

***In vivo* persistence of adoptively transferred
TCR gene-transduced lymphocytes with anti-tumor reactivity
in patients with MAGE-A4 expressing esophageal cancer**

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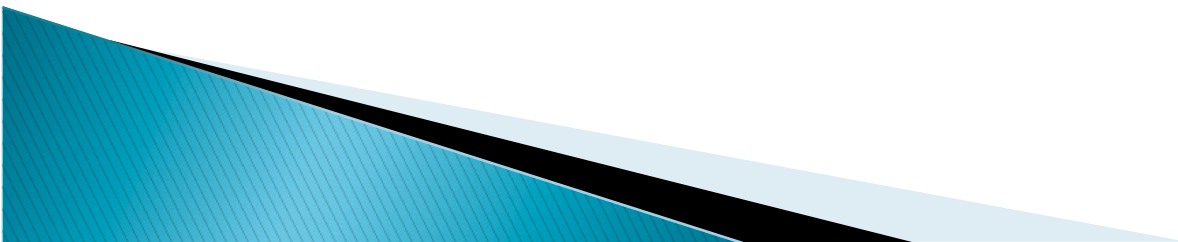
SITC 2013 Annual Meeting, Maryland

COI Disclosure Information

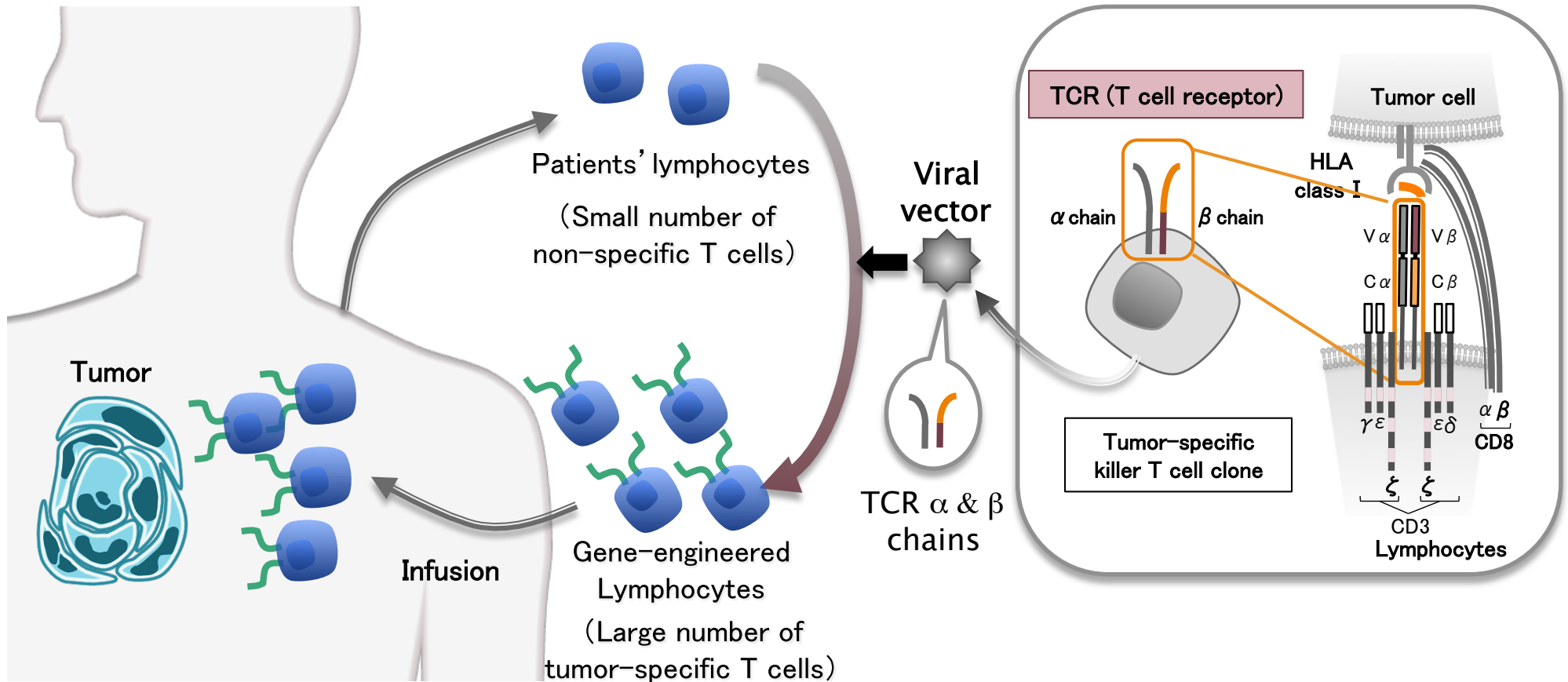
Hiroaki Ikeda

I have the following financial relationships to disclose.

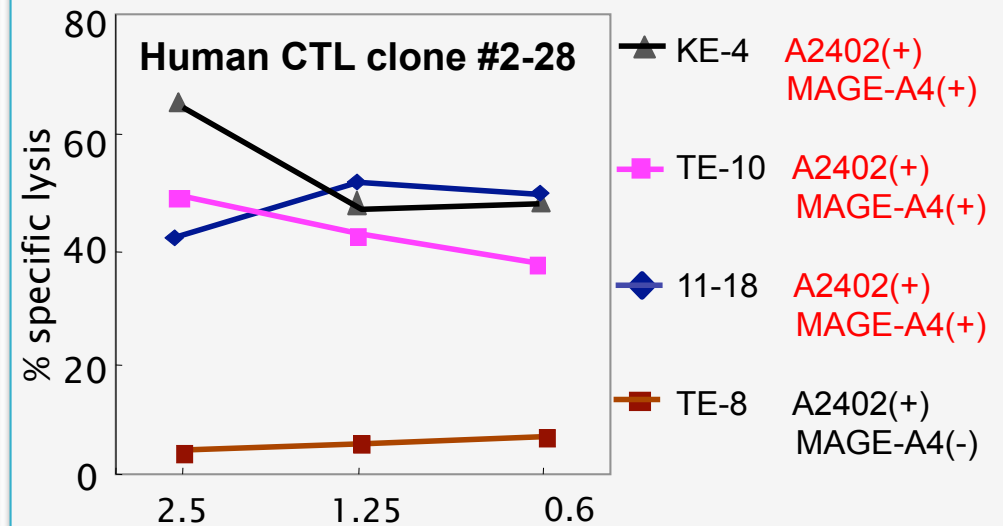
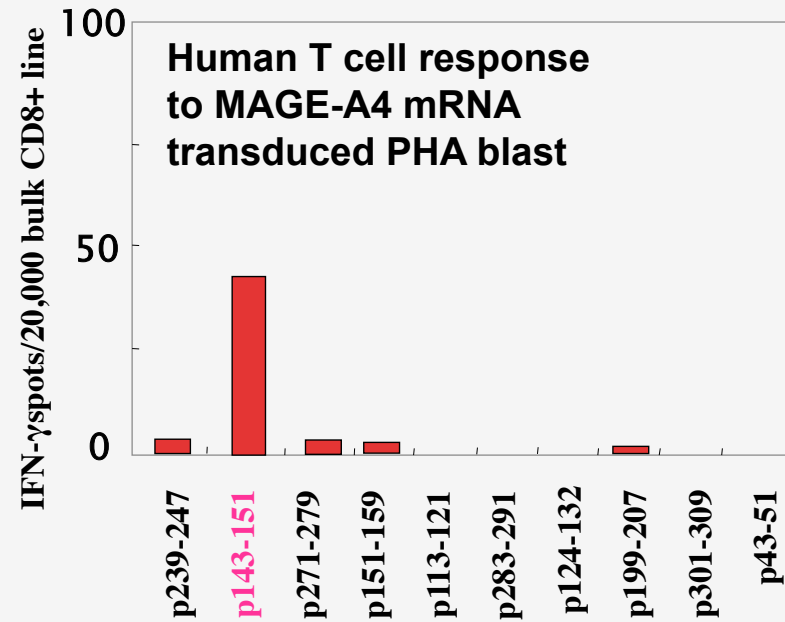
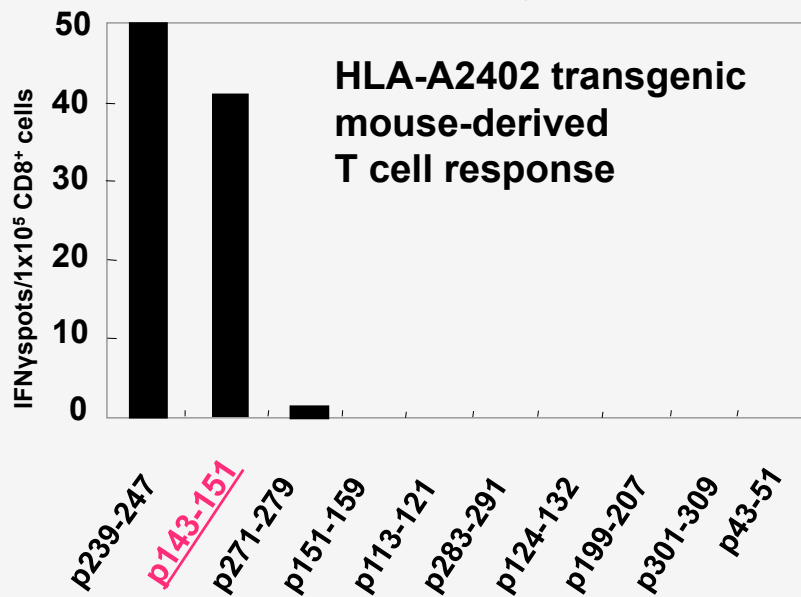
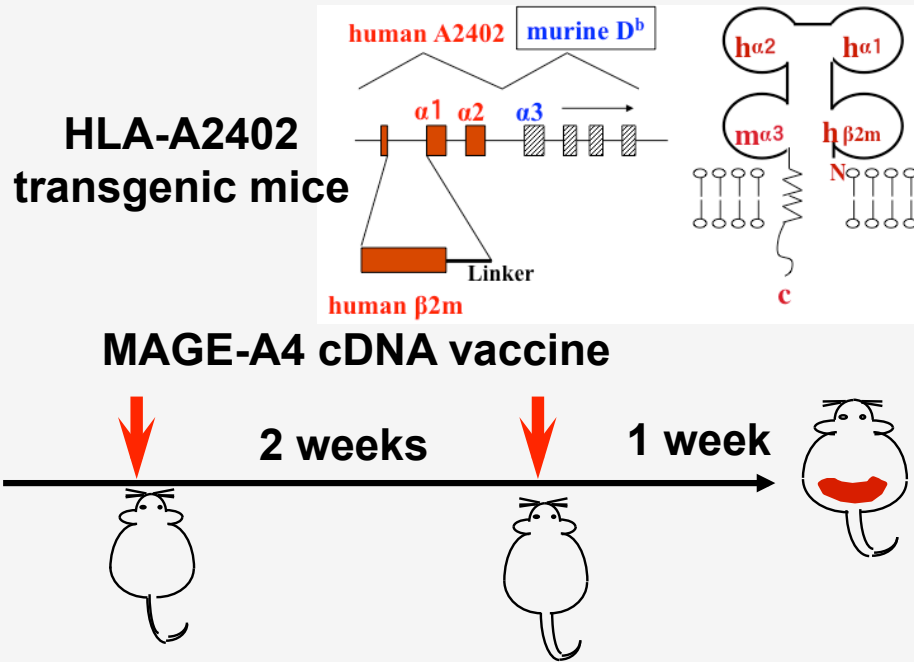
Grant/Research funding from: Takara Bio Inc.



TCR gene therapy of cancer patients

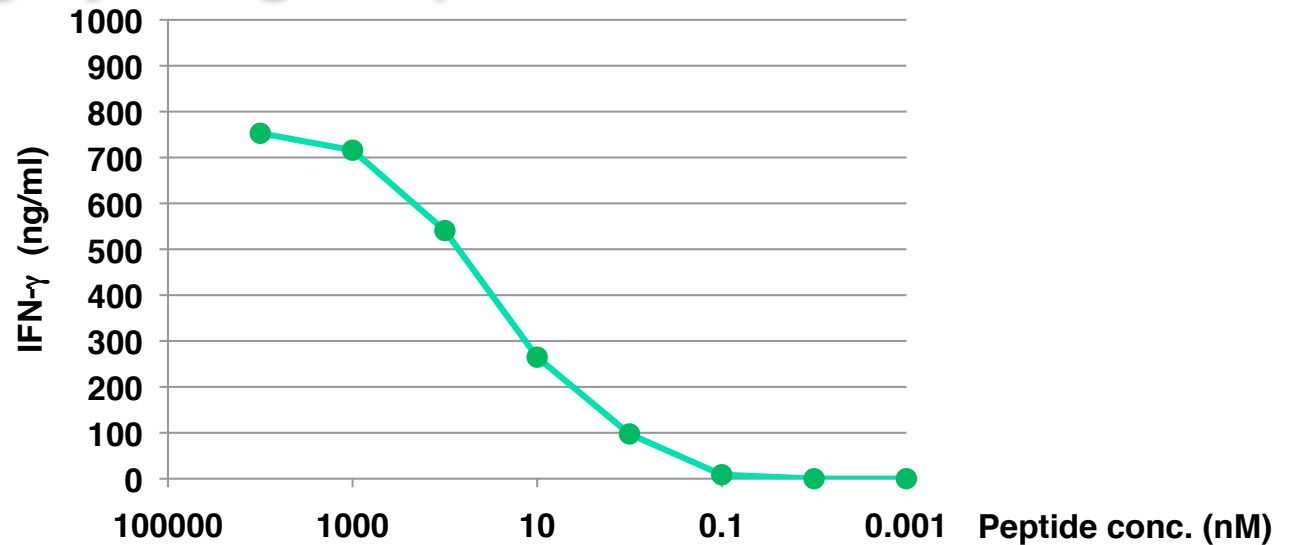


Establishment of MAGE-A4-specific human CTL clones

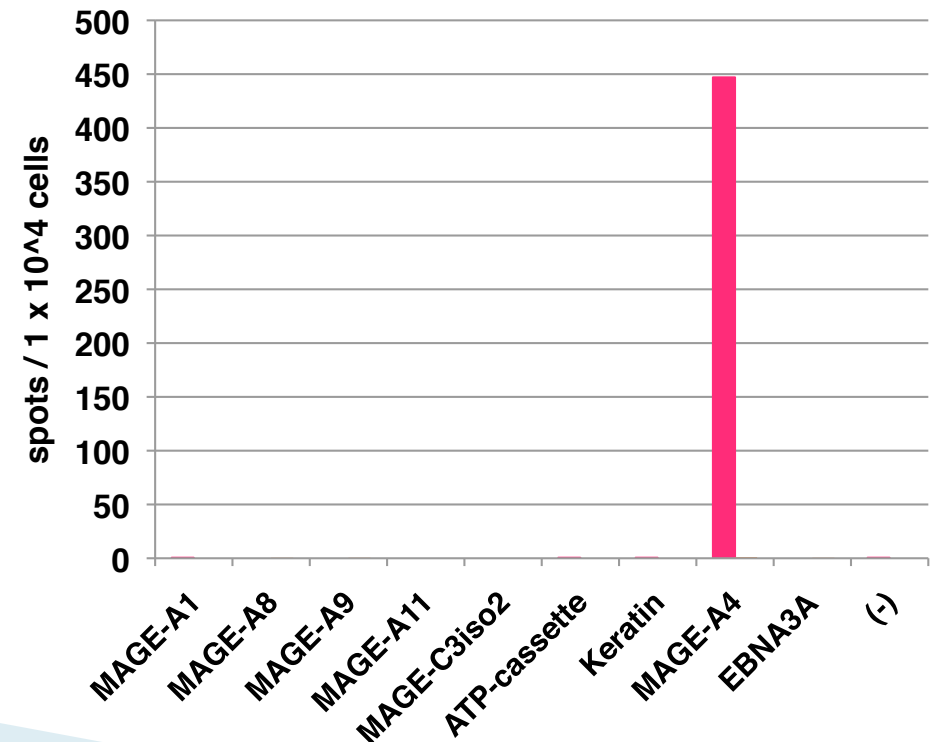


Human CTL clone #2-28 recognizes MAGE-A4 epitope peptide in a highly antigen-specific manner

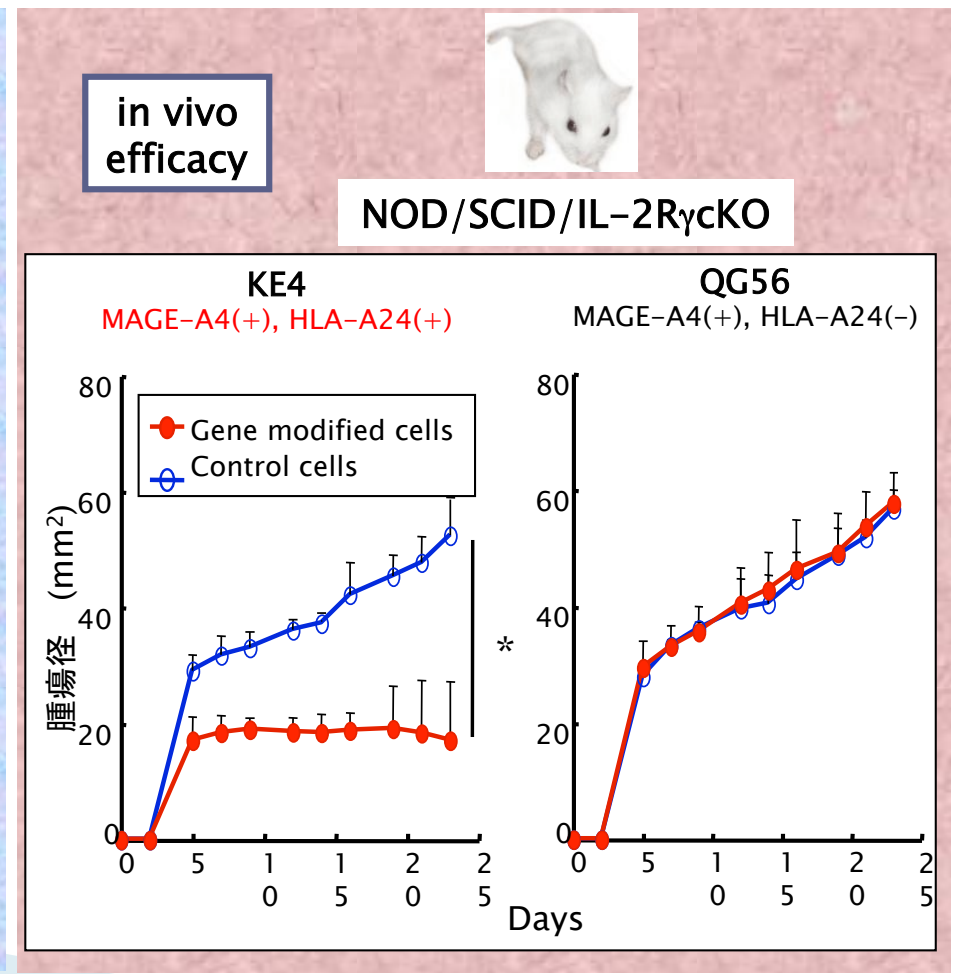
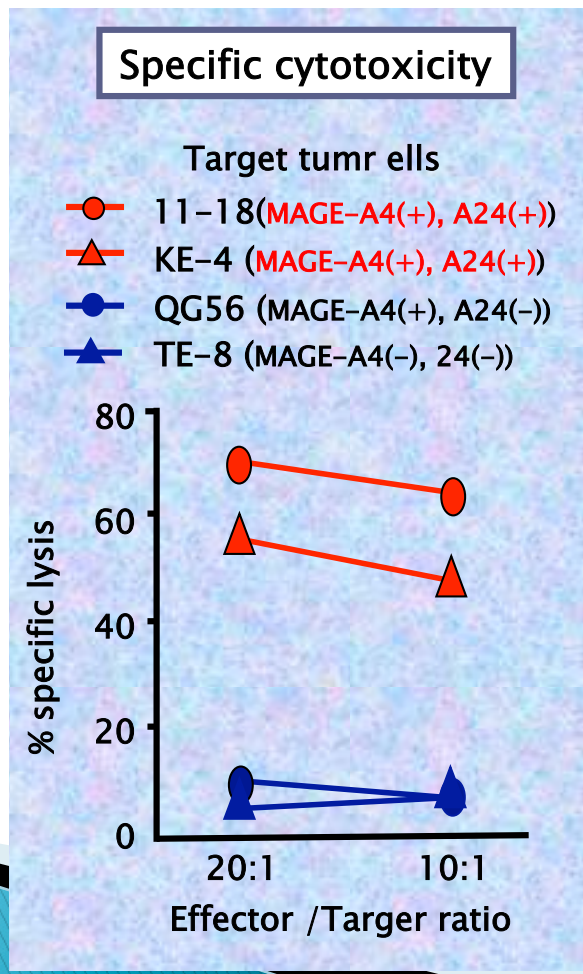
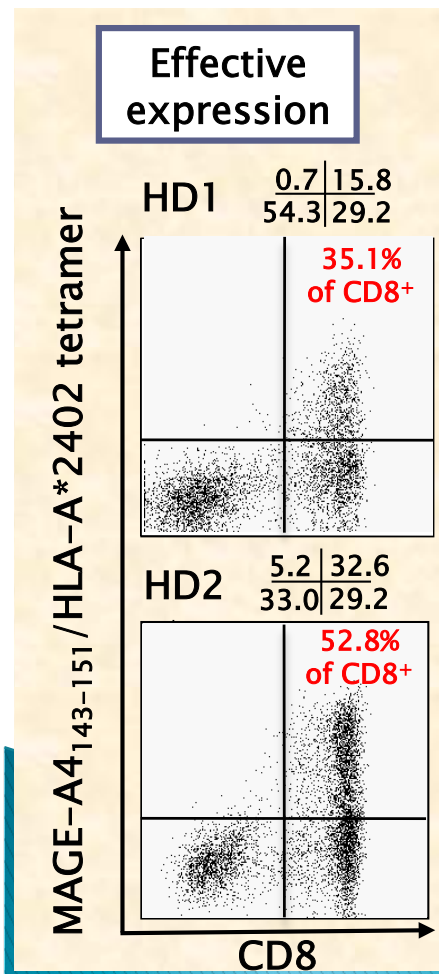
MAGE-A4₁₄₃₋₁₅₁ epitope peptide
NYKRCFPVI



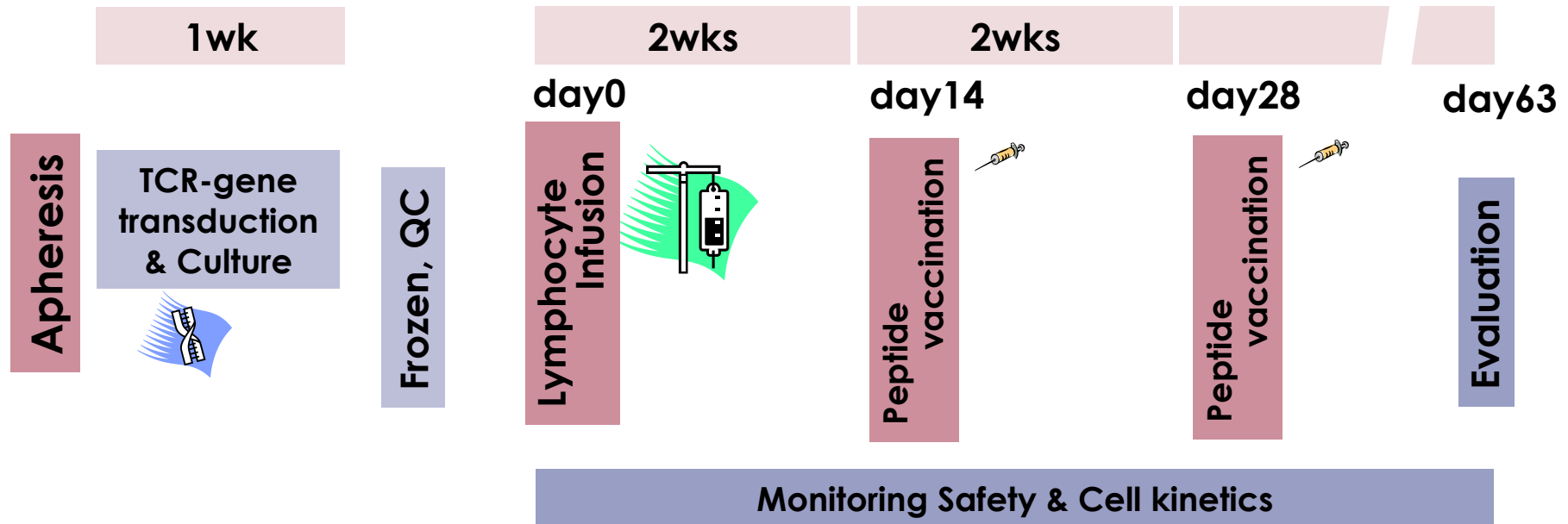
Proteins with homology to MAGE-A4 epitope	Amino Acids
melanoma-associated antigen 9	NYKRYFPVI
melanoma-associated antigen 1	NYKHCFPEI
keratin, type I cytoskeletal 25	DYSRYFPII
keratin, type I cytoskeletal 27	DYSRYFPII
ATP-binding cassette sub-family A member 9 isoform X4	NTKRLNCFPV
melanoma-associated antigen 8	NYKNHFPEI
melanoma-associated antigen C3 isoform 2	KYKDYFPMI
melanoma-associated antigen C3 isoform 1	KYKDYFPMI
melanoma-associated antigen 11 isoform a	NYEDYFPEI



TCR-transduced lymphocytes become reactive to MAGE-A4 expressing tumors



Phase I trial of adoptive transfer of lymphocytes transduced with MAGE-A4-specific TCR gene for patients with esophageal cancer



Patients

MAGE-A4 expression(+) HLA-A*24:02(+)
Esophageal cancer

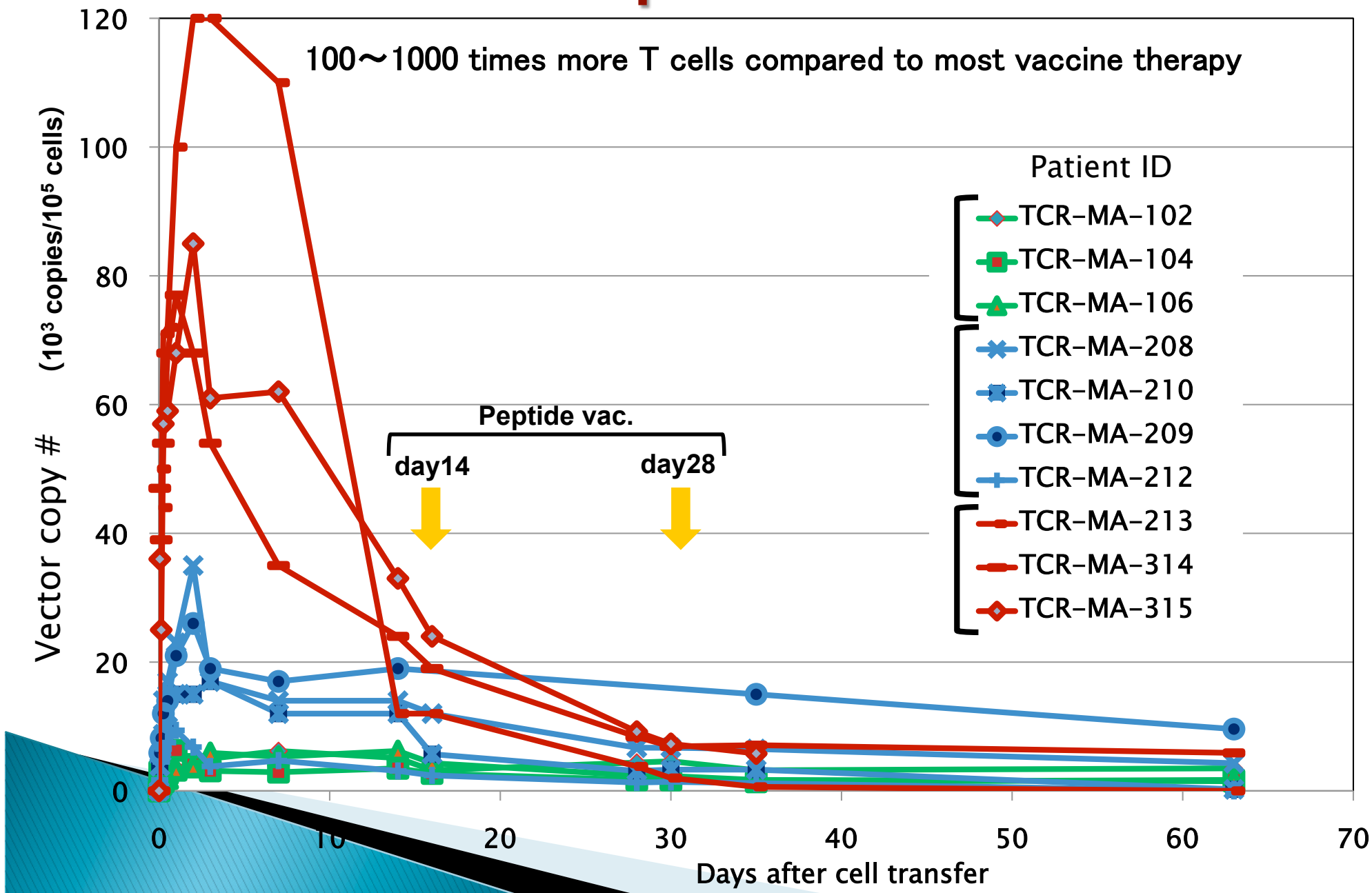
Cell-dose escalating study

2x10⁸ cells infusion for 3 pts
1x10⁹ cells infusion for 3 pts
5x10⁹ cells infusion for 3 pts

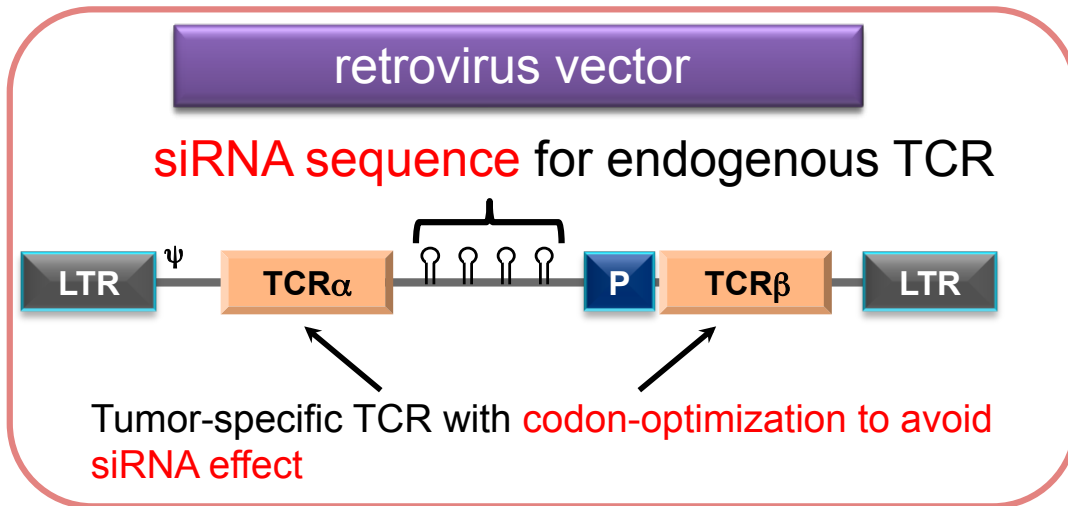
Endpoints

- **Primary Safety**
 - Adverse events
 - RCR(replication competent retrovirus)
 - Cell clonality by LAM-PCR
 - Cell kinetics, Tissue infiltration
- **Secondary**
 - Immune reaction, Tumor response

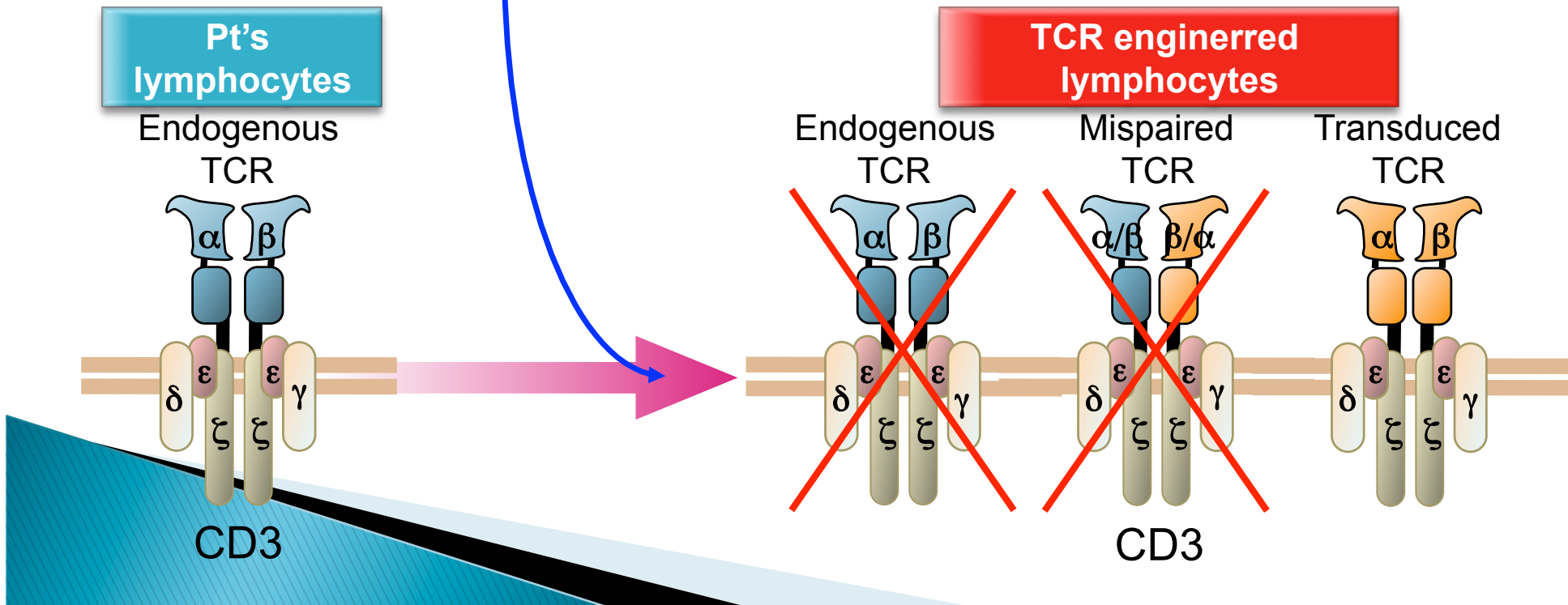
Transferred lymphocytes detected in PBMC in a dose-dependent manner



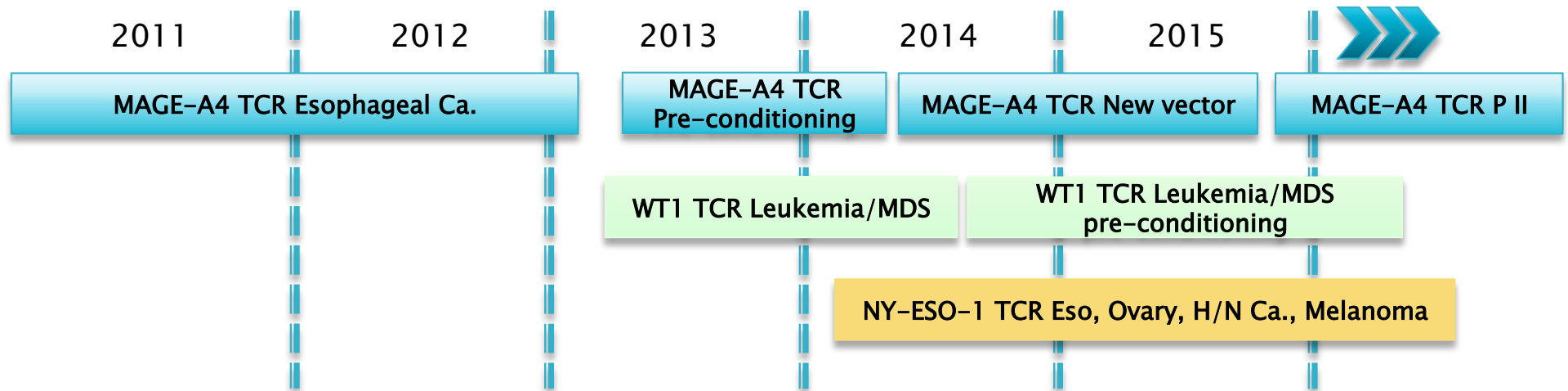
Retrovirus vector that down-regulates endogenous TCR by specific siRNA



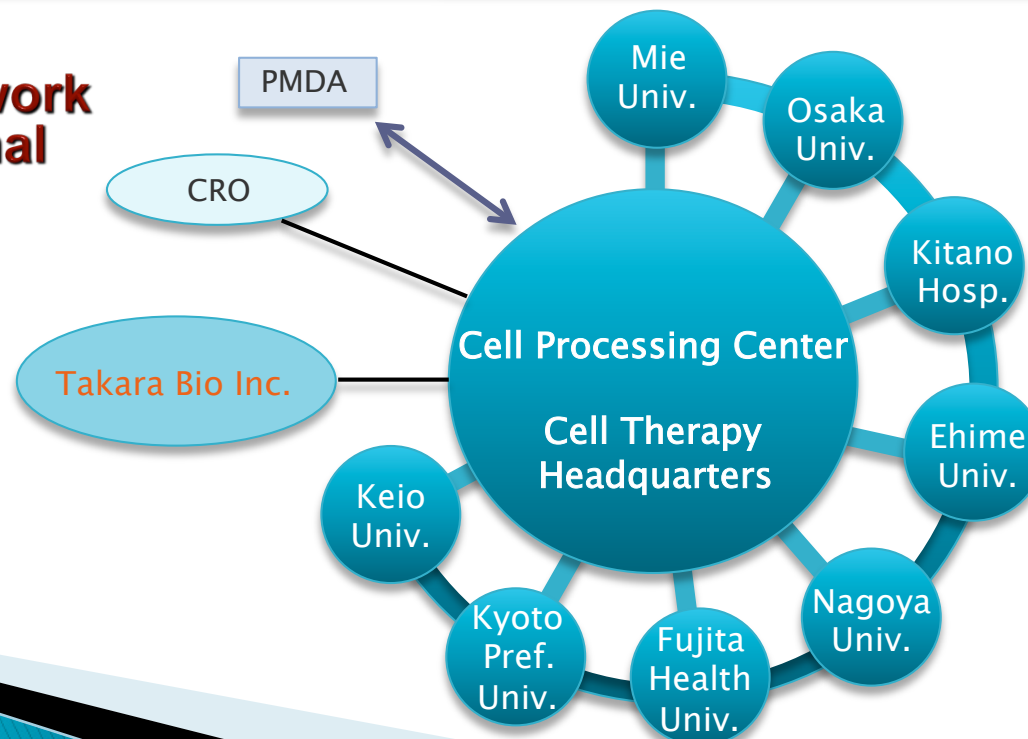
- ✧ Enhance the expression of the tumor-specific TCR
- ✧ Inhibit the creation of self-reactive TCR



Multi-institutional clinical trials



**Collaborative network
of multi-institutional
TCR gene therapy**



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