

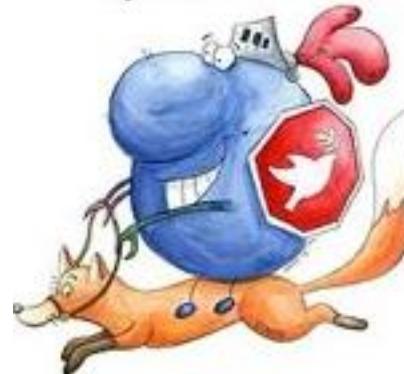
T cells



Cytotoxic T Cell



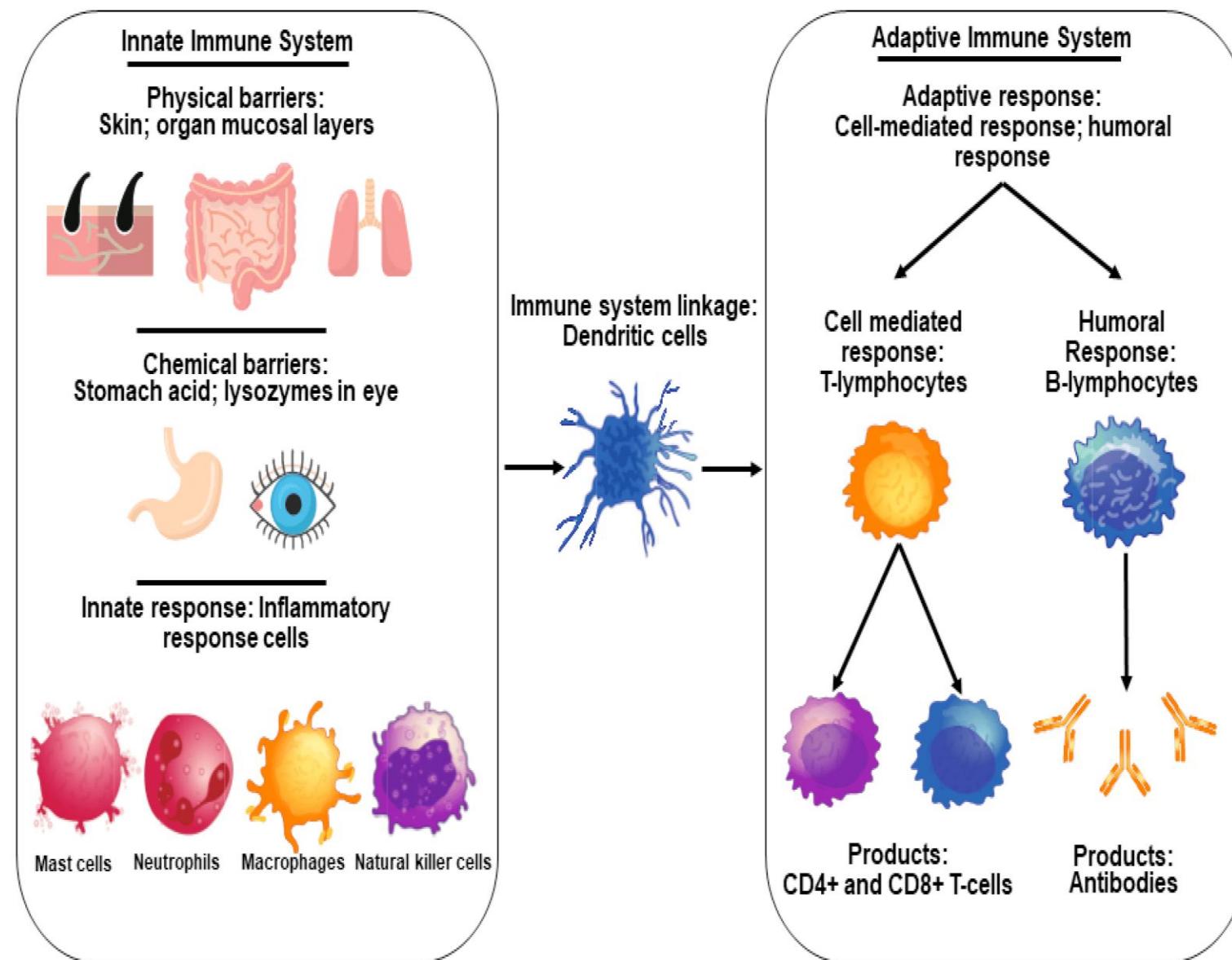
Helper T Cell



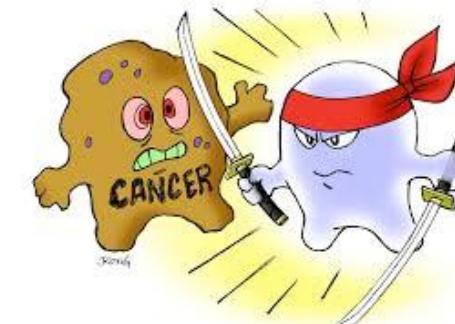
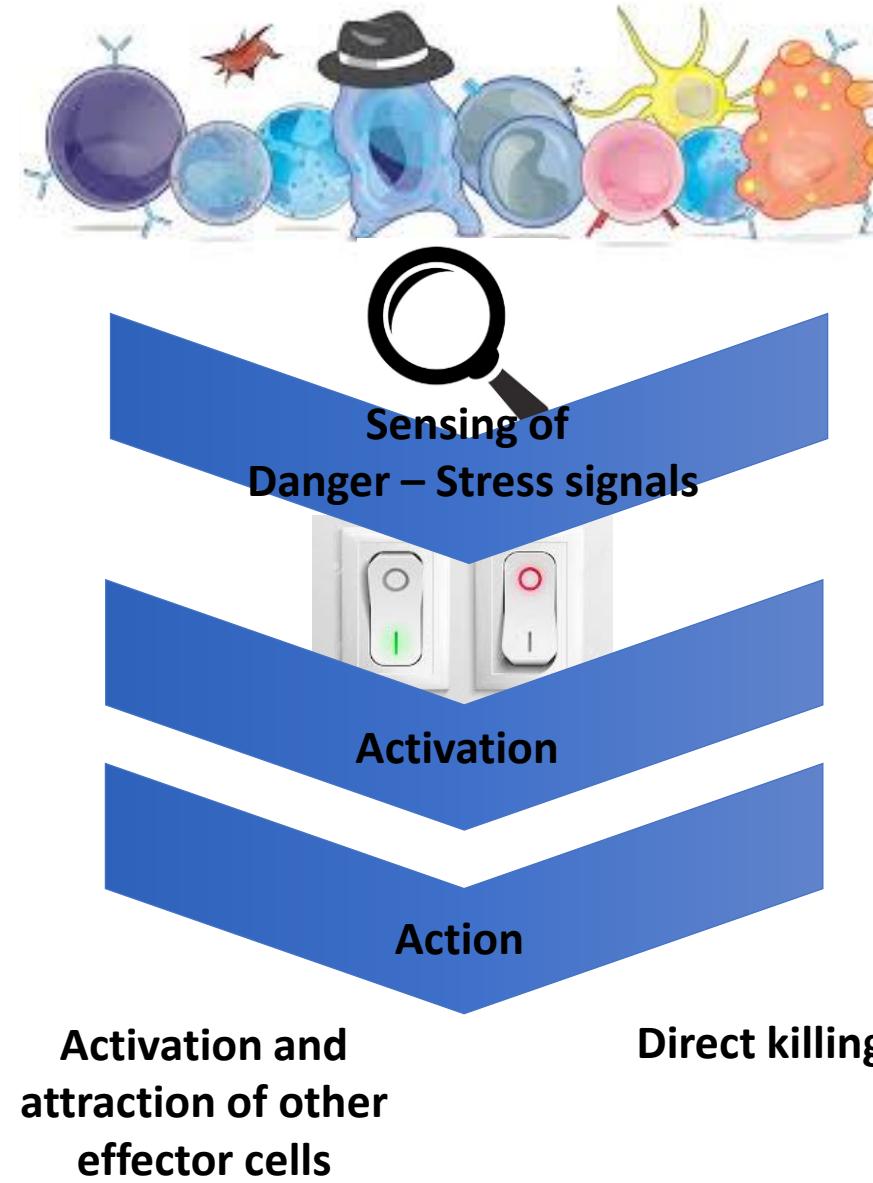
Treg

Hatzioannou A.
Laboratory of Biology, National and
Kapodistrian University of Athens Medical School

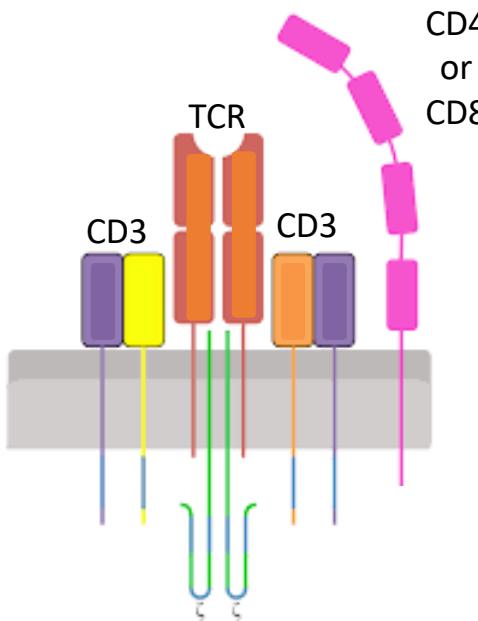
Where do T cells stand in the outline of the immune system?



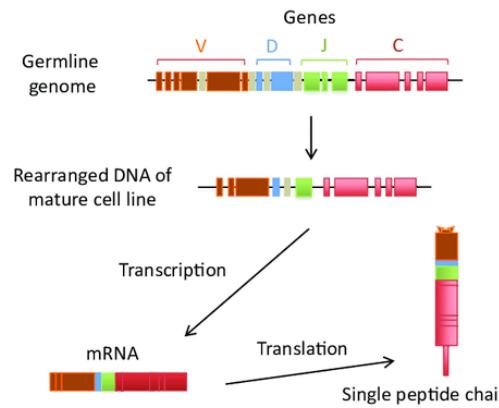
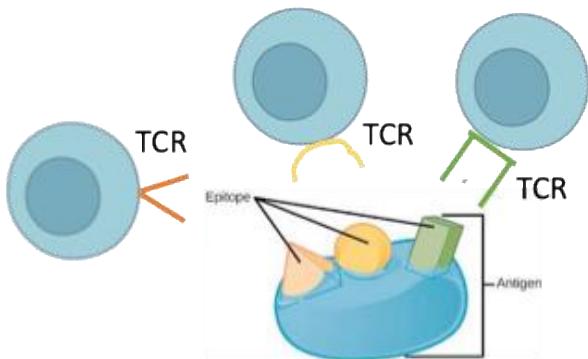
Important steps for T cells to exert their function



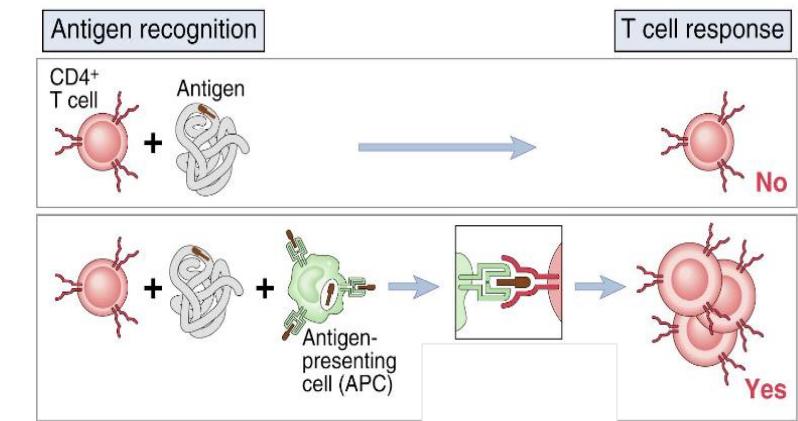
The identity of T cells



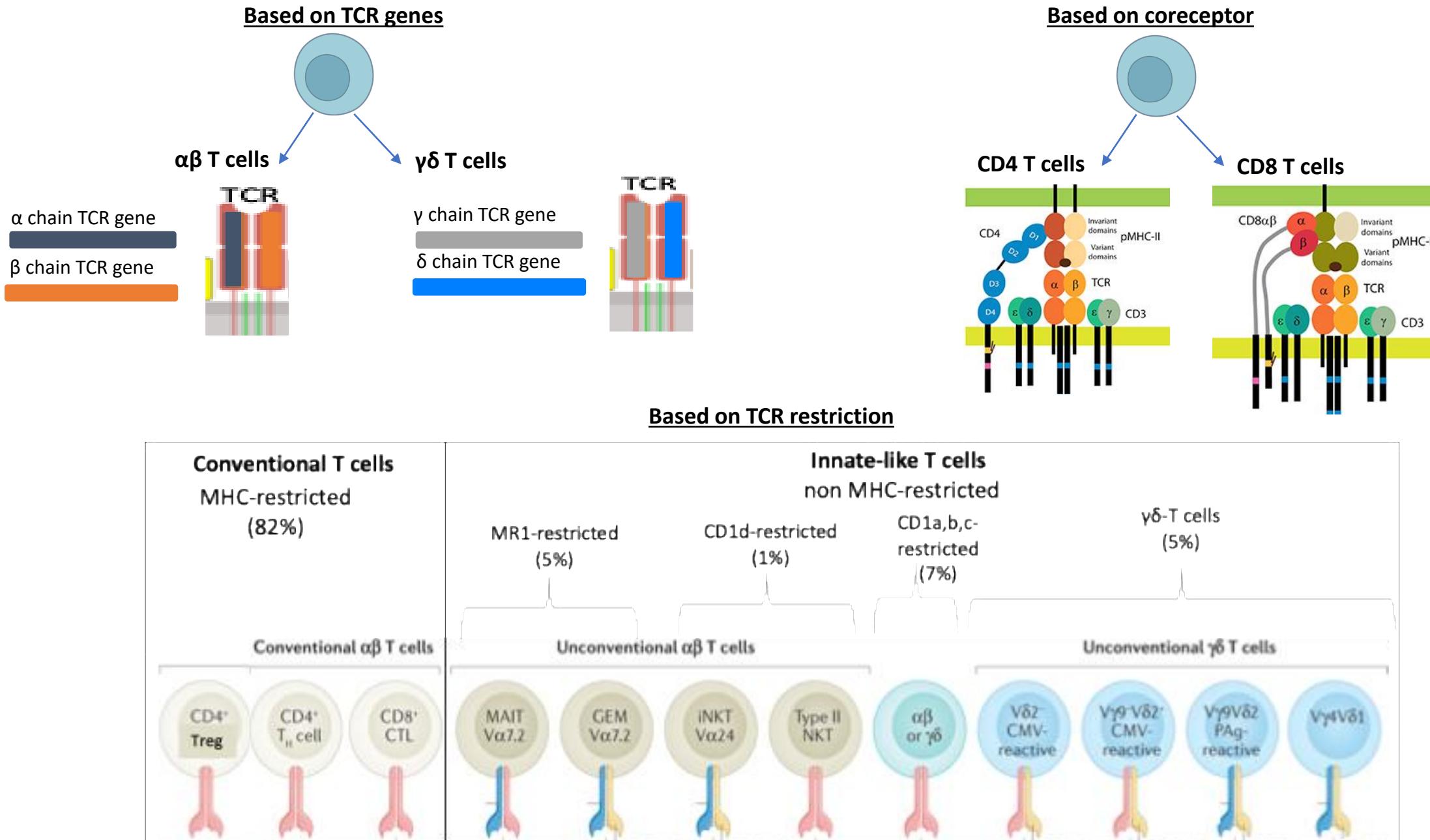
The TCR is responsible for the recognition of antigens and dictate the high specificity of T cells



T cells do not recognize soluble antigens through their TCR

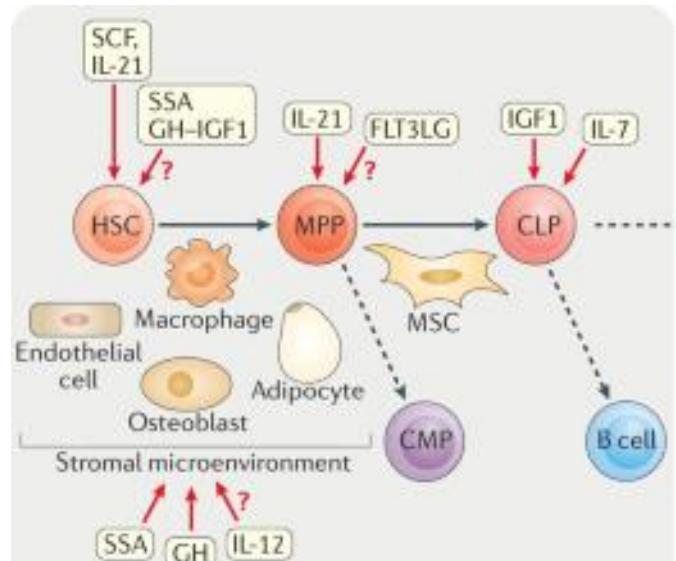
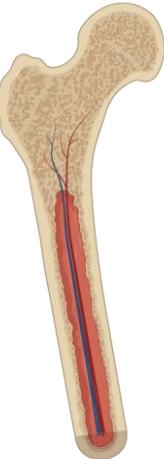


The different flavors of T cells based on their TCR and coreceptors

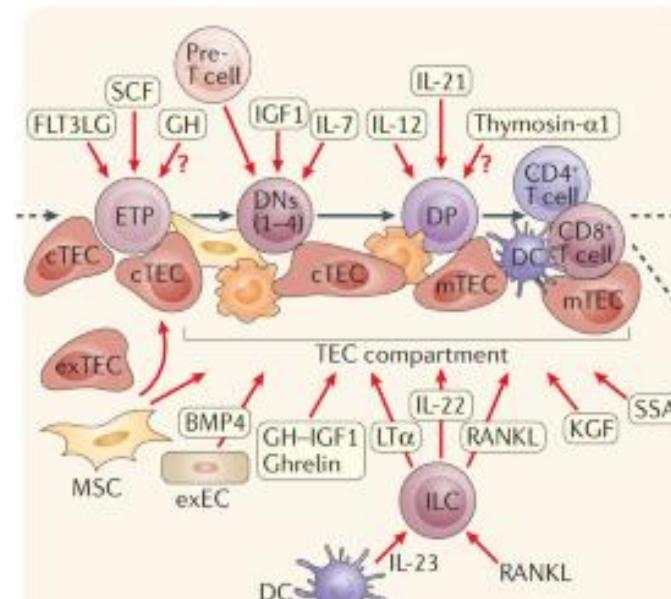
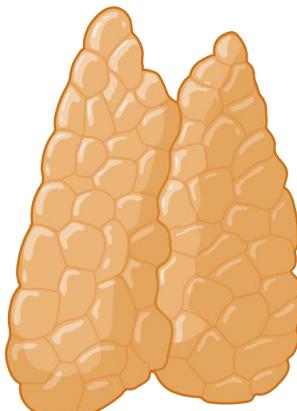


The life cycle of T cells

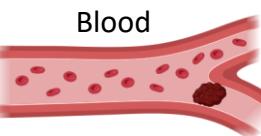
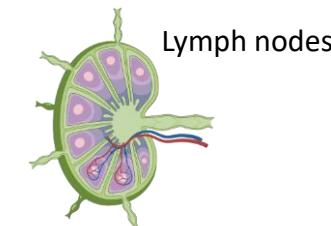
Bonne Marrow



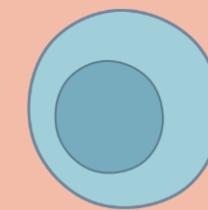
Thymus



Periphery
Secondary lymphoid organs

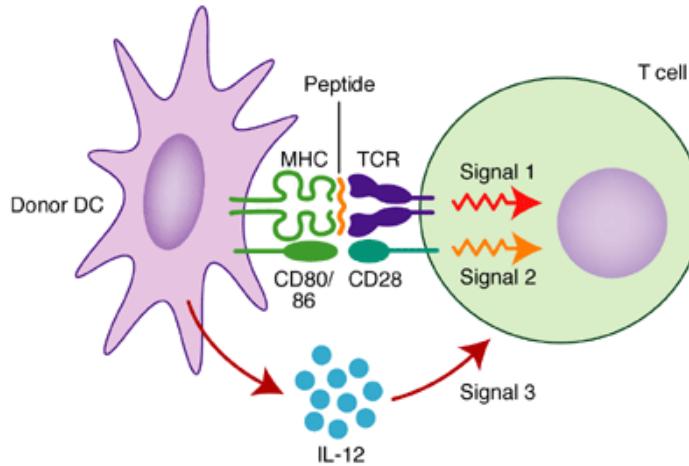


Naïve T cells

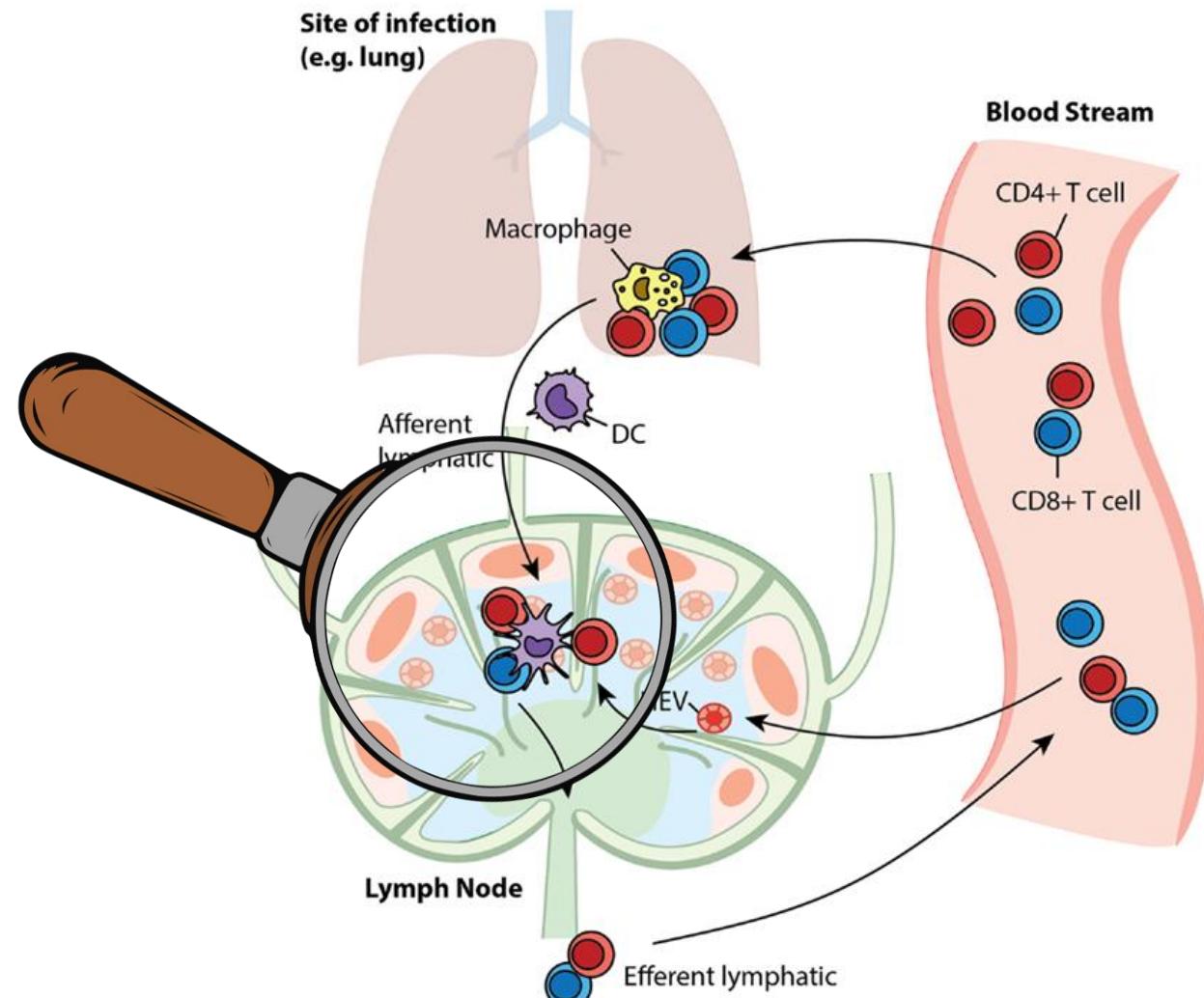
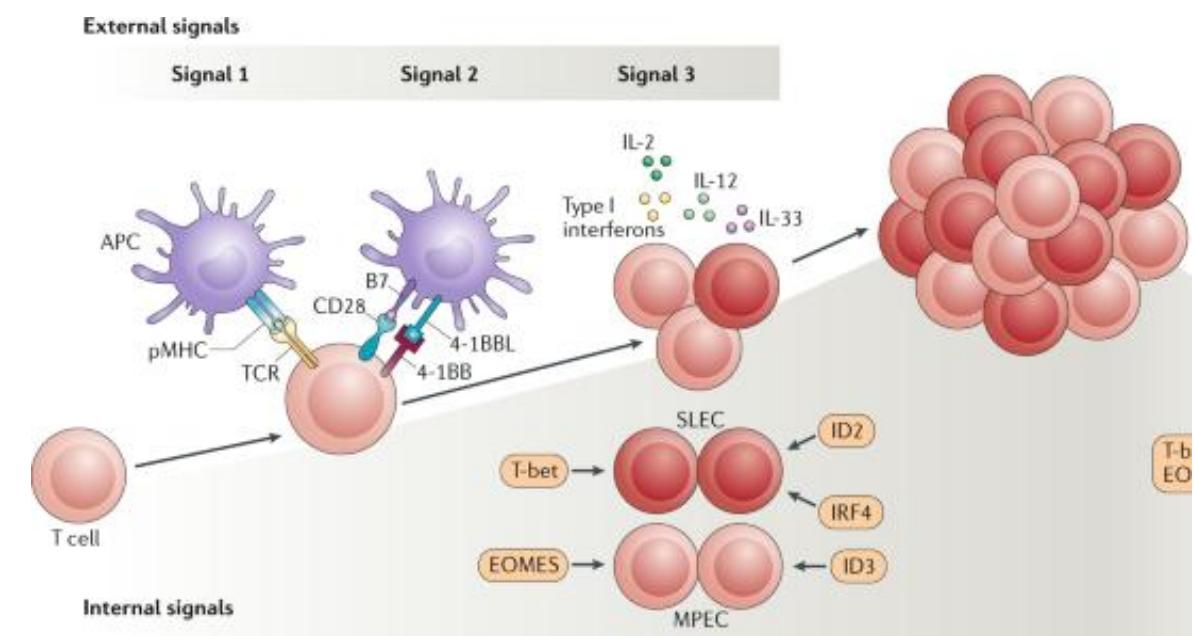


The activation and expansion of naïve T cells in secondary lymphoid organs

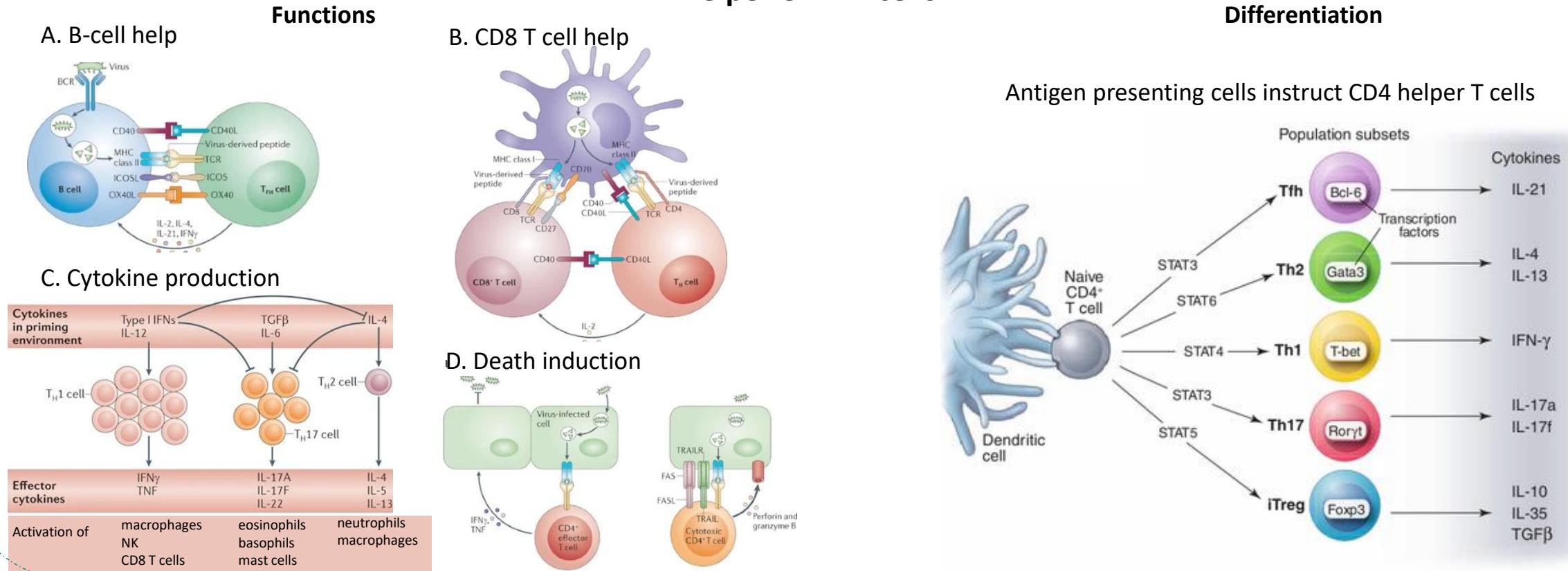
The important three signals for T cell activation



Expansion of T cells

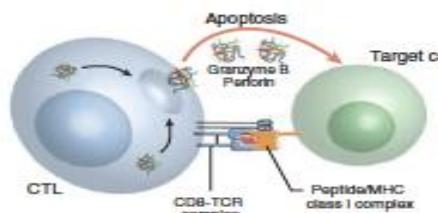
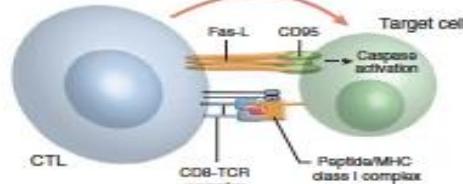


T lymphocytes are the conductors of the immune orchestra

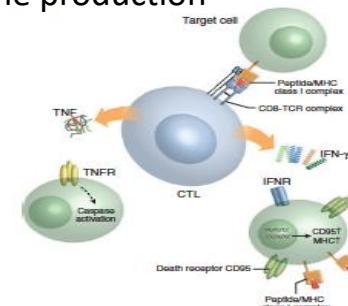


Cytotoxic CD8⁺ T cells

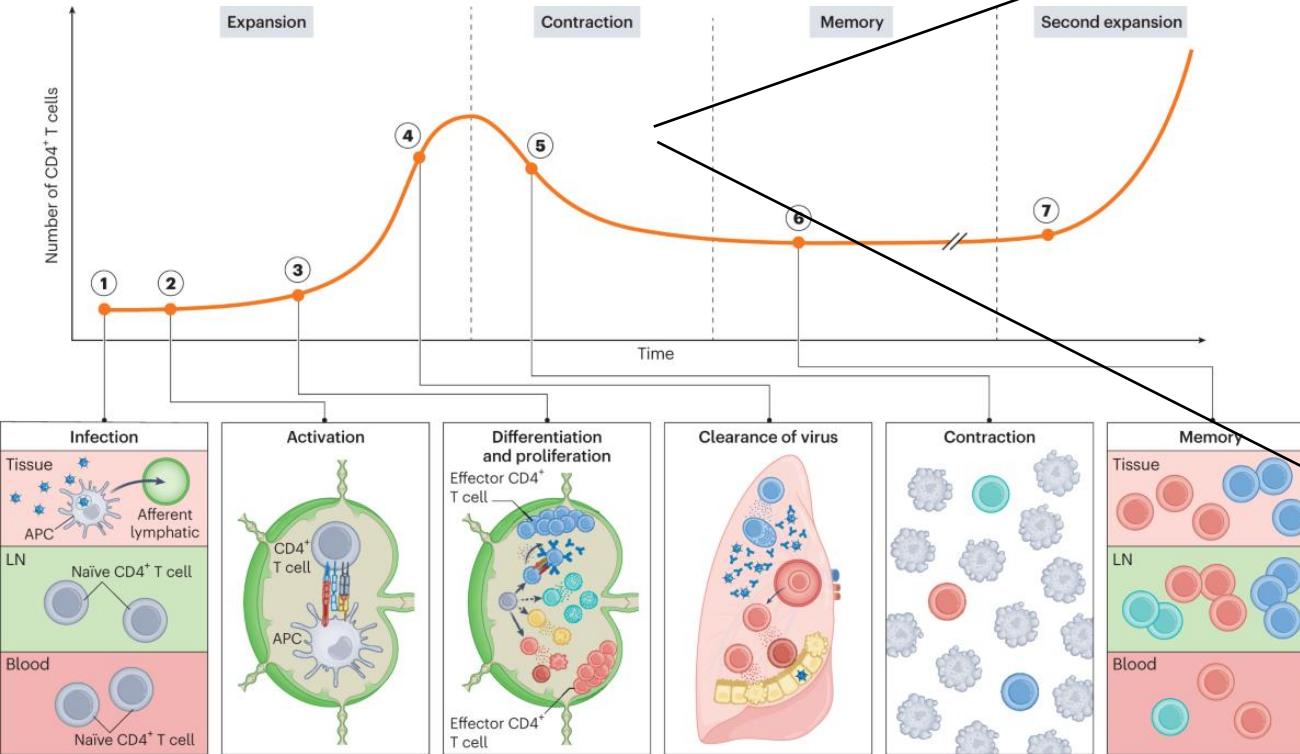
A. Death induction



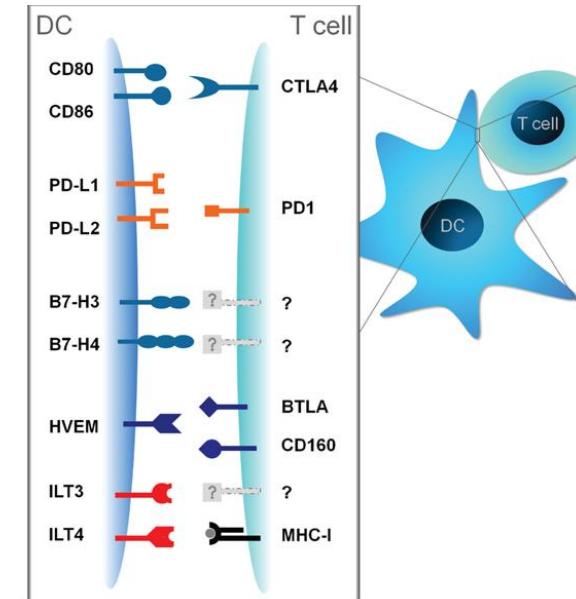
B. Cytokine production



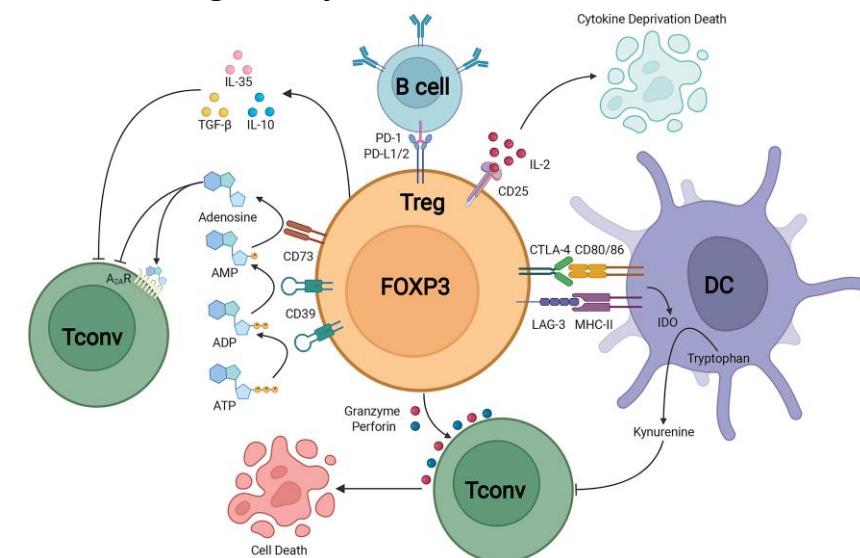
The shut down of the T-cell mediated immune response



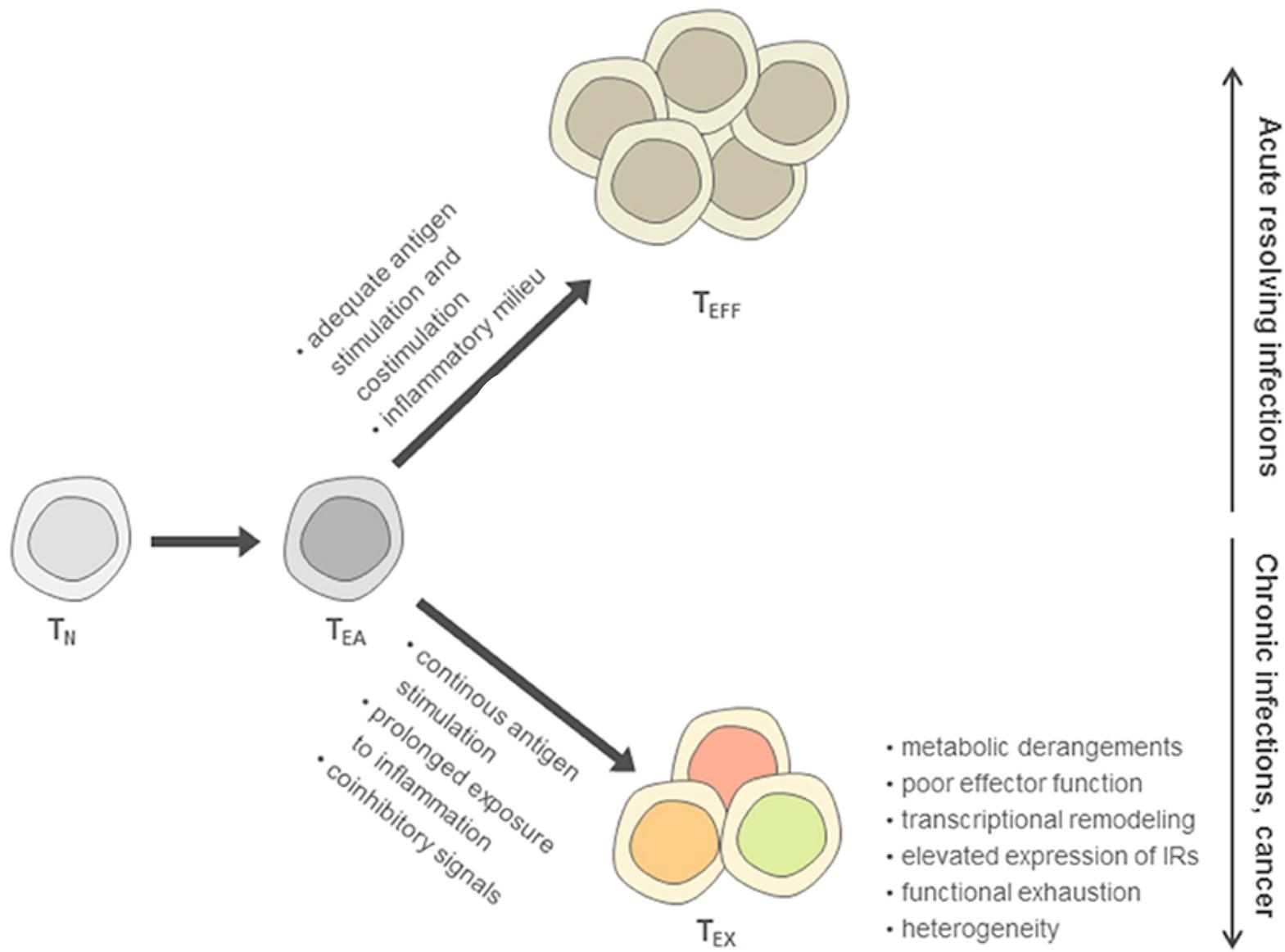
Coinhibitory receptors



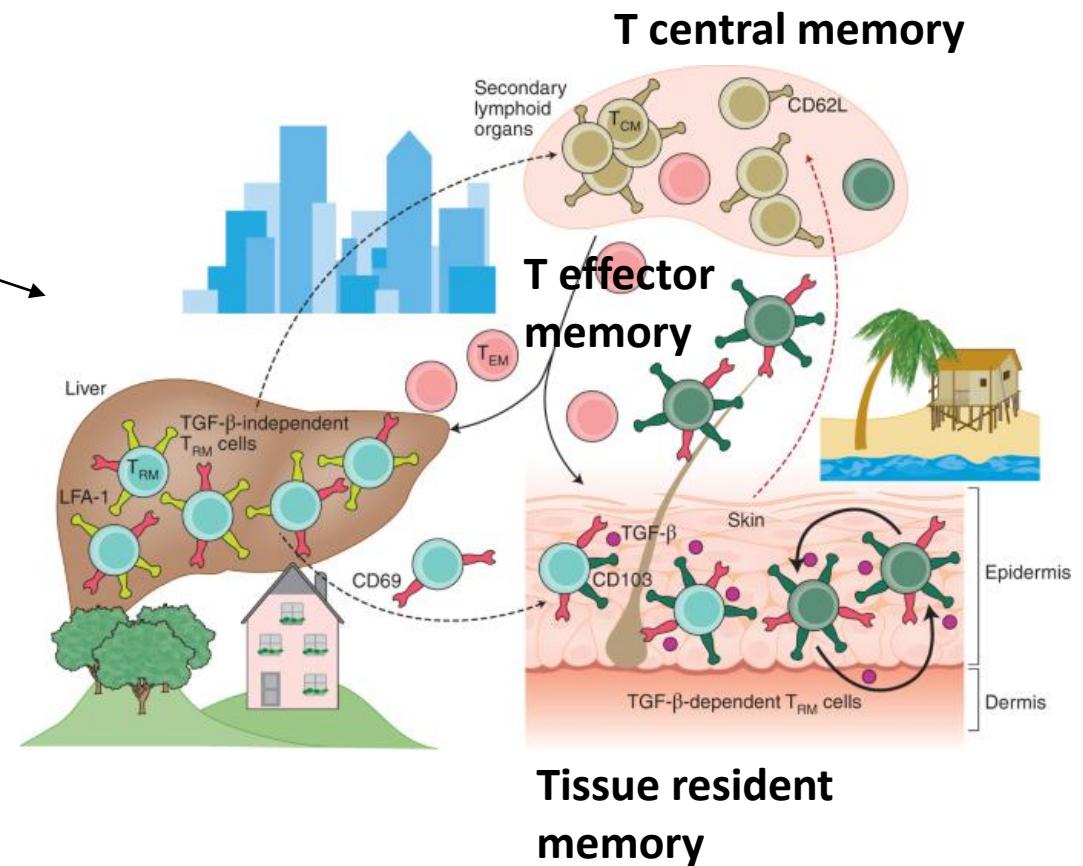
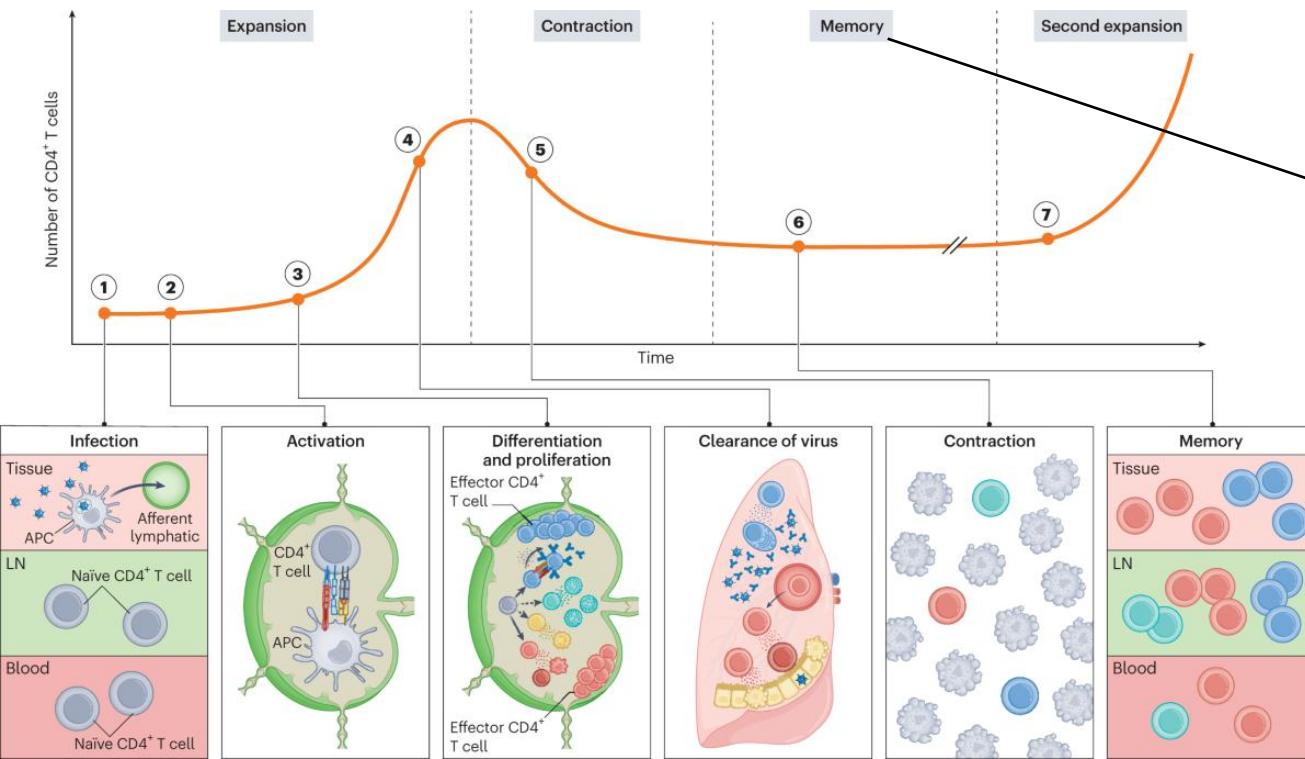
CD4⁺ T regulatory cells



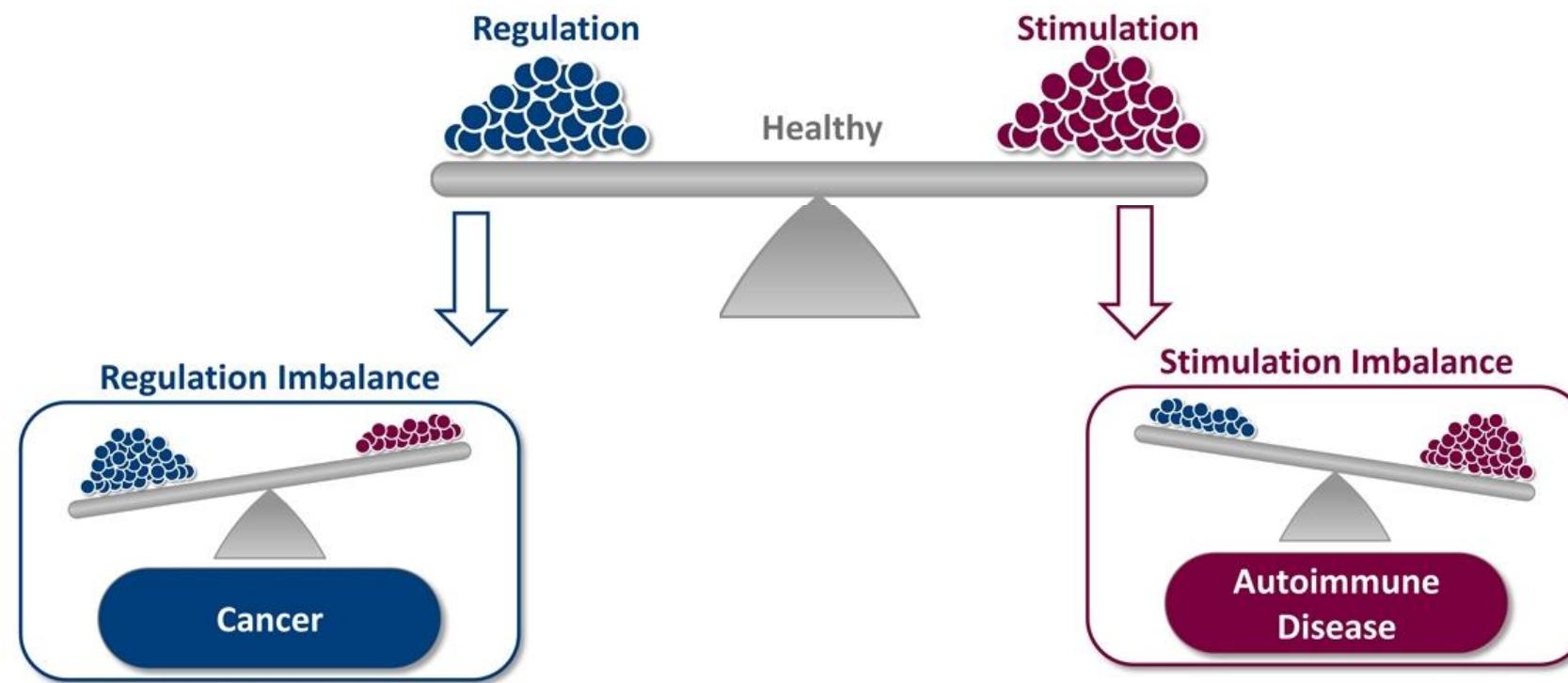
Chronic inflammation induces exhaustion of T cells



The formation of T cell memory



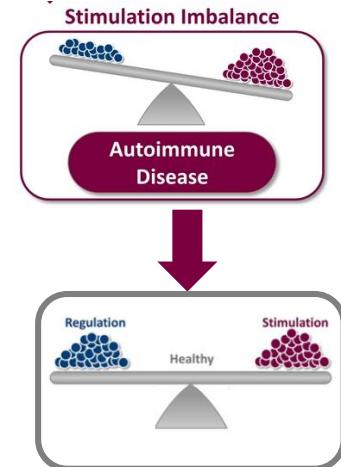
Failure of the balance of T cell stimulation and T cell regulation leads to disease manifestation



T cell based therapies

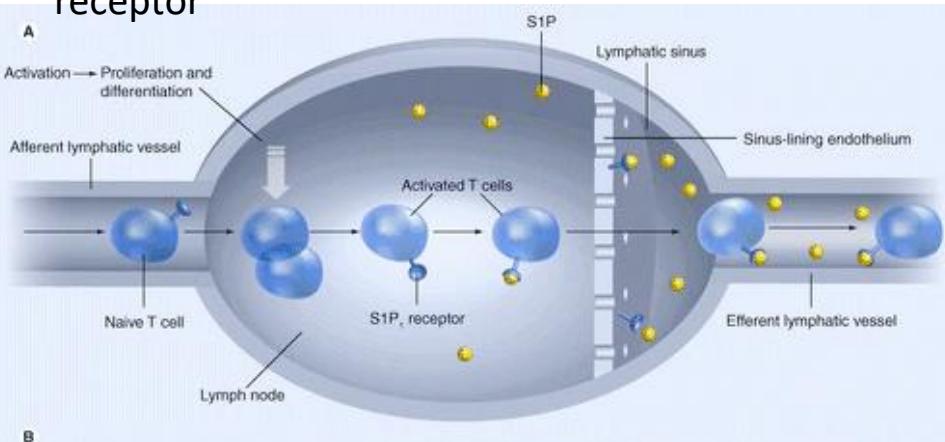
1. T cell depletion

Target molecule	Medicine	Use
CD3e	OKT3 (monoclonal antibody)	transplantation
CD3e	Teplizumab, Otelixizumab, Visiluzimab	in psoriatic arthritis, renal transplantation type 1 diabetes
CD2	BTI-322	acute kidney transplants
CD2	sipilizumab	nonmyeloablative stem cell transplantation, psoriasis

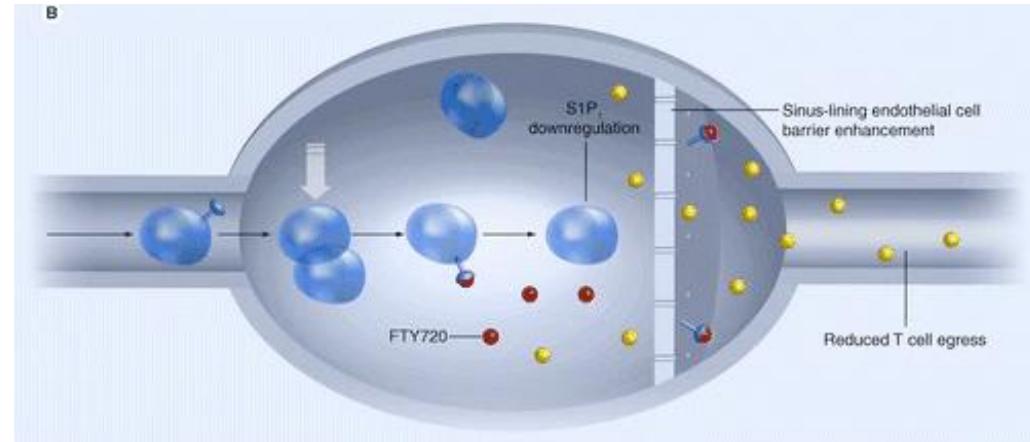


2. Targeting T cell trafficking

Target molecule: Sphingosine 1 – phosphate (S1P) receptor



Medicine: FTY720 (fingolimod)

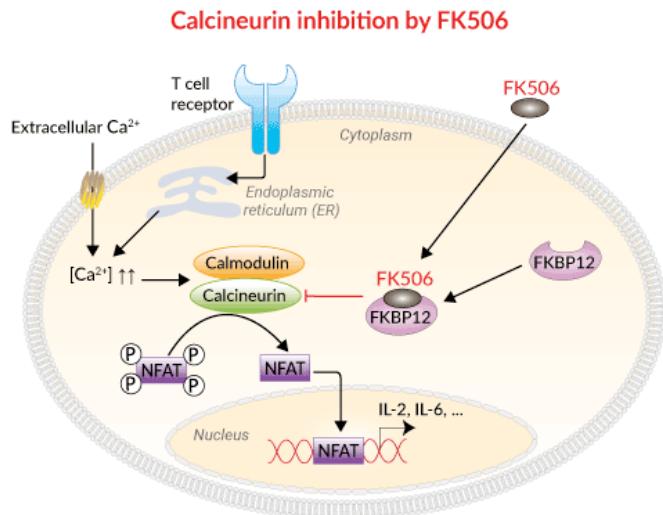


Use

- Transplantation
- Multiple Sclerosis

T cell based therapies

3. Interfering with TCR-mediated signaling

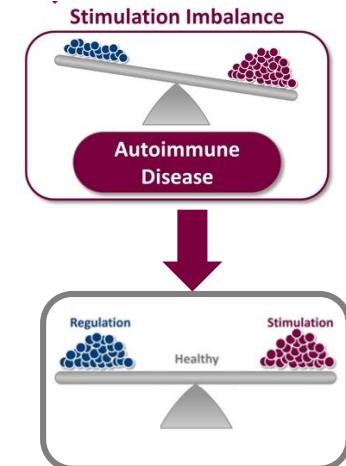


Target molecule: Calcineurin

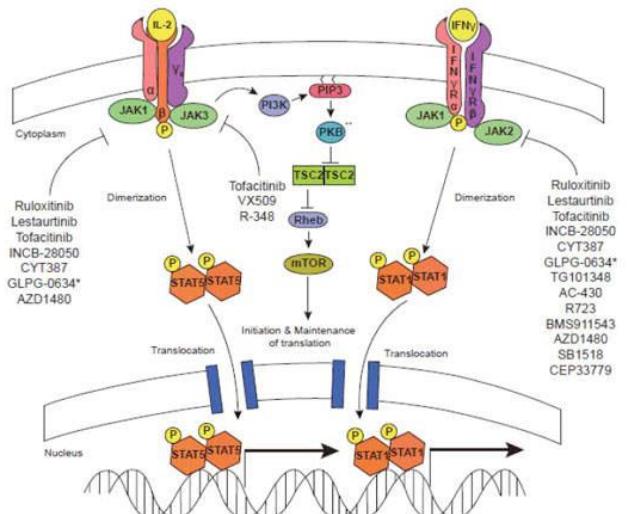
Medicine: Cyclosporine A (CsA) and Tacrolimus (FK506)

Use

- autoimmune diseases
- psoriasis
- atopic disorders
- solid organ transplantations



4. Targeting cytokine signaling



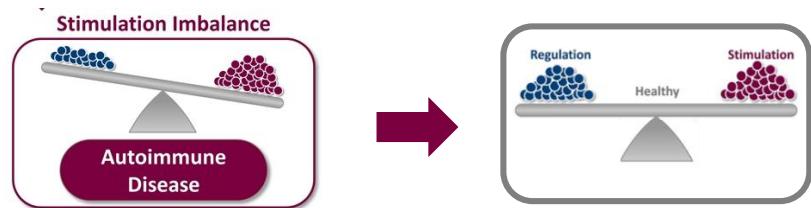
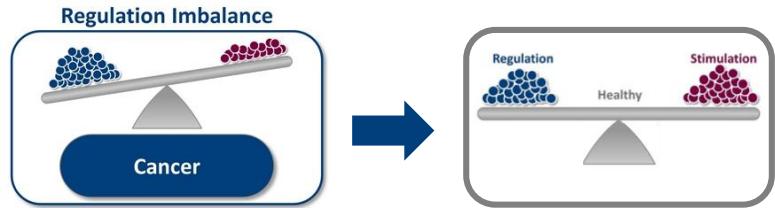
Target molecule: Janus Kinases

Use

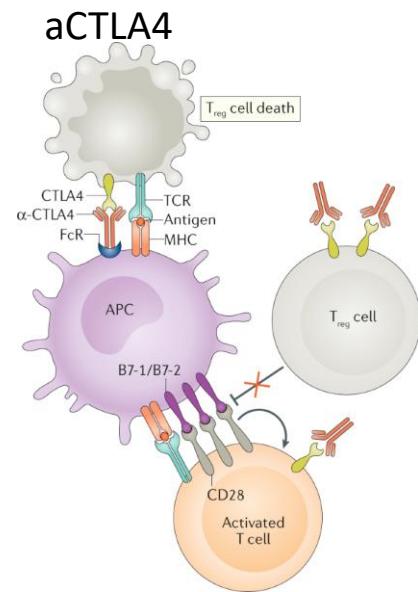
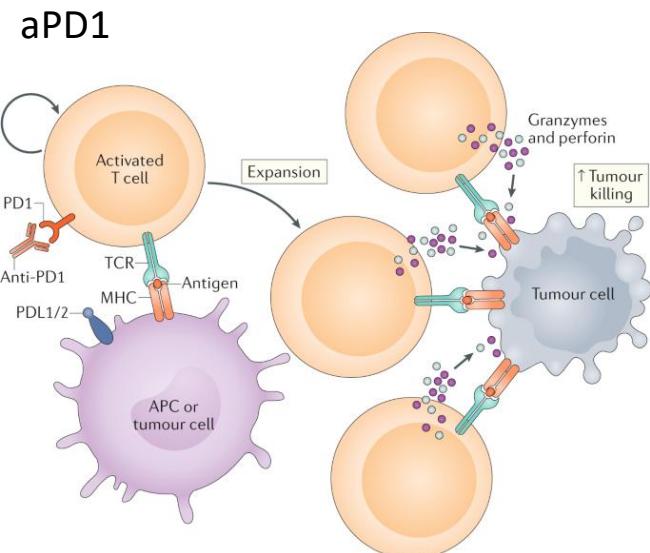
- autoimmune diseases

T cell based therapies

5. Targeting coinhibitory molecules

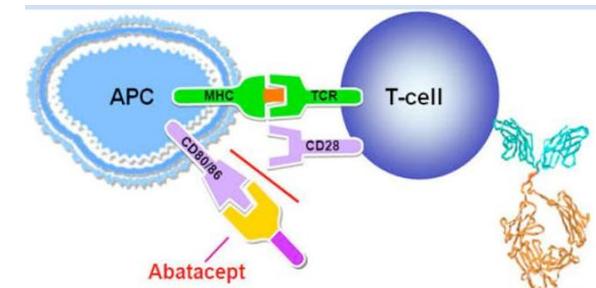
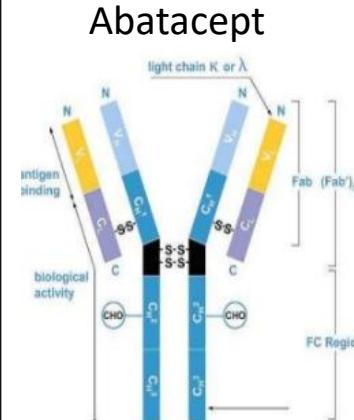


Blocking inhibitory molecules in cancer



VS

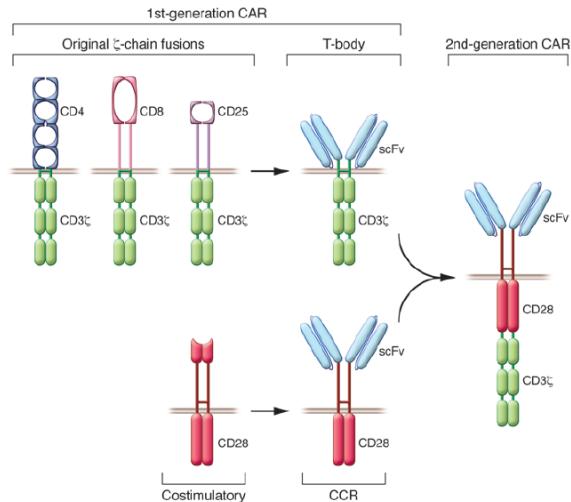
Activating inhibitory molecules in autoimmunity



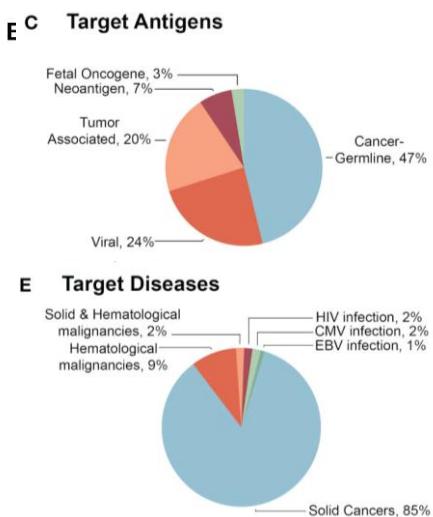
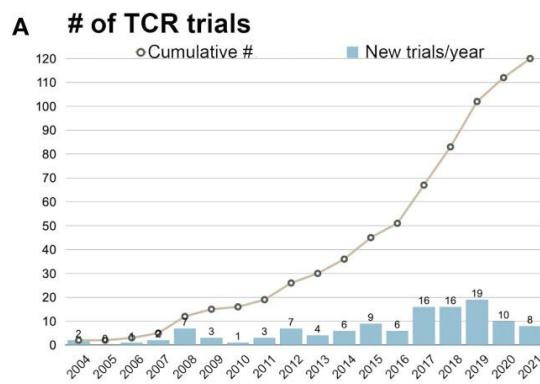
T cell based therapies

6. Engineering T cells

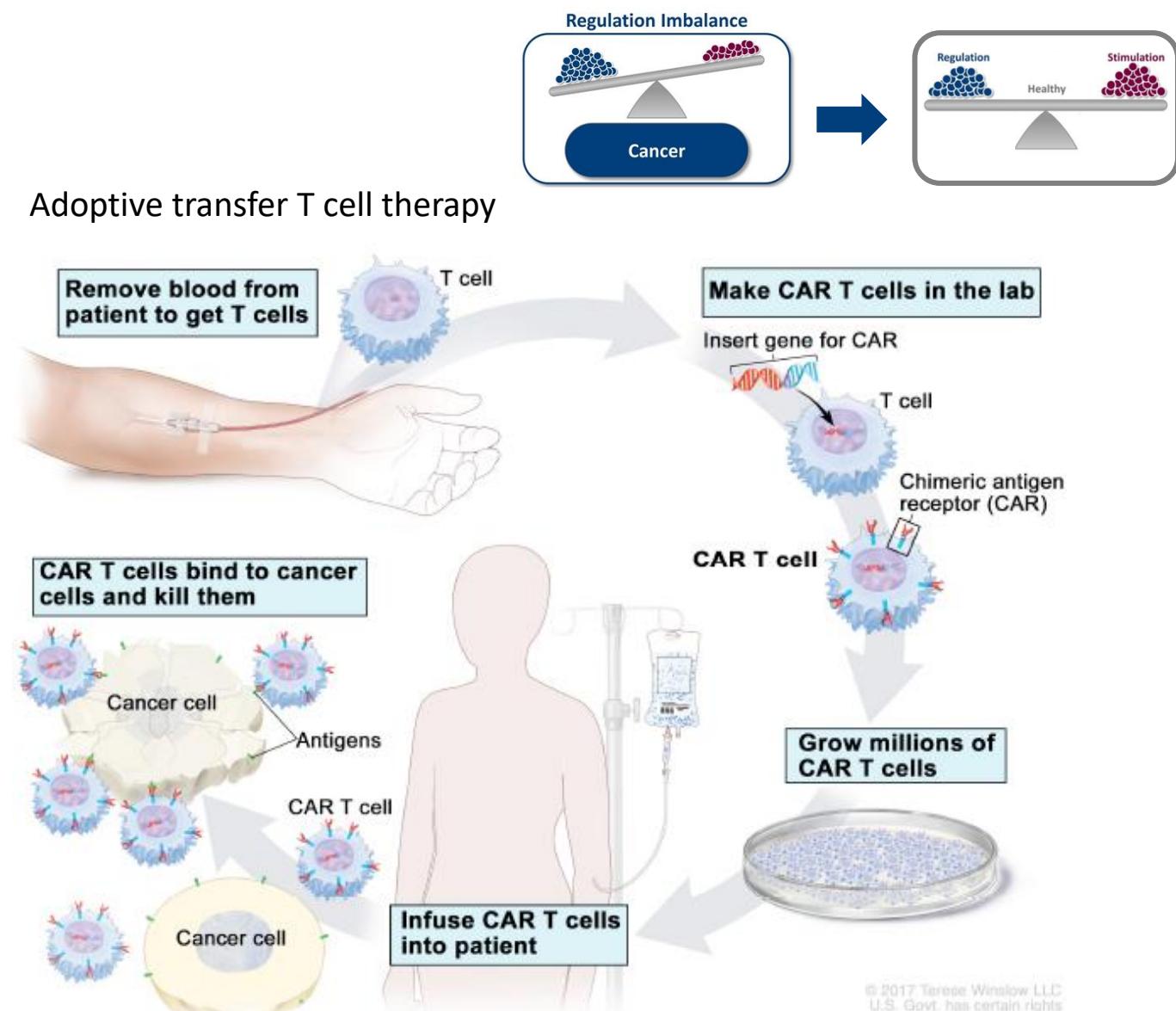
CAR T cells



TCR-engineered T cells (TCR T)



Adoptive transfer T cell therapy

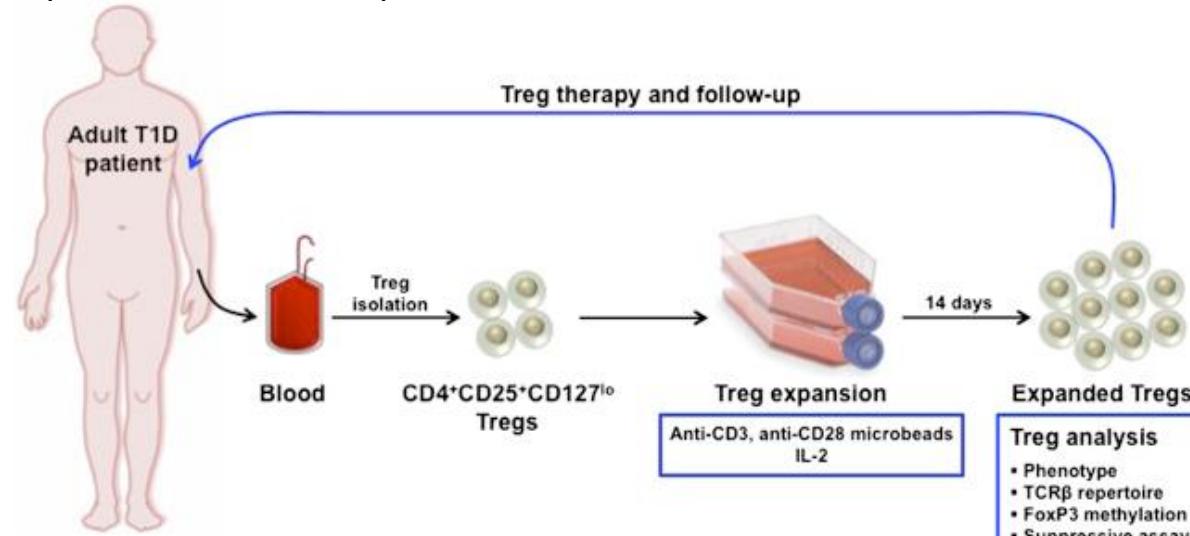


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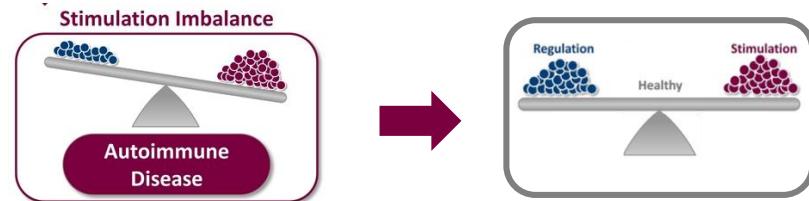
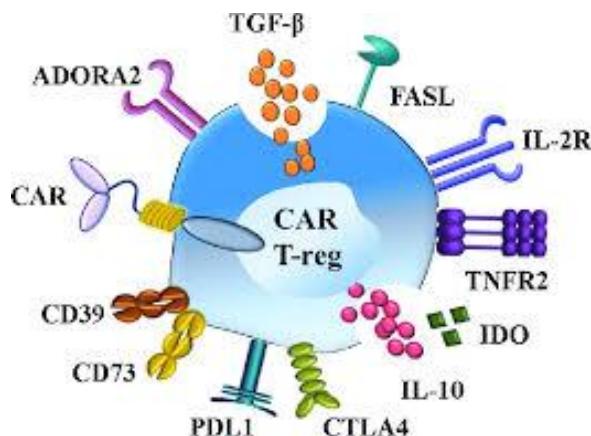
T cell based therapies

7. Tregs

Adoptive transfer therapies



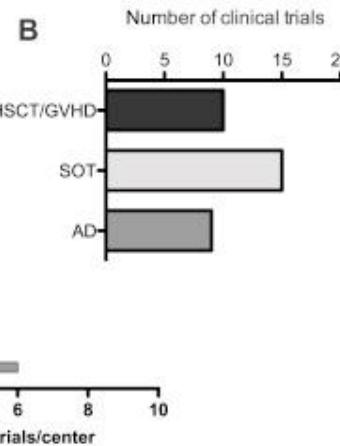
CAR Tregs



A

Universitaria di Bologna, ITA
Universidade de Lisboa, POR
Hospital de Santa Maria, POR
University Hospital Liege, BEL
Katholieke Universiteit Leuven, BEL
Hôpitaux de Paris, Hospital Certeil, FRA
Guy's Hospital London, GB
King's College Hospital, GB
The Churchill Hospital Oxford, GB
Charité University, Berlin, GER
Boris Petrovsky Scientific Center of Surgery Moscow, Russia
Russian State Medical University, Russia
Nanjing Medical University, China
Second Xiangya Hospital of Central South University, China
University of Alberta, Edmonton
University of Iowa Health Care
Duke University
University of Kentucky Medical Center
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University of Texas
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Masonic Cancer Center University of Minnesota
Dana-Farber Cancer Institute, Boston
Brigham and Women's Hospital, Boston
University of Pittsburgh
Massachusetts General Hospital
University of California San Francisco
Stanford University

Autoimmune diseases
Solid organ transplant
GVHD/GVHD





TEACELL



thank you

Η σημασία των Τ λεμφοκυττάρων – Τ κυτταρικές ανοσοανεπάρκειες

Ανοσοανεπάρκεια	Αιτία	Αποτέλεσμα
Φυλοσύνδετη βαριά συνδυασμένη ανοσοανεπάρκεια	Μεταλλάξεις στην κοινή αλυσίδα γ (γc) - υπομονάδα μεταβίβασης σήματος υποδοχέα κυτταροκινών	Μειωμένη επιβίωση και αναστολή της ωρίμανσης των Τ λεμφοκυττάρων
Αυτοσωμική βαριά συνδυασμένη ανοσοανεπάρκεια	Μεταλλάξεις σε ένα ένζυμο, την απαμινάση της αδενοσίνης	Αναστολή της ωρίμανσης των Τ λεμφοκυττάρων
Σύνδρομο DiGeorge	Ανεπαρκή ανάπτυξη θύμου	Αναστολή της ωρίμανσης των Τ λεμφοκυττάρων
Συνδρομο επίκτητης ανοσοανεπάρκειας (AIDS)	Ιός HIV	Εξάλειψη των CD4+ Τ λεμφοκυττάρων

Ευπάθεια σε λοιμώξεις

Ευπάθεια σε καρκίνο