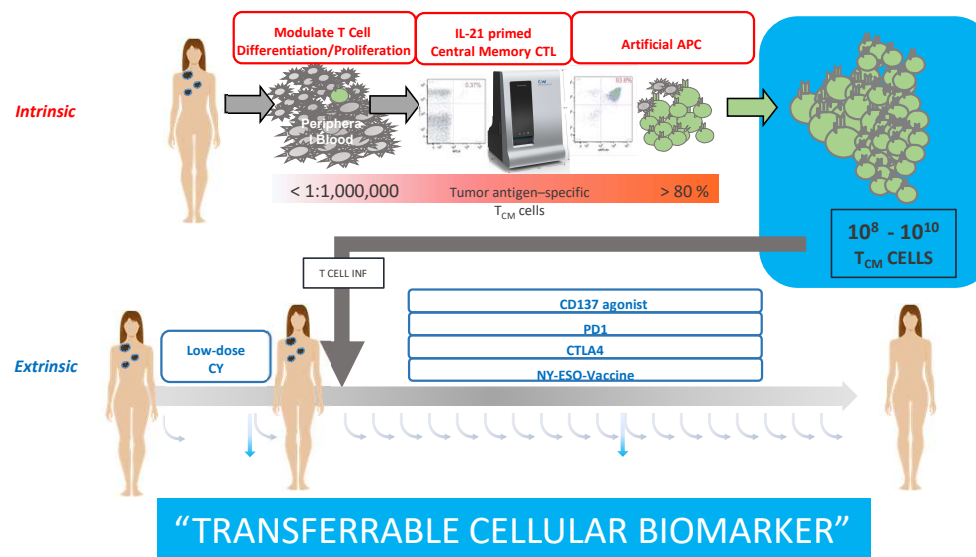
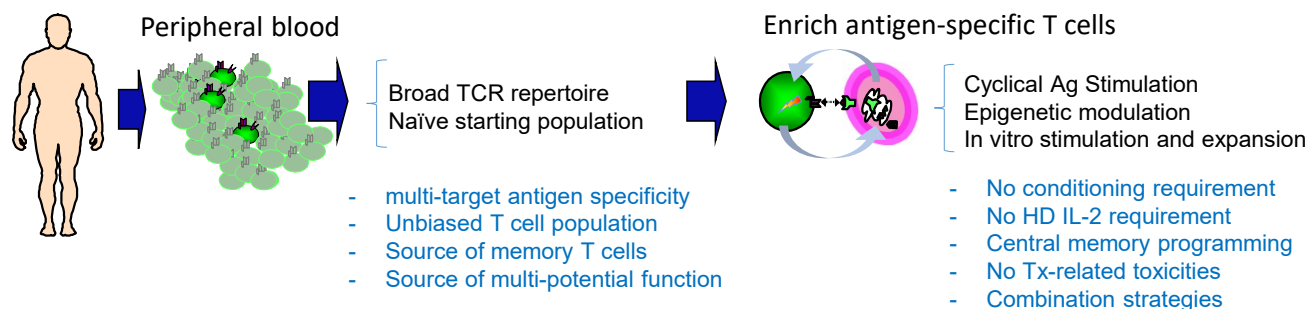
Multiple Tumors

Combination Tx



Endogenous T Cell Therapy					
Disease	Antigen	Design	Year	n	PR/CR
Melanoma	MART-1	Alone	2002 - 10	4	1/0
	gp100	CTLA4	2012 - 10	3	1/1
	tyrosinase		2016 - 10	7	2/2
Leukemia	WT1	CD4	2008 - 9	4	1/1
Merkel	T antigen		2014 - 10	8	3/2
Breast	NY-ESO		2007 - 1	0	
Ovarian	Col6A3/PRAME	anti-CD137	2019 - 3	Pending	
Sarcoma	NY-ESO	Vaccine	2019 - 1	Pending	
Uveal Melanoma	SLC45A2	CTLA4	2018 - 3	Pending	
TOTALS				66 pts	34
66 patients treated (does not include highlighted : ovarian, sarcoma, uveal melanoma TETC					
PR = 34 patients / 66					
CR = 7 (> 18 months)					

Endogenous T Cell (ETC) Therapy:





The people who did all the work

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Yongming Xue
Yating Li

Ying Ma
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Samantha Delaney

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- Parker Institute for Cancer Immunotherapy
- CPRIT
- Stand Up to Cancer-AACR/CRI
- NIH National Cancer Institute

- Cancer Research Institute
- Damon Runyon
- Sister Institutions Network Funding (GAP)