CAR-T Hücreleri Transplantasyon Alanına Girebilir mi?

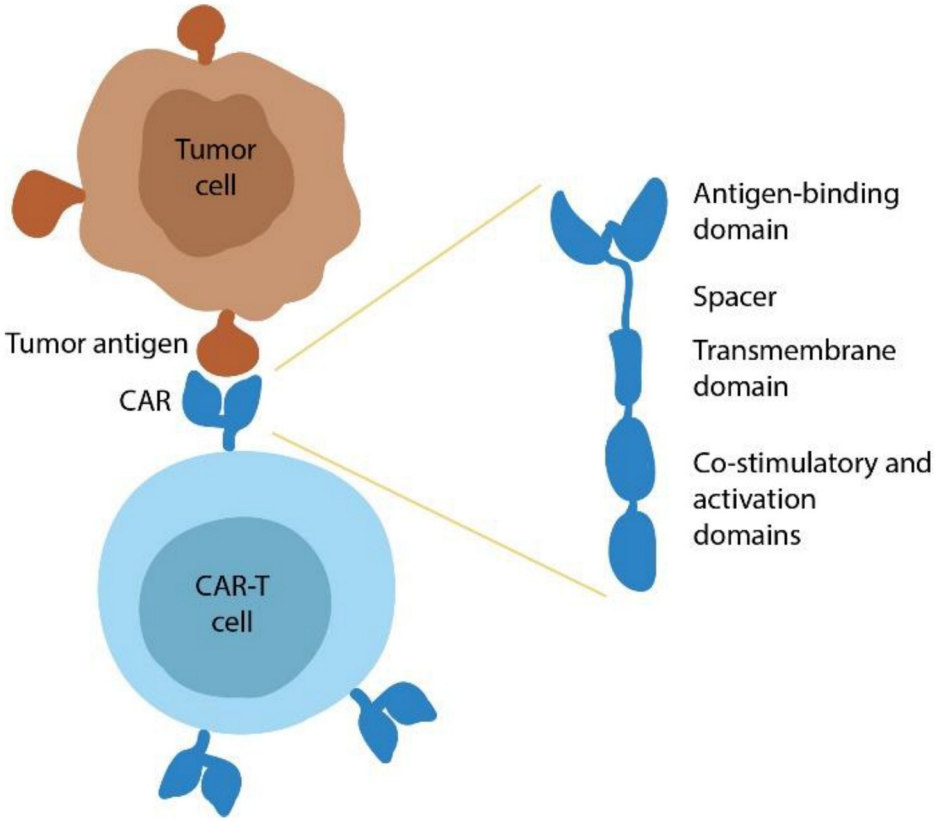
Prof. Dr. Tülay Kılıçaslan Ayna

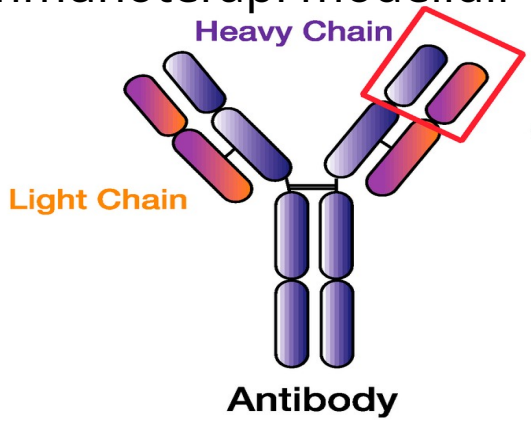
İzmir Katip Çelebi Üniversitesi Tıp Fakültesi Tıbbi Biyoloji AD
İKÇÜ Hücre Doku Organ Nakli Araştırma ve Uygulama Merkezi

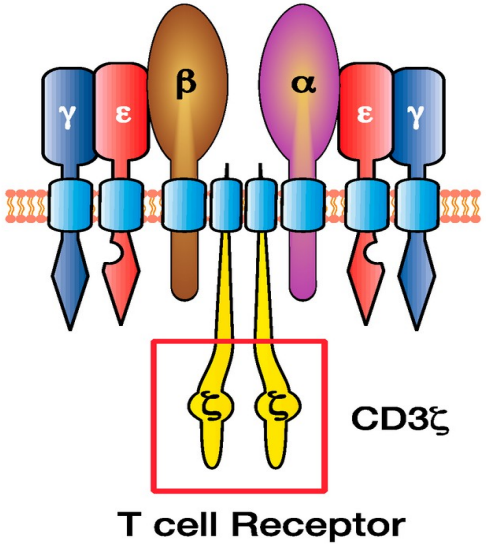
İzmir 23-24 Ekim 2025

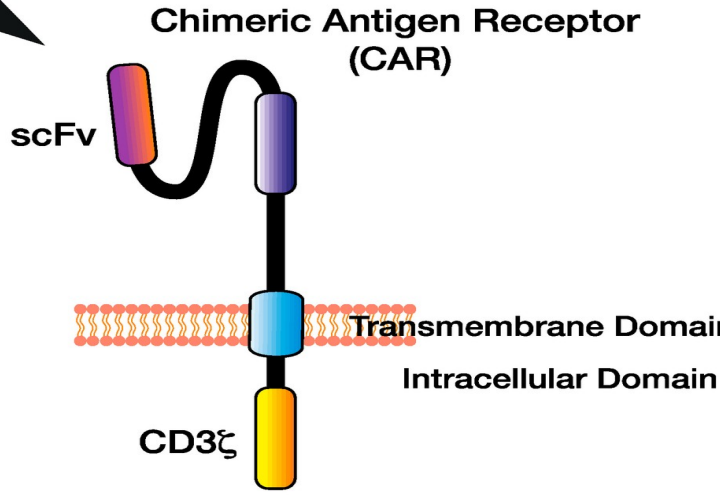
Kimerik Antijen Reseptör (CAR)-T

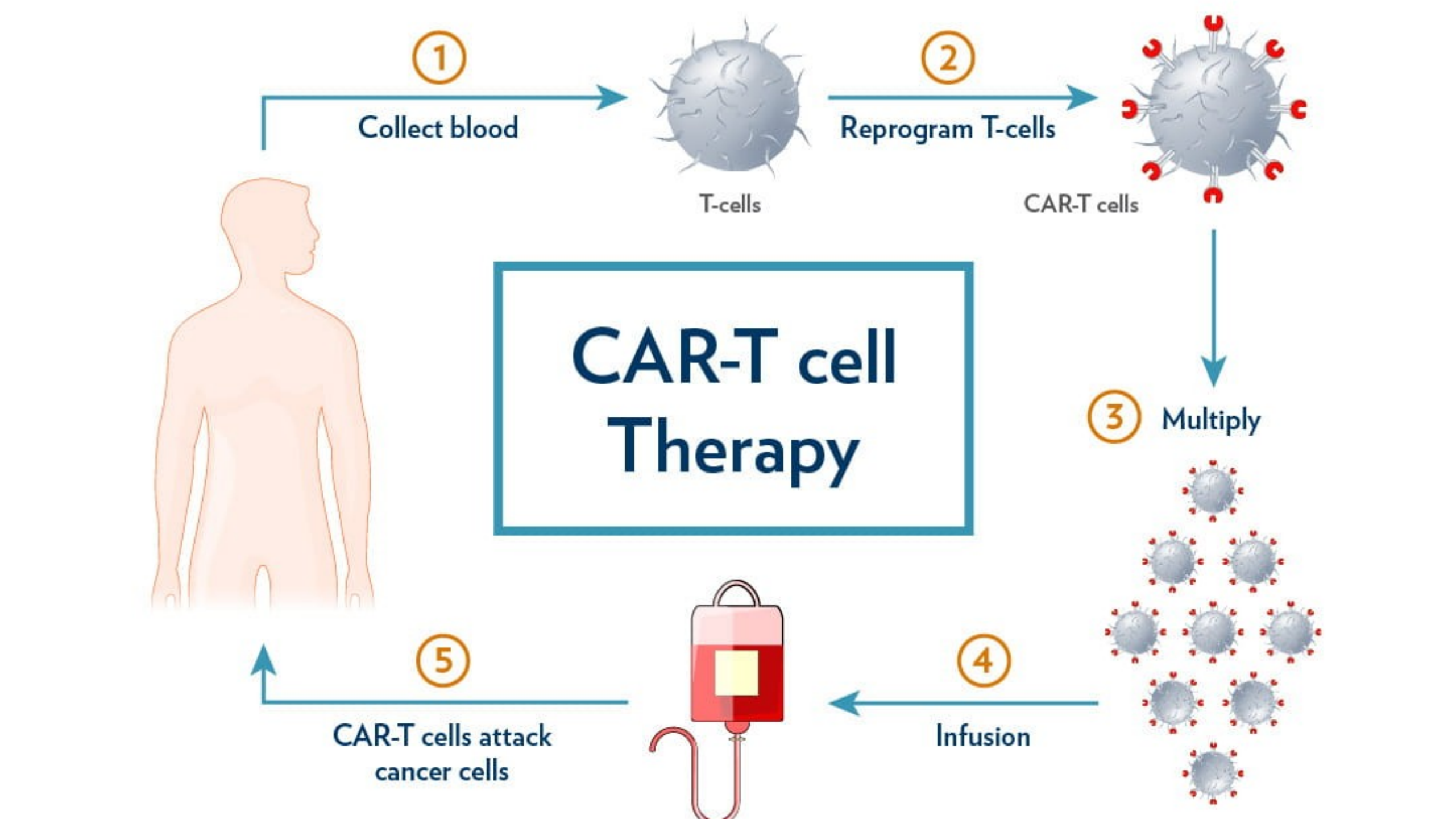
Genetik olarak tasarlanmış otolog veya allojenik hücresel immünoterapi modelidir



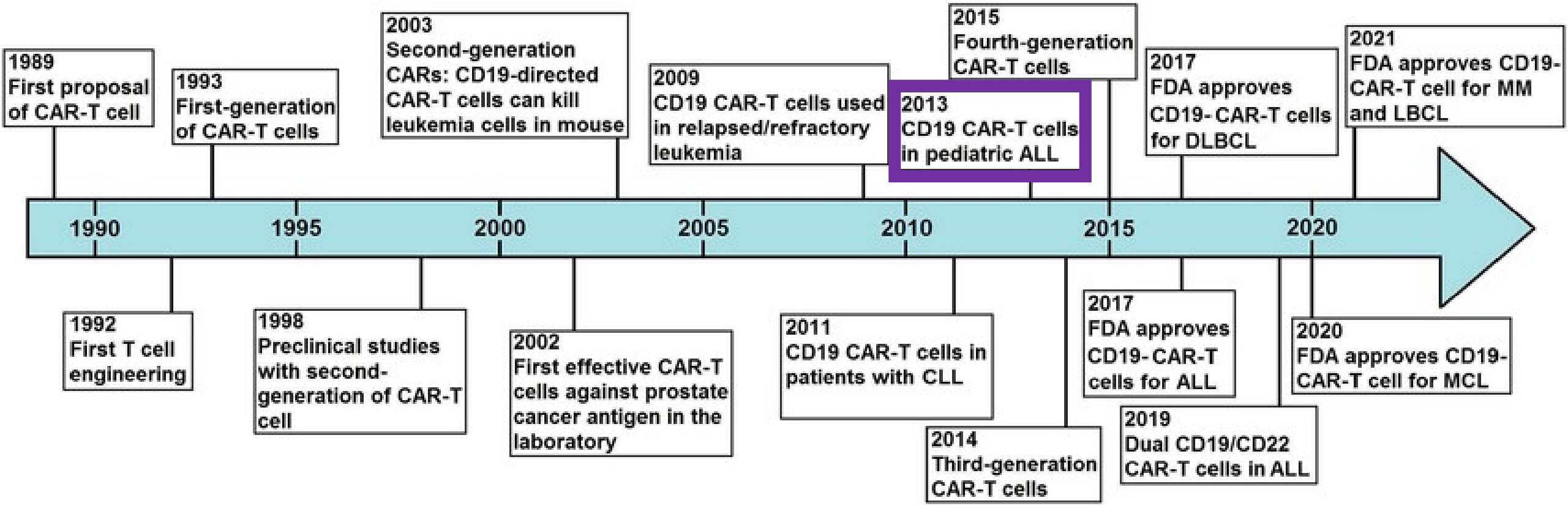






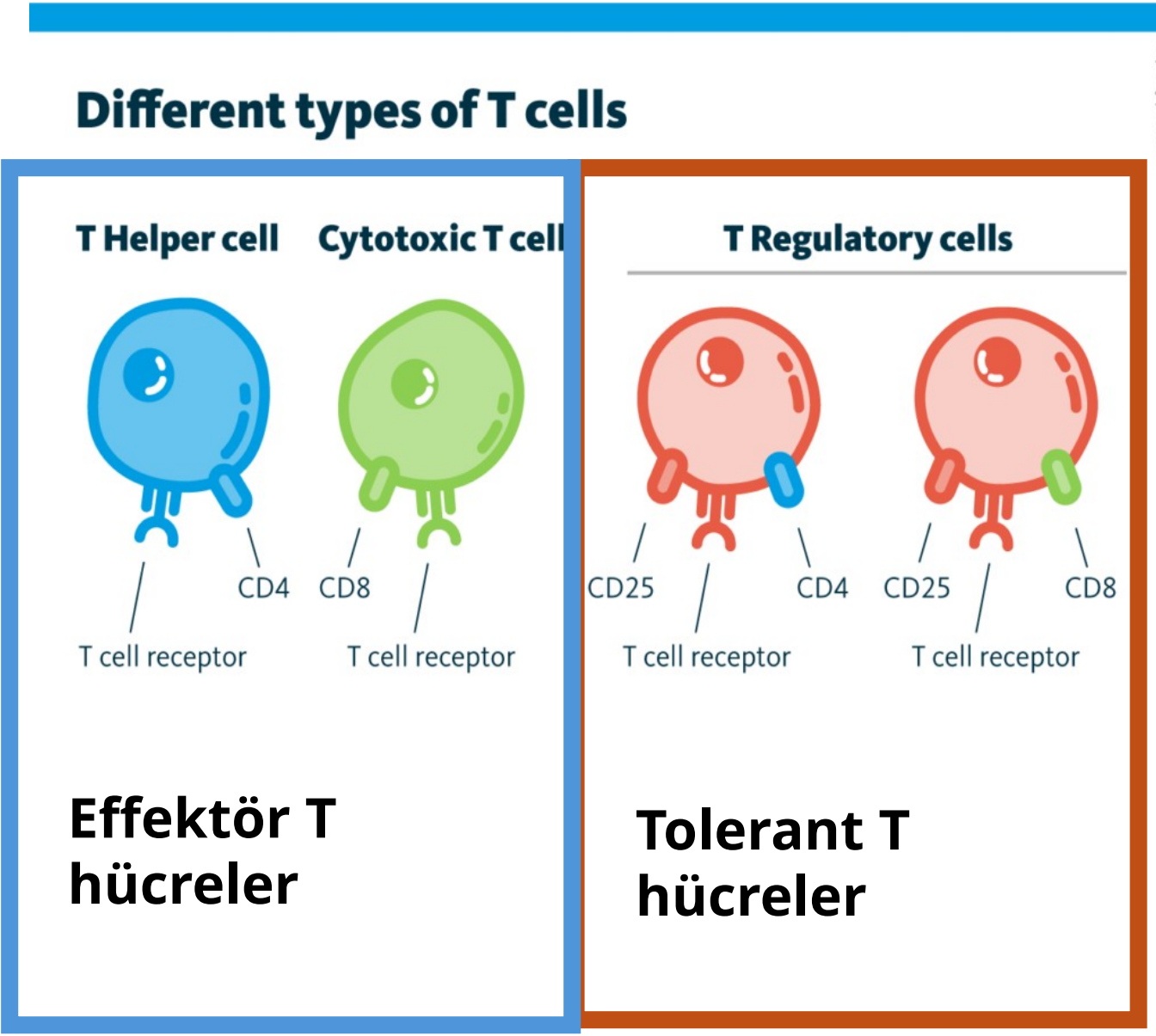

1
Collect blood
T-cells
2
Reprogram T-cells
CAR-T cells
CAR-T cell Therapy
3
Multiply
4
Infusion
5
CAR-T cells attack cancer cells

Kimerik Antijen Reseptör



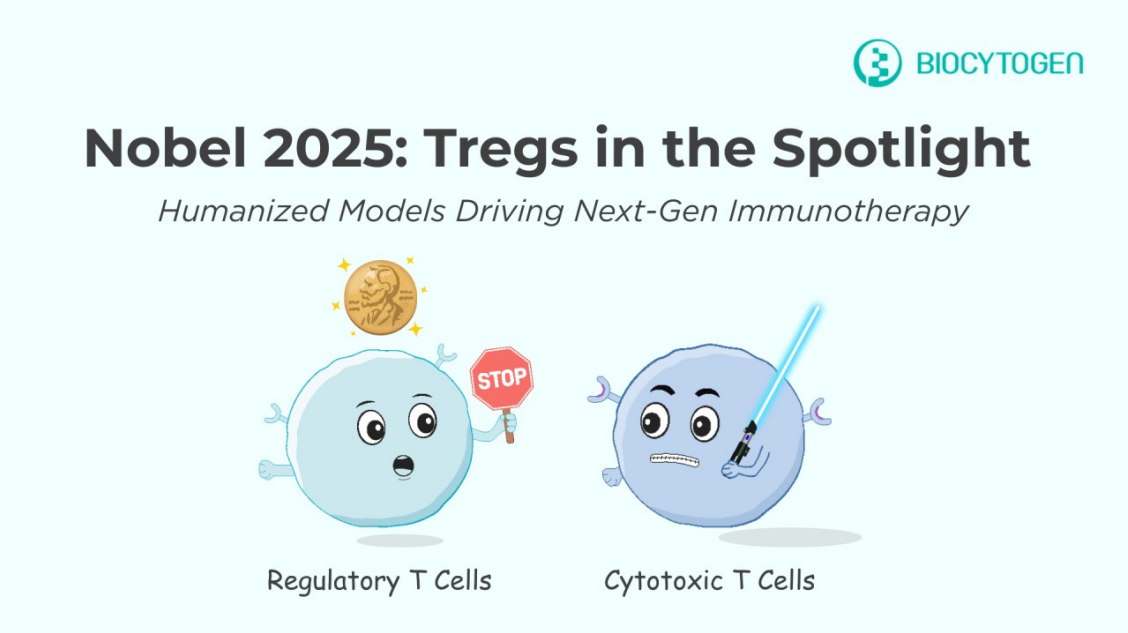
Emily Whitehead

Organ Transplantasyonu

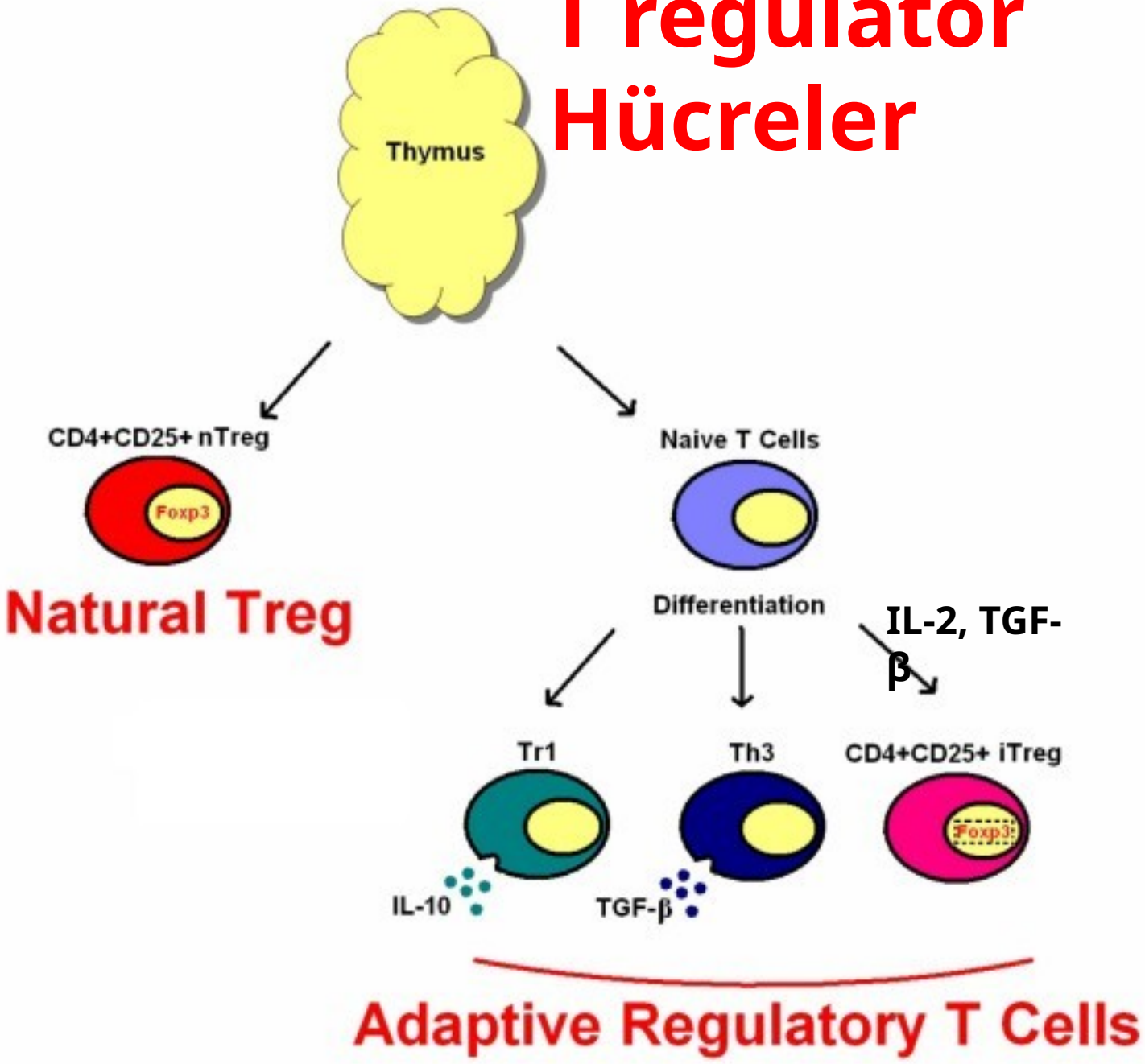


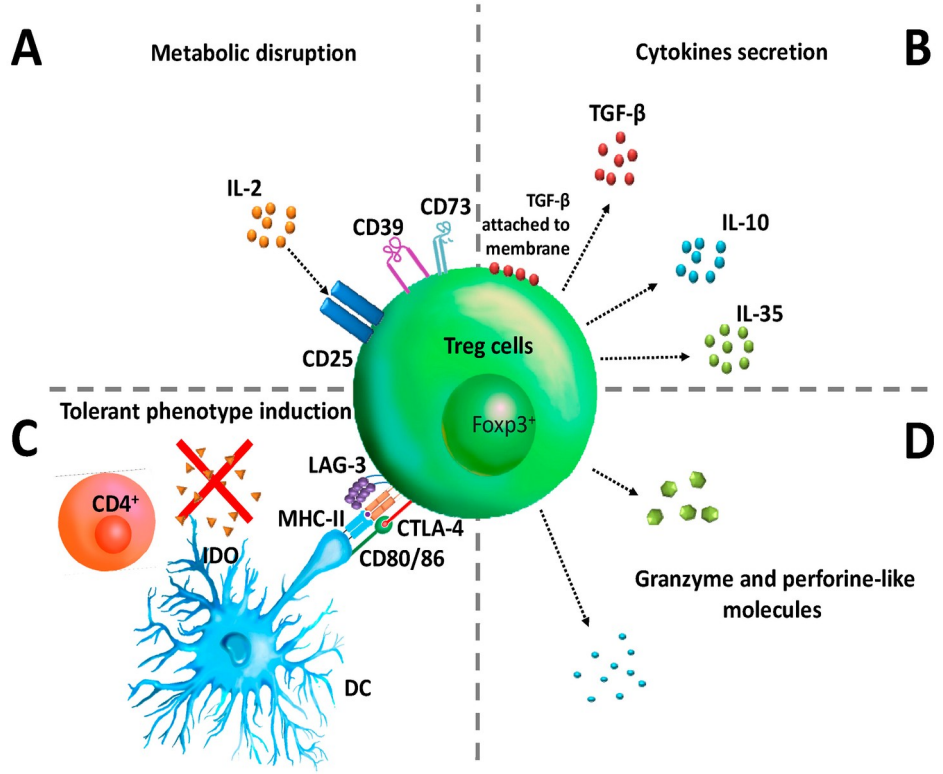
Teff greft infiltrasyonunu önleyerek greft bölgesindeki Treg hücrelerine baskınlık sağlamak,

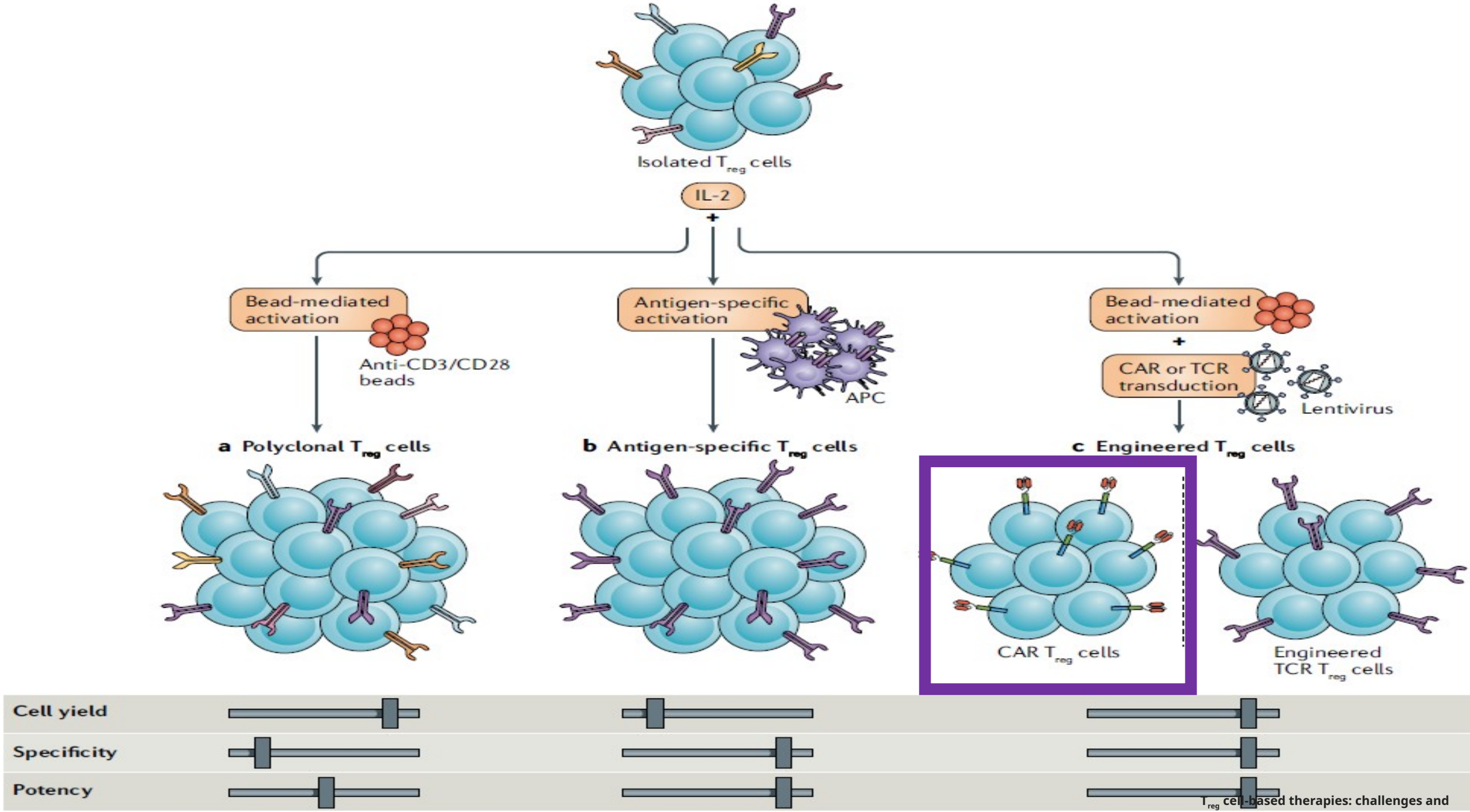
Treg sayısını artırmak



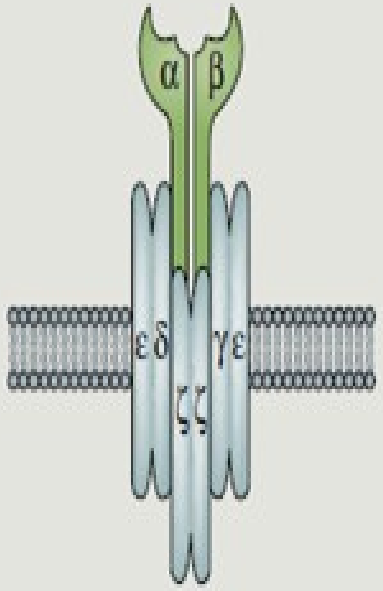
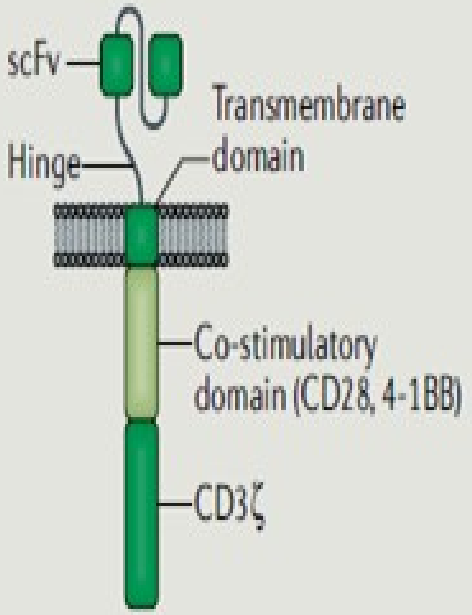
T regülatör Hücreler

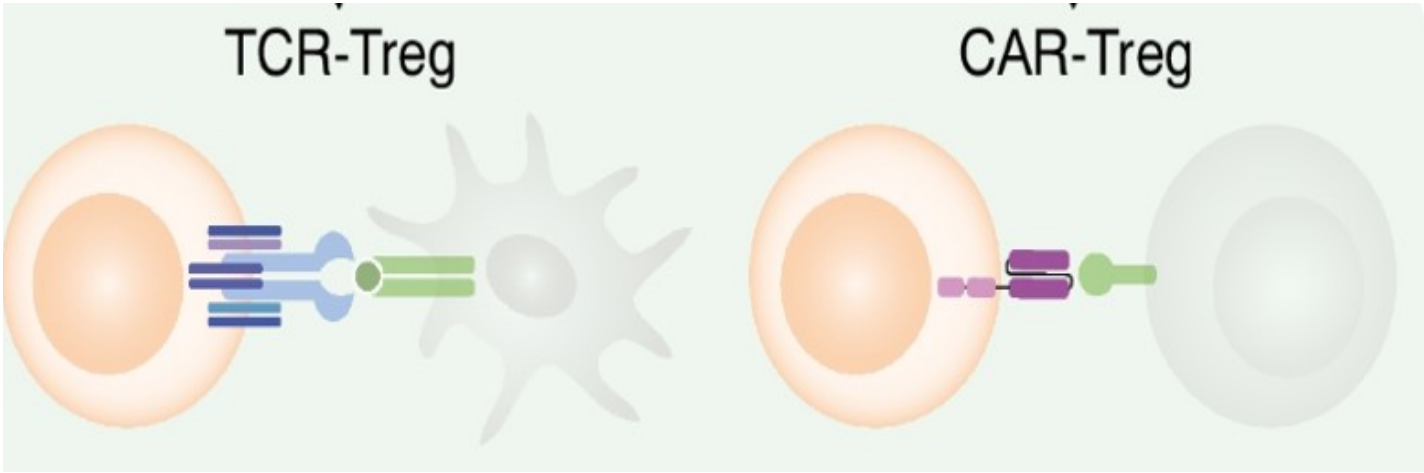




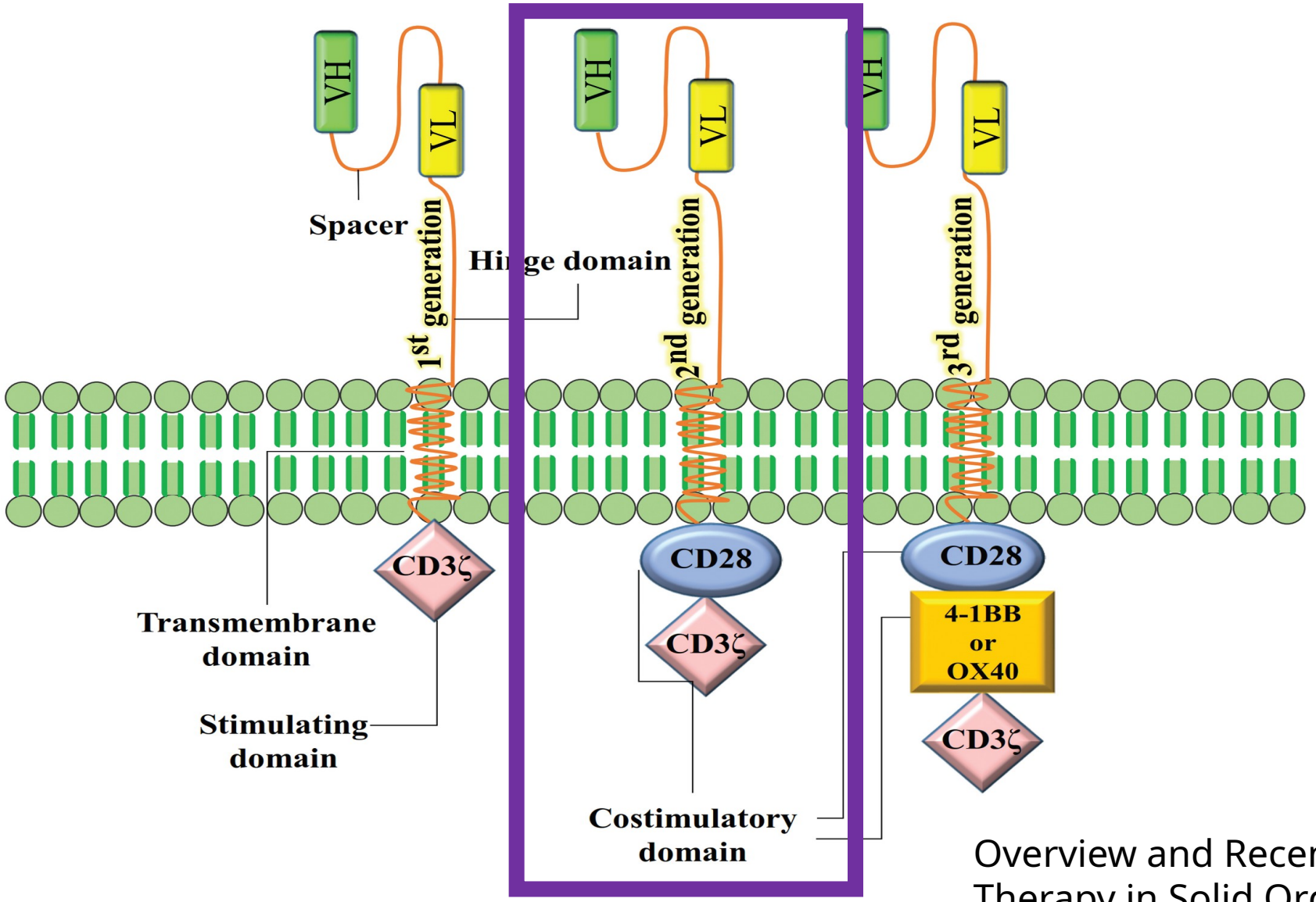


T_{reg} cell-based therapies: challenges and

Engineered TCRs	CARs
	
Multi-protein complex	Single protein
Low affinity	High and adjustable affinity
Recognition is MHC-restricted	Recognition is MHC-independent (broader applicability)
Recognize processed extracellular and intracellular antigens bound to MHC molecules	Recognize whole proteins, including MHC–peptide complexes and extracellular antigens present in the ECM
Risk of mispairing with endogenous TCR	CRS reported with CAR T cell ACT but unlikely with CAR T_{reg} cells



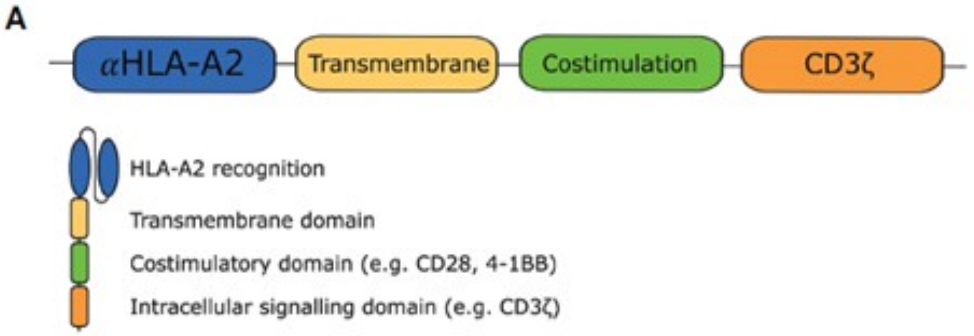
CAR-T Reg

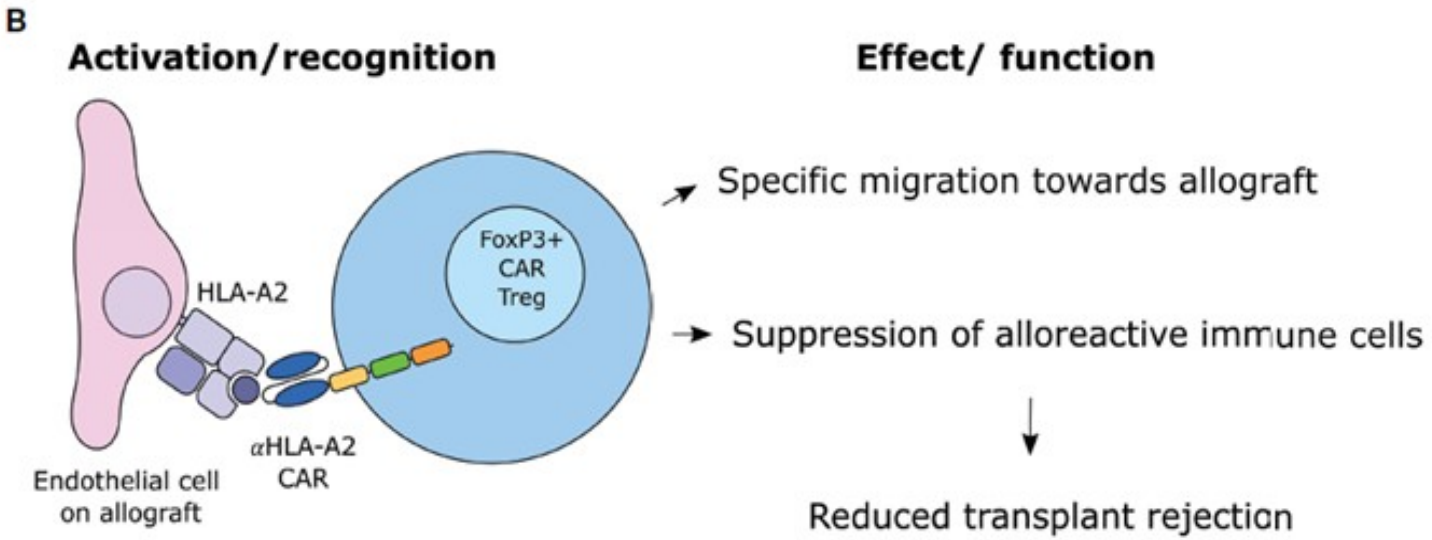


2008-Elan Elinav

Overview and Recent Advances of Regulatory T cell Therapy in Solid Organ Transplantation

Tx de neden T Reg ????
Neden A2 CAR-T Reg ???





Jeffrey Bluestone

Katherine G. MacDonald

HLA-A2 CAR T Reg

The Journal of Clinical Investigation

RESEARCH ARTICLE

Alloantigen-specific regulatory T cells generated with a chimeric antigen receptor

Katherine G. MacDonald,[1] Romy E. Hoeppli,[1] Qing Huang,[2] Jana Gillies,[1] Dan S. Luciani,[1] Paul C. Orban,[1] Raewyn Broady,[2] and Megan K. Levings[1]

American Journal of Transplantation 2017; 17: 917–930
Wiley Periodicals Inc.

doi: 10.1111/ajt.14175

Prevention of Allograft Rejection by Use of Regulatory T Cells With an MHC-Specific Chimeric Antigen Receptor

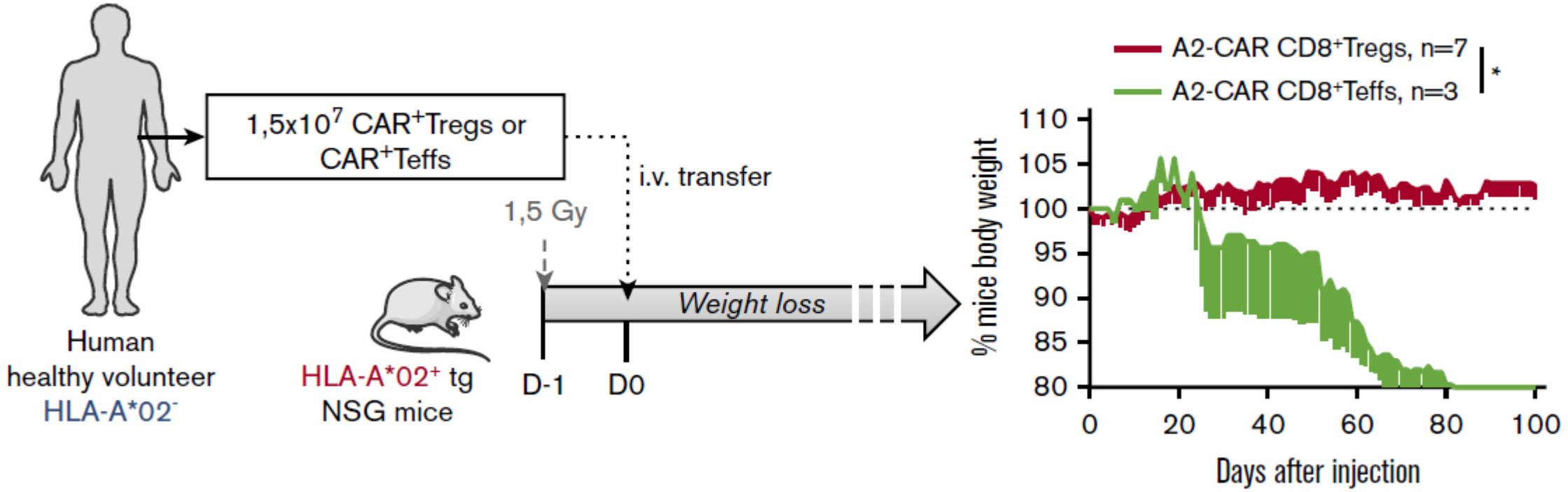
A2 CAR-Treg'ler ile yapılan adaptif hücre tedavisi umut

American Journal of Transplantation 2017; 17: 931–943
Wiley Periodicals Inc.

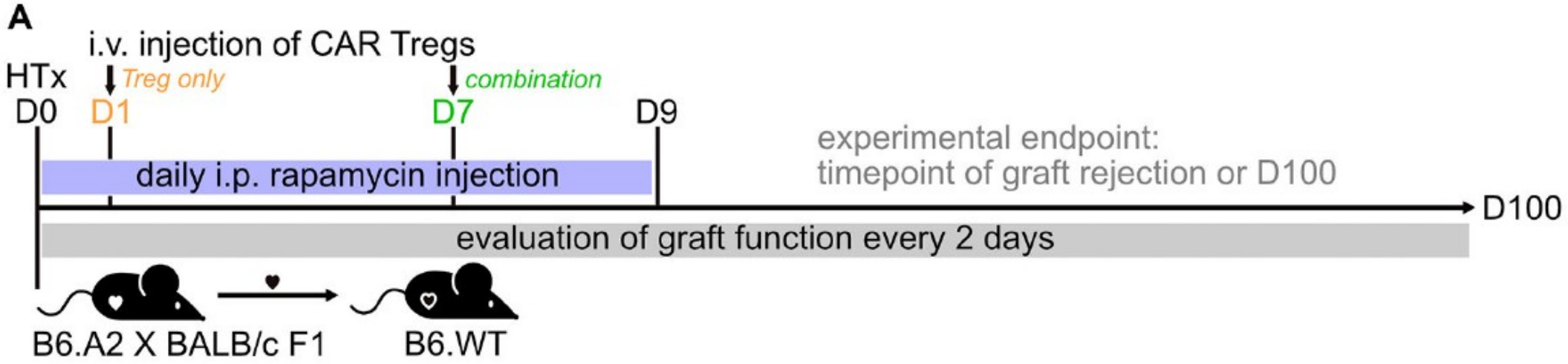
doi: 10.1111/ajt.14185

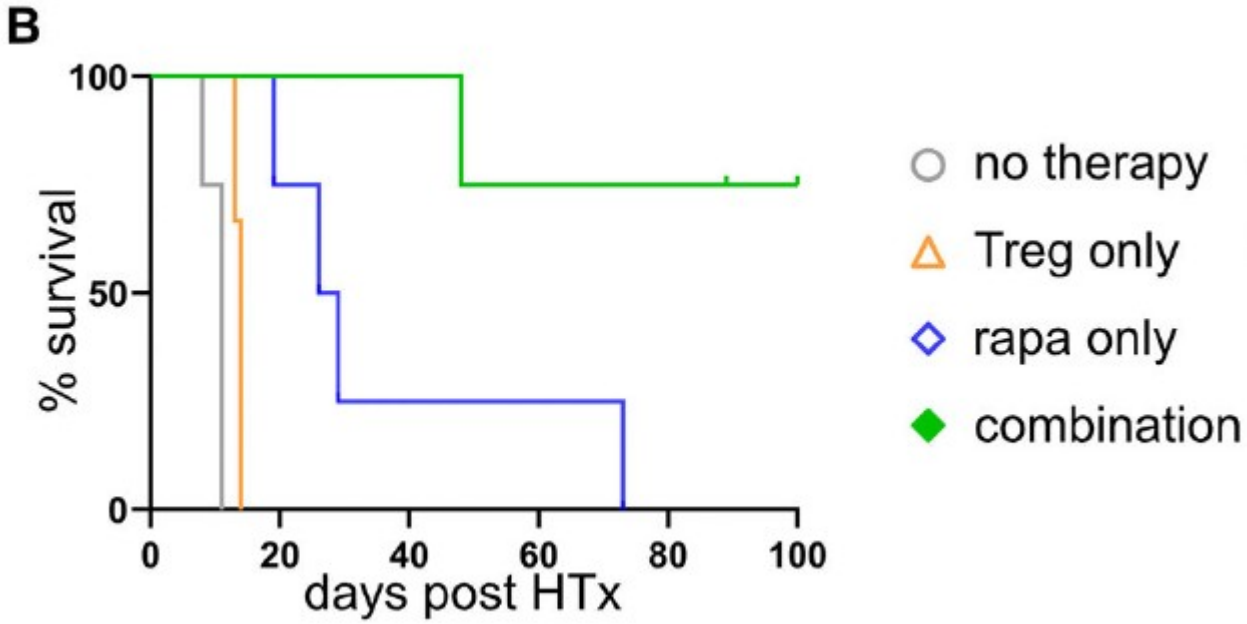
Expression of a Chimeric Antigen Receptor Specific for Donor HLA Class I Enhances the Potency of Human Regulatory T Cells in Preventing Human Skin Transplant Rejection

- İnsan **CD8⁺CD25⁺FOXP3⁺ Treg hücreleri** izole edildi.
- Bu hücreler **HLA-A2'ye özgü CAR (A2-CAR)** ile transdükte edildi.
- **In vitro** baskılama kapasitesi ve aktivasyon profili değerlendirildi.
- **In vivo** olarak iki NSG fare modeli kullanıldı:
- **İnsan deri grefti reddi modeli**
- **İnsan PBMC kaynaklı GVHD (graft-versus-host disease) modeli**



Human CD81 Tregs expressing a MHC-specific CAR display enhanc
suppression of human skin rejection and GVHD in NSG mice-2019





ClinicalTrials.gov

NCT04817774
NCT05234190

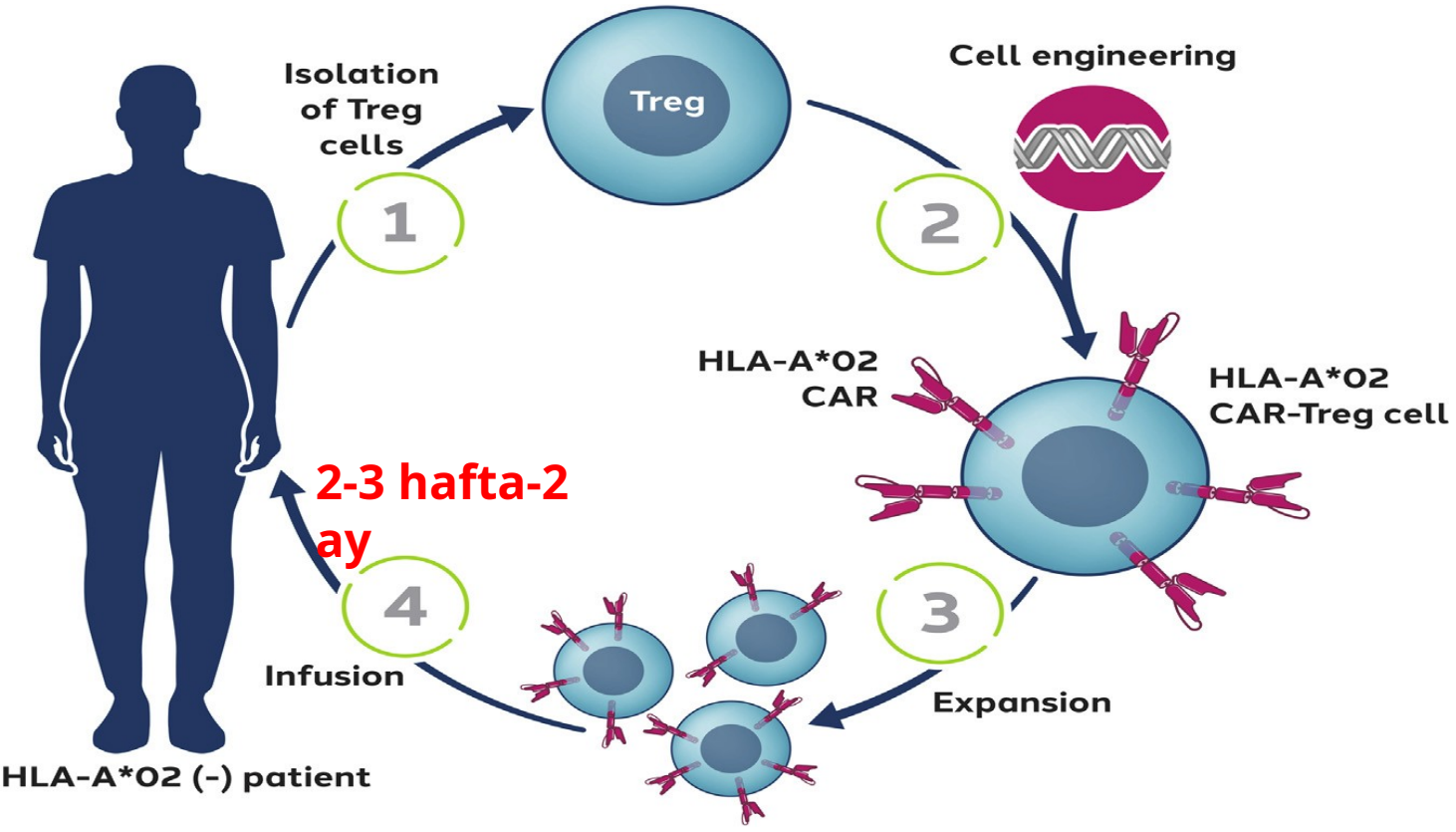
Anti-HLA-A2-CAR Tregs prolong vascularized mouse heterotopic heart allograft survival-2022

TX200-TR101-

NCT04817774

The STEADFAST study is registered on clinicaltrials.gov as NCT04817774 and on EudraCT as 2019-001730-34.

Retx,
DSA (+),
Yüksek PRA
Kontrolsüz enfeksiyon,
Aktif malignite öyküsü



Sangamo Therapeutics

Table 1. Key inclusion and exclusion criteria of transplant recipients and transplant donors in the STEADFAST study

Inclusion criteria	Exclusion criteria
Transplant recipients	
Aged between 18 and 70 yrs (inclusive)	HLA identical to the prospective organ donor
Diagnosis of ESRD and currently waiting for a new kidney from an identified live donor	Known hypersensitivity or contraindications for IS
Single-organ recipients (kidney)	Prior organ transplant
Normal or nonclinically significantly abnormal electrocardiogram	Evidence of HIV, syphilis, EBV, HBV, or HCV infection or prespecified hepatic and hematologic laboratory abnormalities
HLA-A*02 negative[a]	Positive flow-cytometric crossmatch using donor lymphocytes and recipient serum
HLA-A*69 negative[a,b]	PRA > 20% recent or historic
Adequate venous access for leukapheresis, and no other contraindications for leukapheresis[a]	Current, recent, or historical donor-specific antibodies
	Previous treatment with any desensitization procedure
	Underlying renal disease with a high risk of disease reoccurrence in the transplanted kidney
	Concomitant clinically active local or systemic infection
	Systemic immunosuppressive agents administered for other indications
	Significant unstable or poorly controlled acute or chronic diseases or laboratory abnormality (except ESRD) which, in the opinion of the investigator, could confound the results of the study or put the subject at undue risk, including high risk of renal thrombotic event
	Current or previous history of malignancy (within the last 5 yr)
Transplant donors	
Age ≥18 yr	Evidence of HBV or HCV infection
ABO blood type compatible with the organ recipient	
Negative serology result for HIV and syphilis	
HLA-A*02 positive[c]	

Study Design: Human Leukocyte Antigen Class I Molecule A*02-Chimeric Antigen Receptor Regulatory T Cells in Renal Transplantation

Katharina Schreeb[1], Emily Culme-Seymour[1], Essra Ridha[1], Céline Dumont[1], Gillian Atkinson[1], Ben Hsu[1] and Petra Reinke[2]

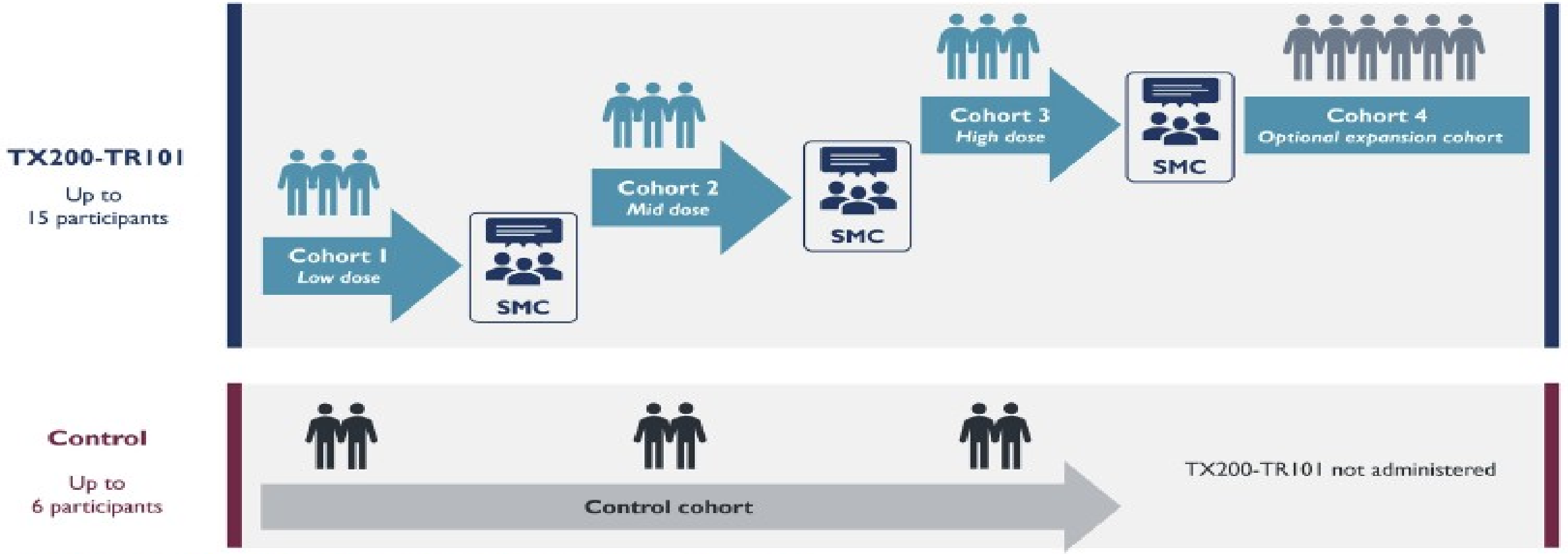
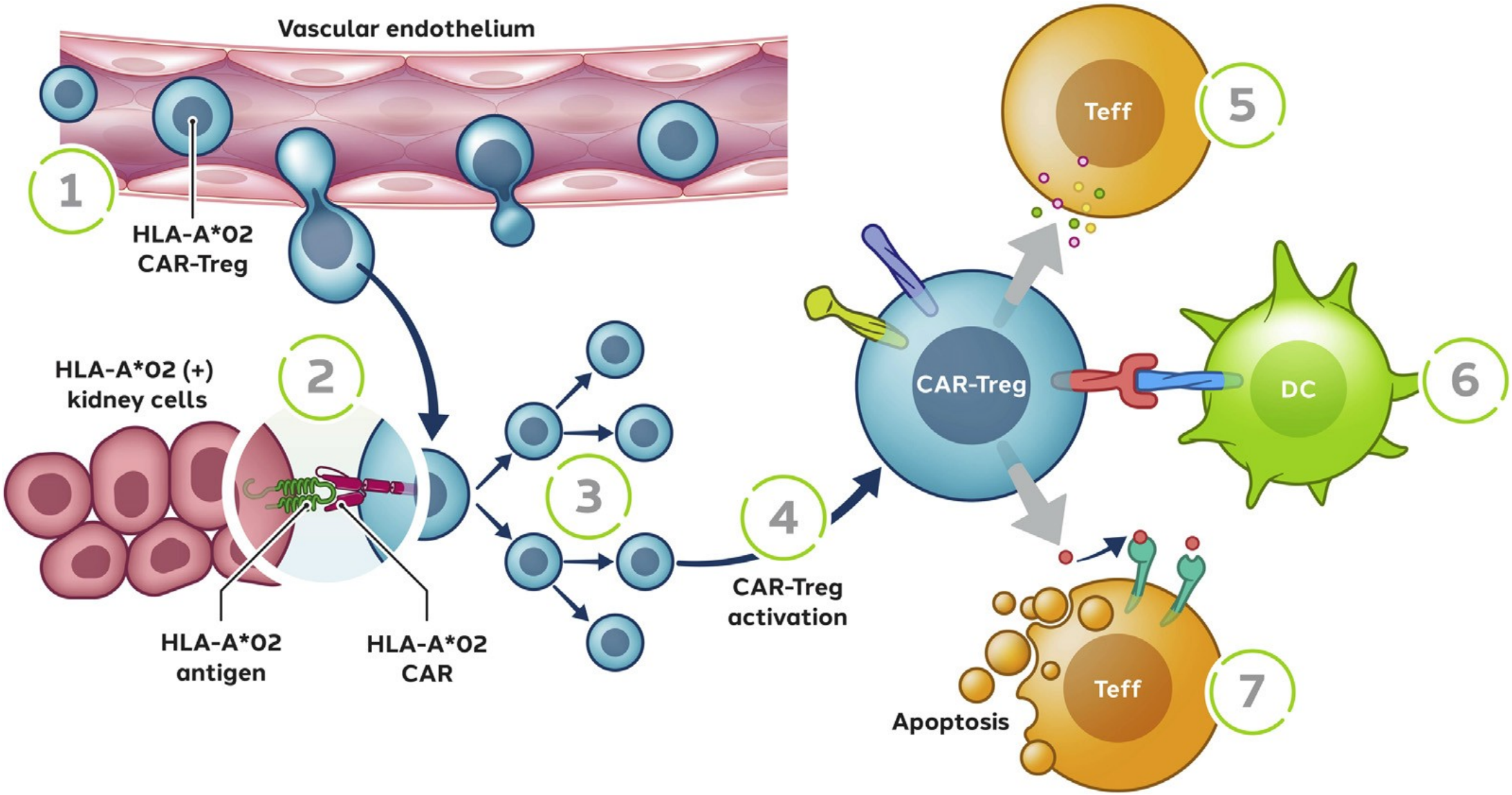


Figure 3. STEADFAST study scheme. SMC, Safety Monitoring Committee.



Bitiş tarihi :
29.10.2025

TX200-KT03-NCT05234190

Neden CAR-T reg

1. Graft kaybını azaltmak

2. Diğer İmmunsupresiflere ola ihtiyacı azaltmak

Long-Term Follow-Up of TX200-TR101 (STEADFAST Long Term)

ClinicalTrials.gov ID NCT05987527
Sponsor Sangamo Therapeutics
Information provided by Sangamo Therapeutics (Responsible Party)
Last Update Posted 2025-05-14

Bitiş tarihi : 2039

Download | Save | + Expand a

Study Details | Researcher View | No Results Posted | Record History

On this page
Study Overview
Contacts and Locations
Participation Criteria
Study Plan

Study Overview

Brief Summary

This long-term follow-up study is being conducted to collect long-term (up to 15 years post-infusion) safety and tolerability data from subjects enrolled in studies evaluating TX200-TR101.

MMF'in 2. haftadan itibaren kademeli olarak doz azaltılması ve 49. haftaya kadar mümkünse kesilmesi,

Nihai hedef: Tacrolimus tek başına ve düşük doz seviyede sürdürebilmesi hedeflenmektedir.

CAR-T reg çalışmalarında

- Hücre izolasyonu,
- Saflık,
- Verim,
- Expansiyon,
- Vektör üretimi/ transdüksiyonu,
- Stabilite
- İn vivo kalıcılık
- Taşınma
- Ürün salım testleri
- Hücre ürünündeki çeşitlilik
- Bireysel farklılıklar

Teşekkür ederim.