Basic Immunology

Lecture 9th

Organization and rearrangement of the antigen receptor genes

Key issues in the antigen receptor gene expression

- **Every somatic cell** possesses TcR/BcR genes – **structure**?
- **Only T cells (TcR) and B cells (BcR)** can produce proteins – **induction and regulation of expression?**
- The overwhelming **majority of genetic elements encode V-region,** whereas in **BcR/TcR proteins the larger part is constant region – process of rearrangement and (limited) diversity**

Organization of the Ig genes

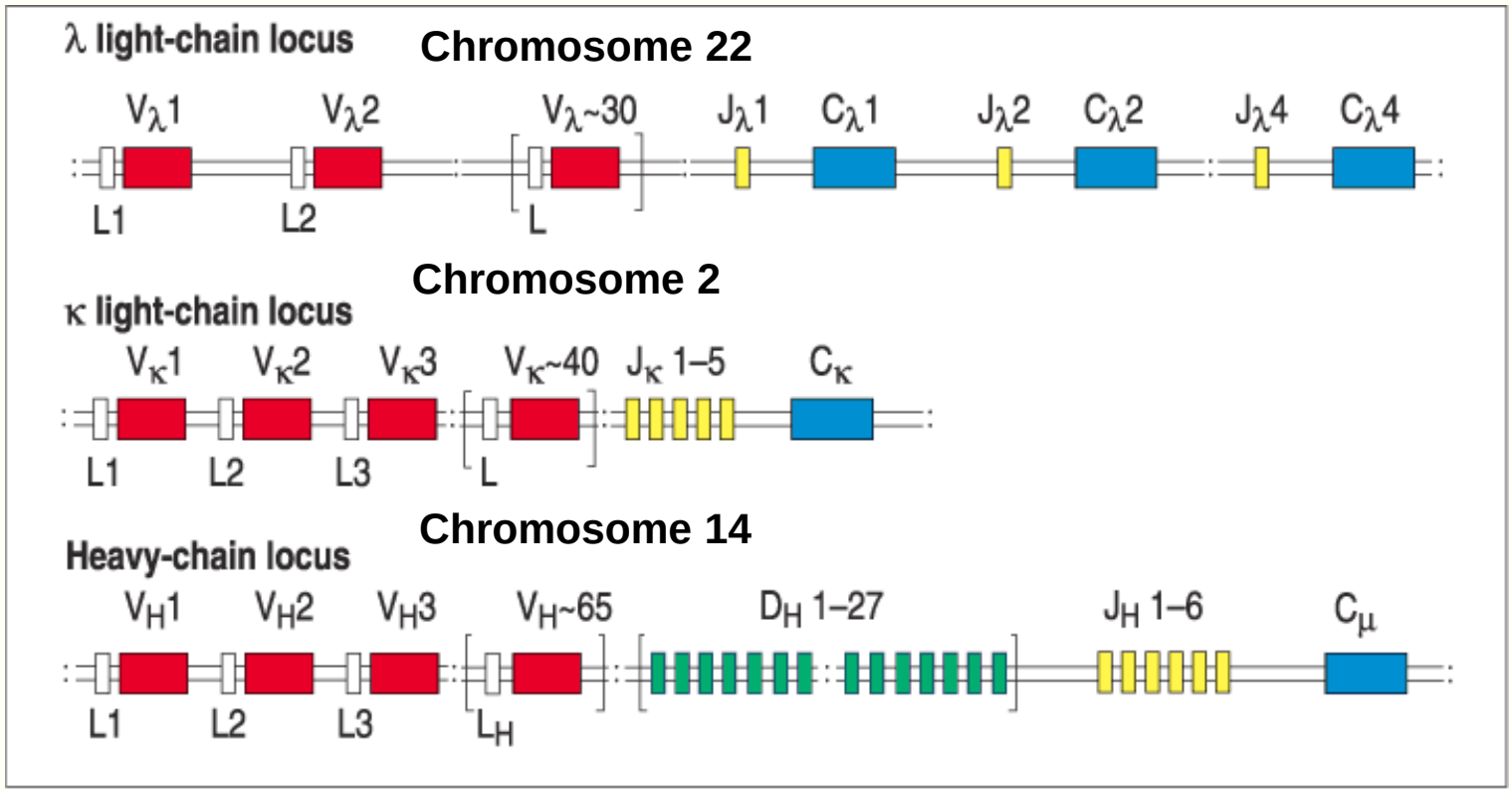
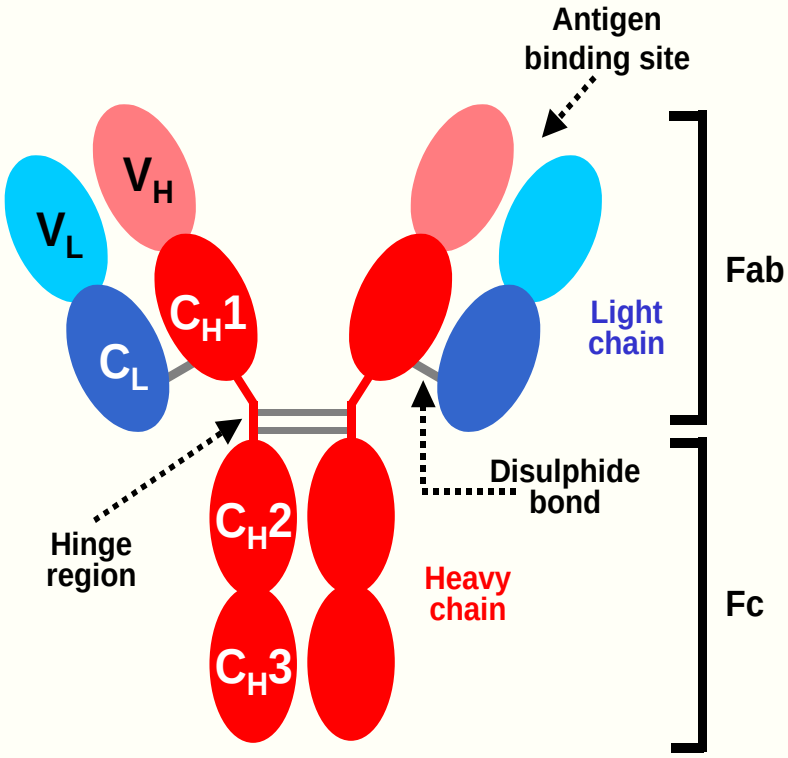


Fig 4.4 © 2001 Garland Science



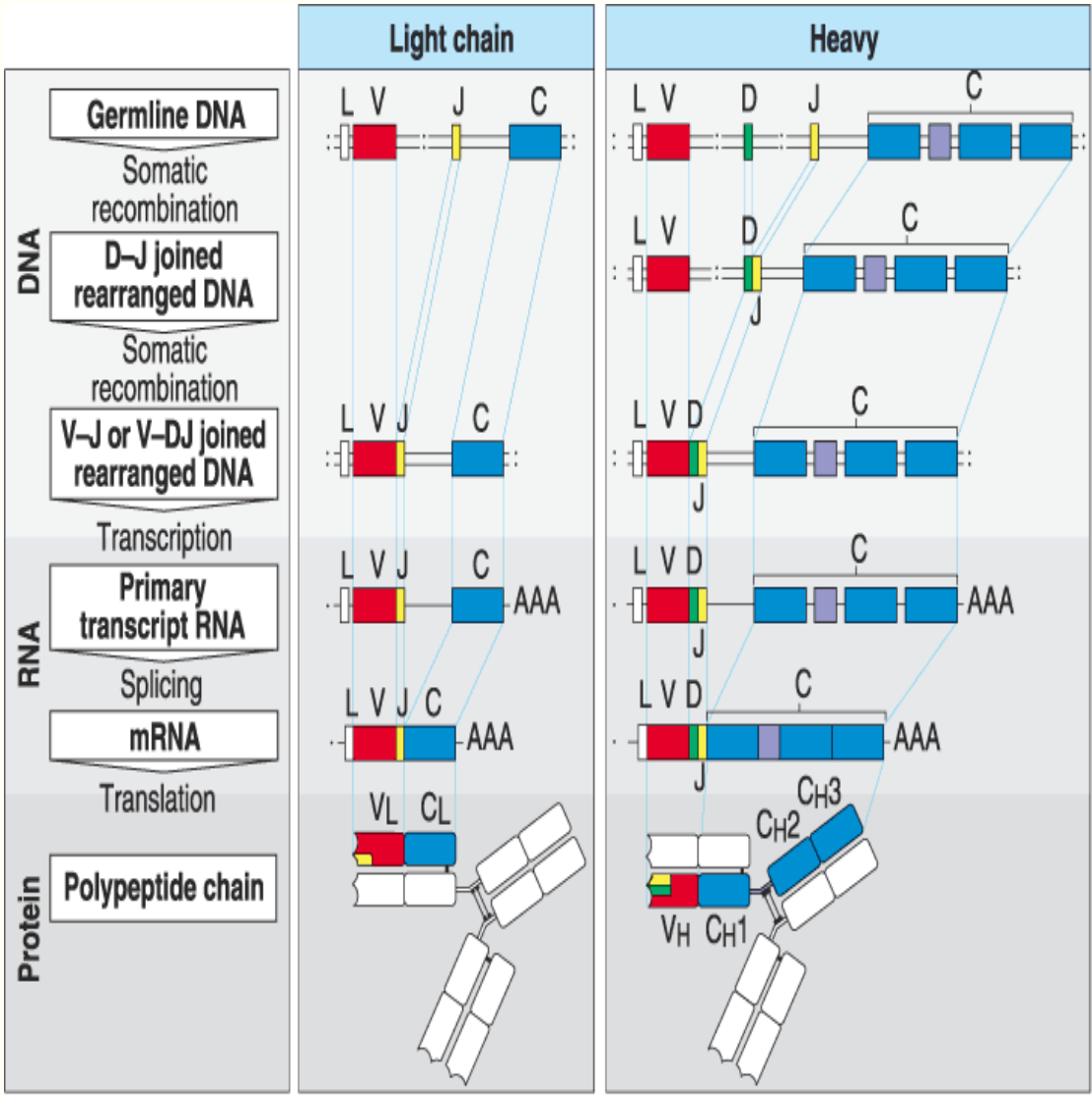


Fig 4.2 © 2001 Garland Science

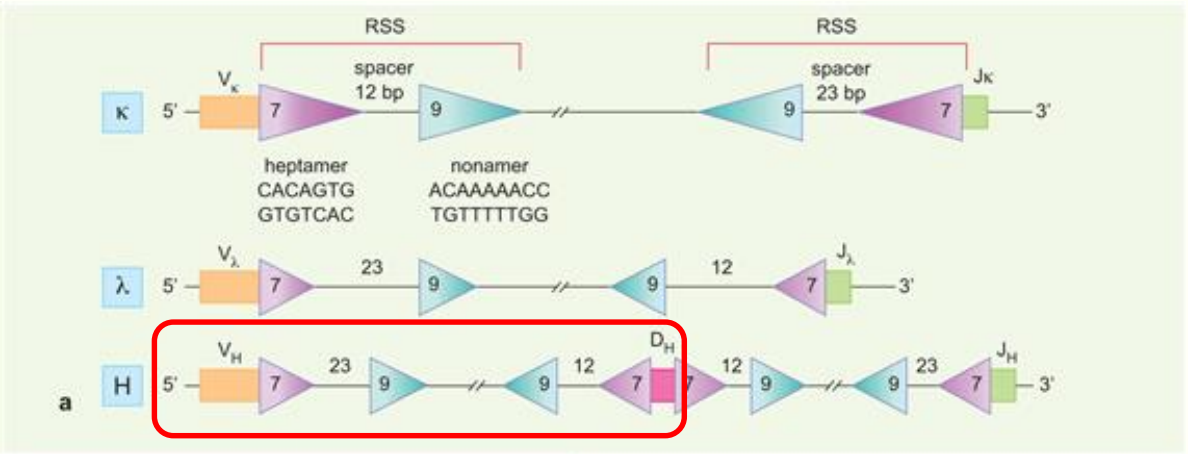
TdT: N-insertion/CDR3

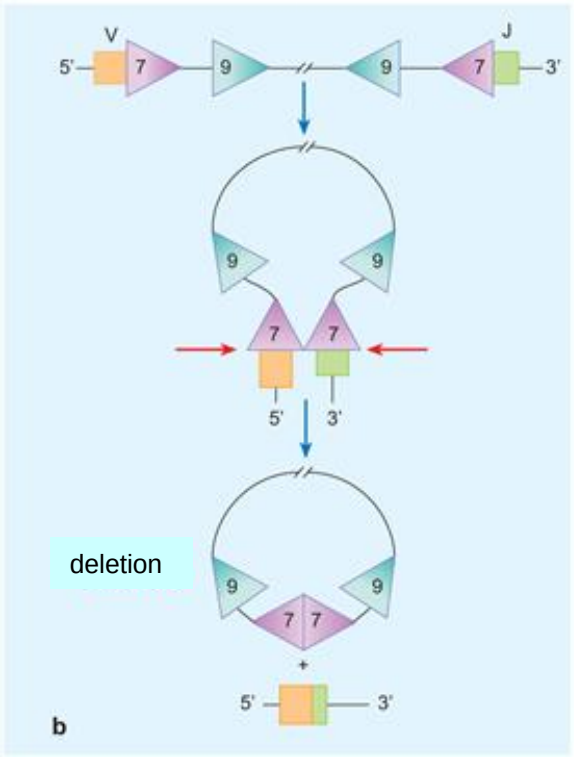
1. Allelic exclusion (H)
2. Unsuccessful rearrangement → death
3. Isotype exclusion (L)

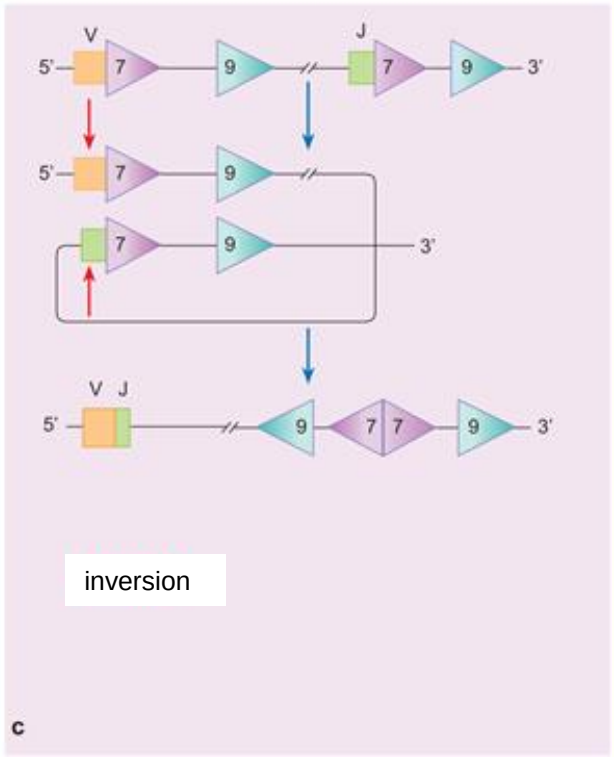
Recombinase activating genes:

RAG-1, RAG-2

VDJ joining and role of RSS







Orientation: 7/9 spacer nucleotide sequences and 12/23 base pairs rule

Recombination Signal Sequence (RSS –VDJ-recombinase)

Establishment of Ig diversity

- **Number and recombination** of Ig V/D/J segments**.**

  V_H: CDR1*/2*

  V_HDJ_H: CDR3

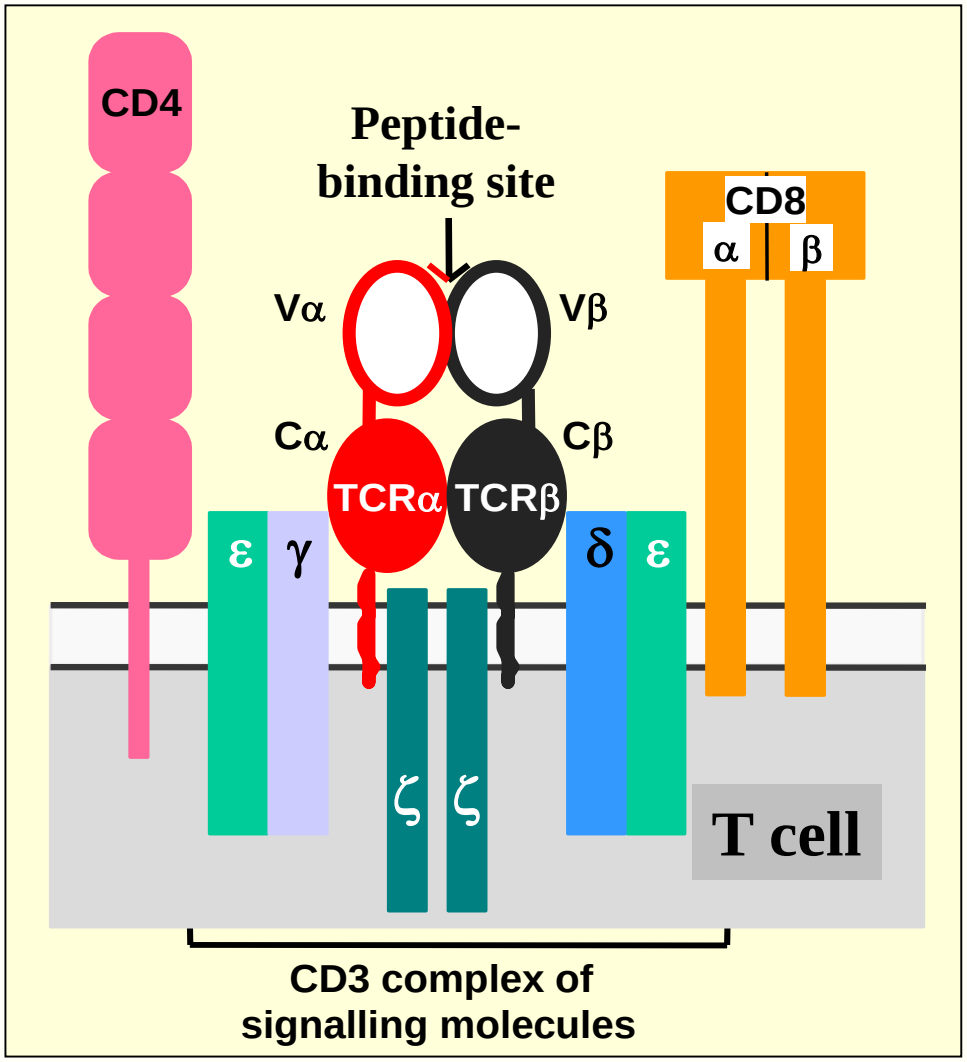
- **Effect of TdT –** CDR3 (in its absence B-1 dominance)**.**

- **Association of subunits** (IgH/IgL)**.**

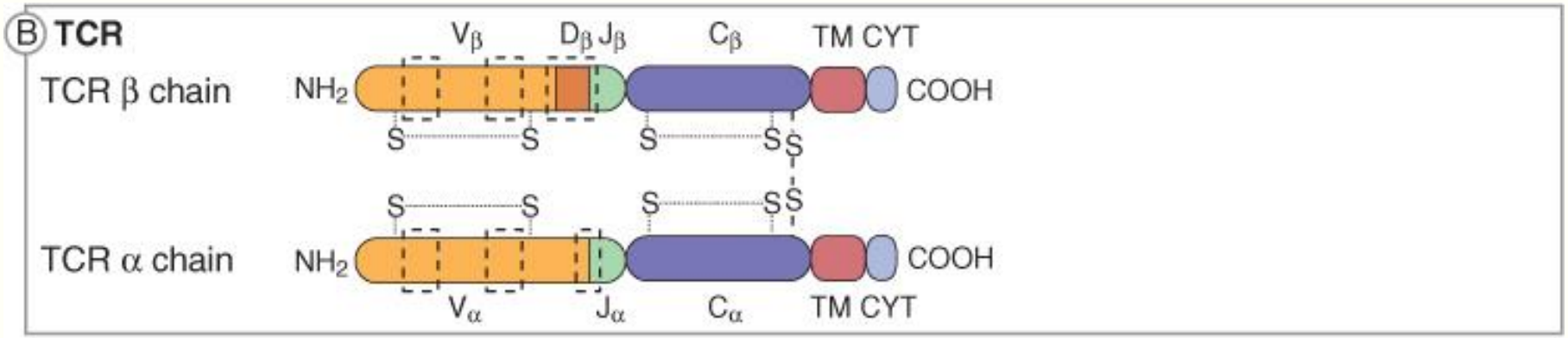
T-cell receptor (TcR)

Types of TcR

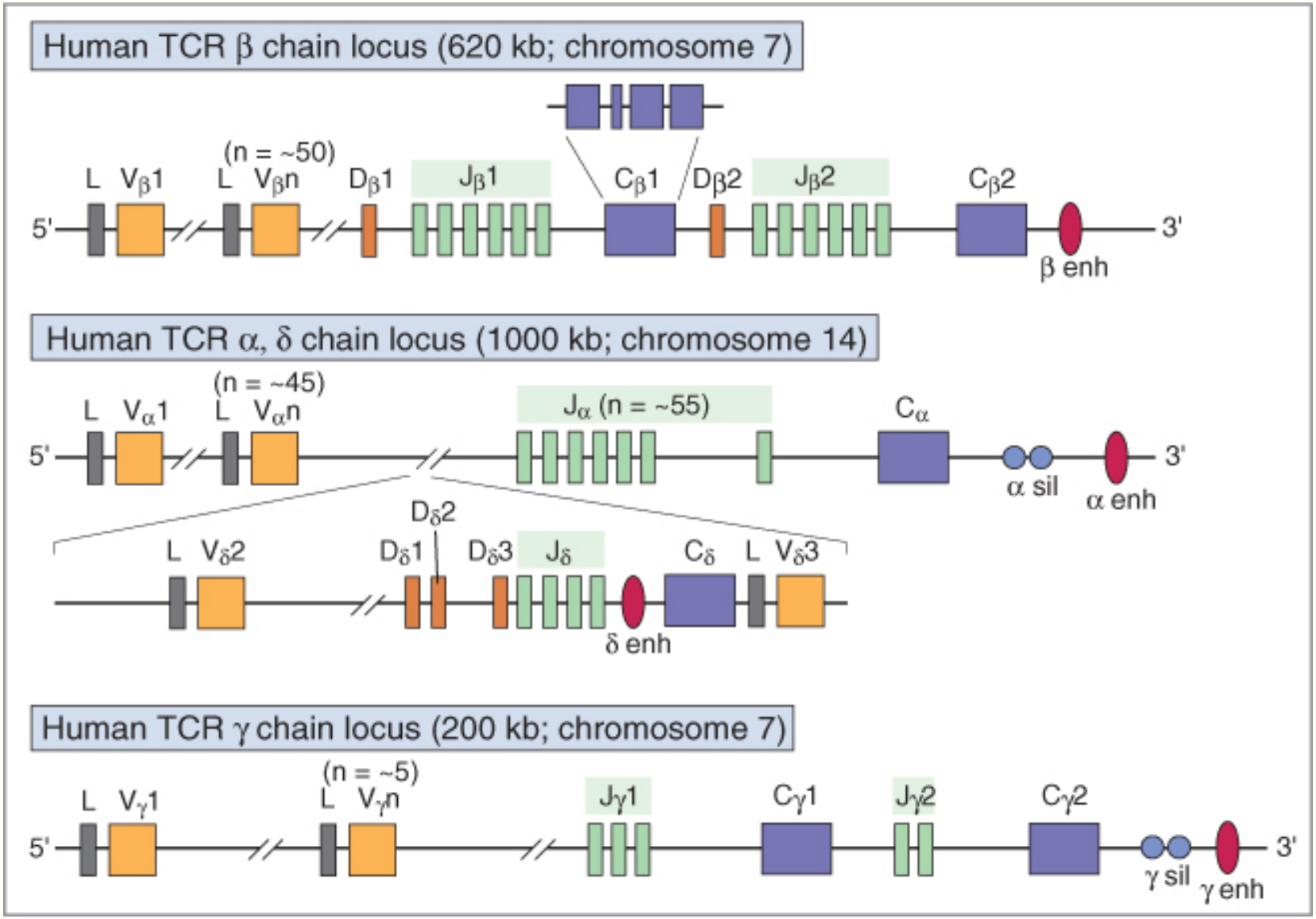
1. αβ
2. γδ



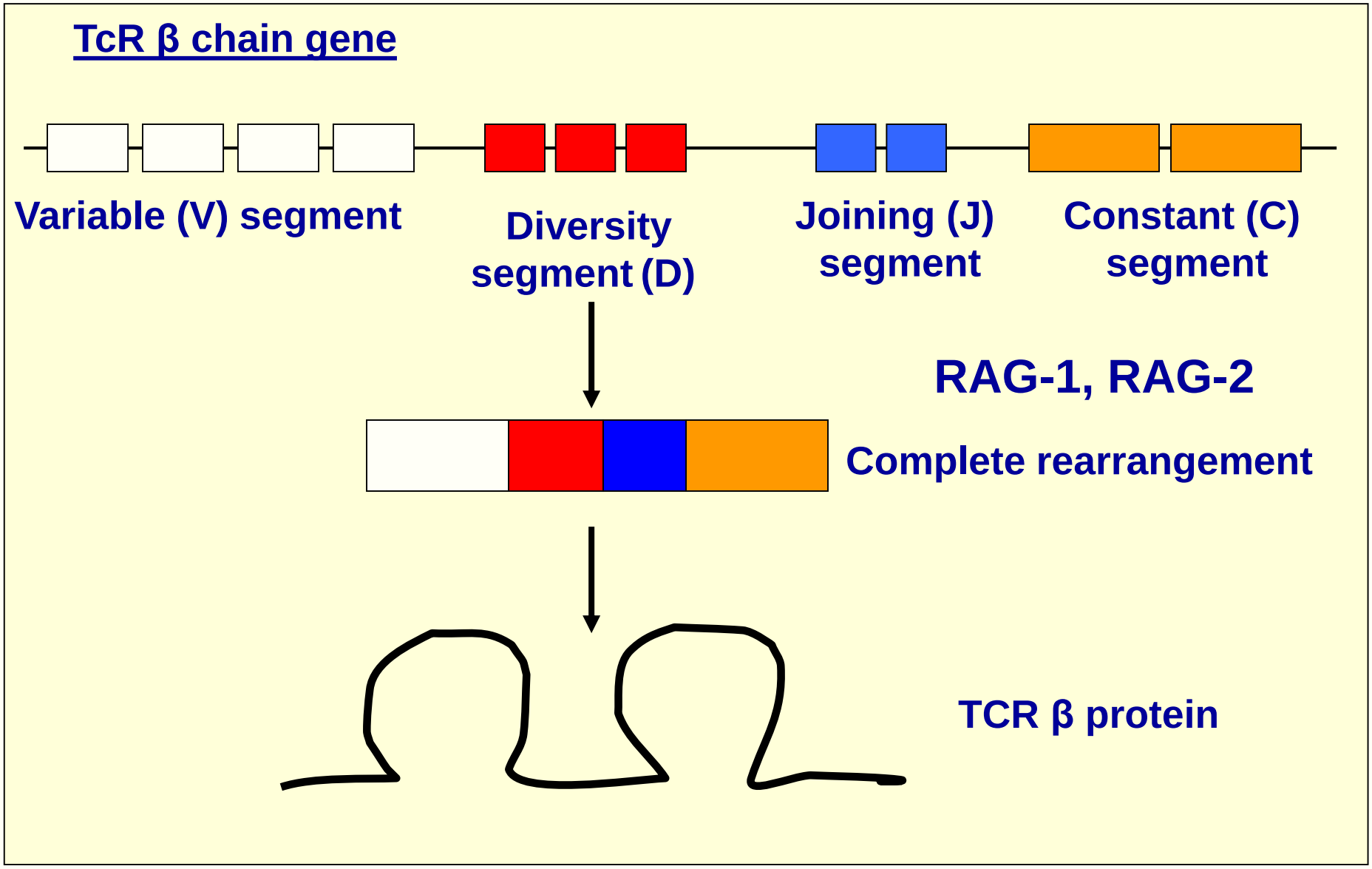
TcR α-β chain structure



TcR-genes

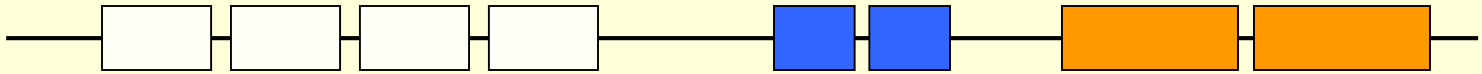


TcR-gene rearrangement I.



TcR gene rearrangement II.

TcR α chain



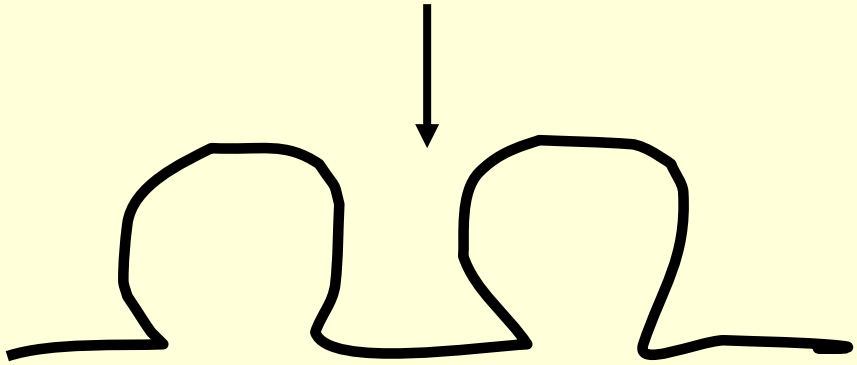
Variable (V) segment

Joining (J) segment

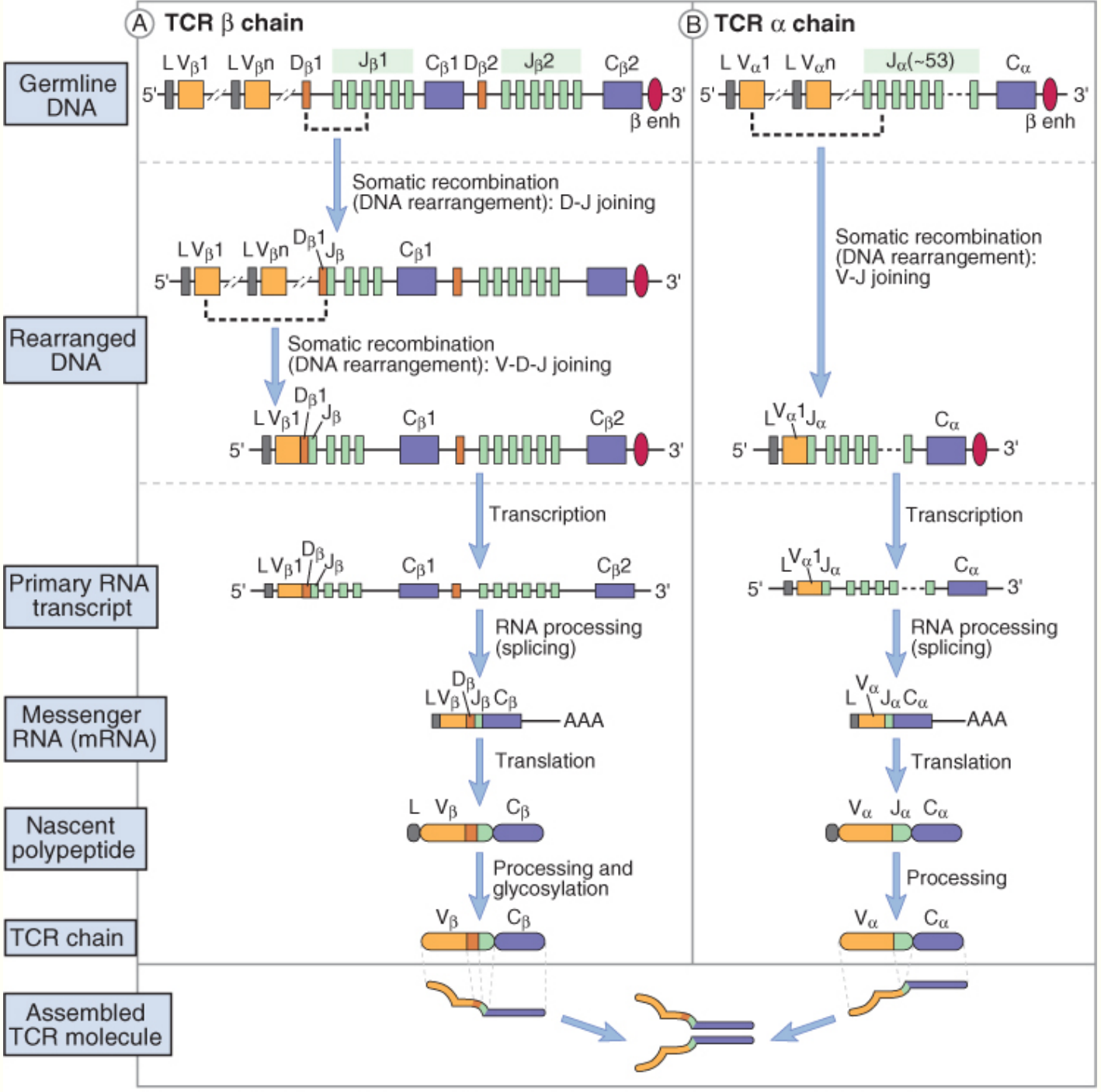
Constant (C) segment

1. β/δ rearrangement
2. α/γ rearrangement

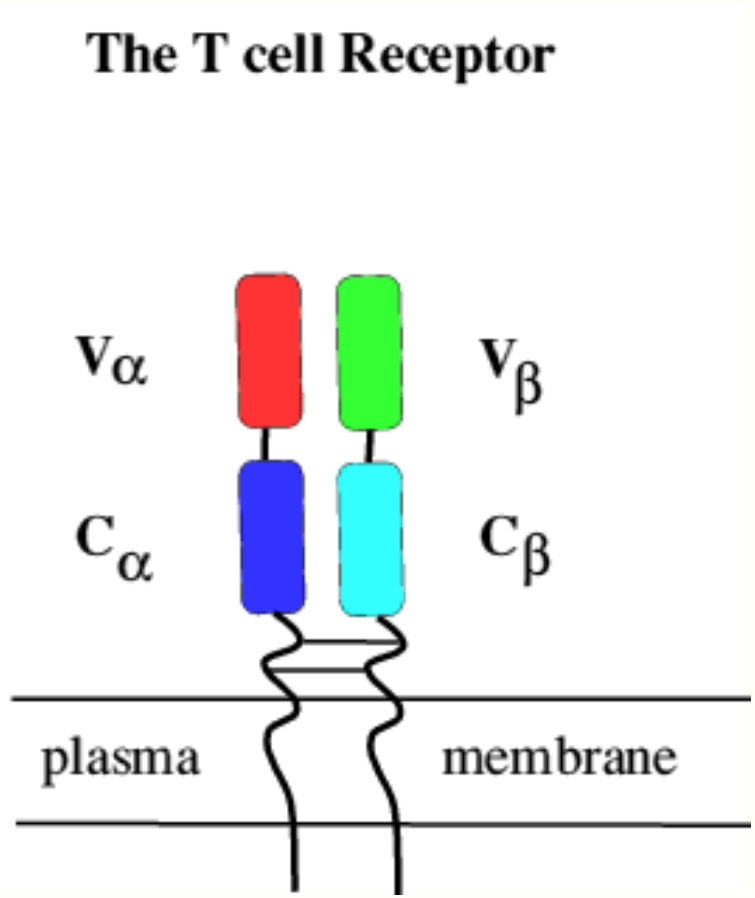
Complete rearrangement

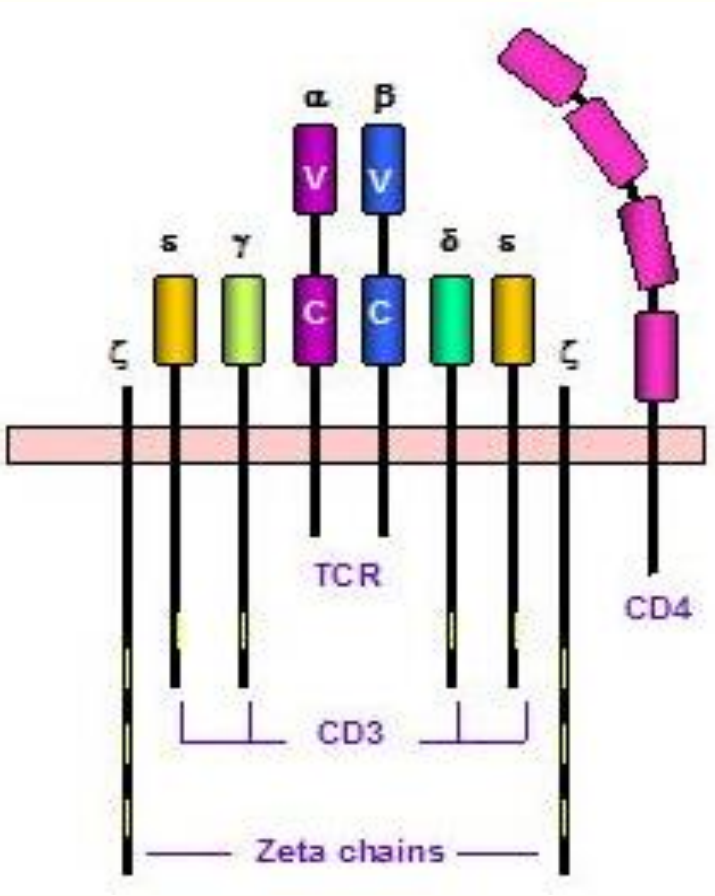


TCR α protein

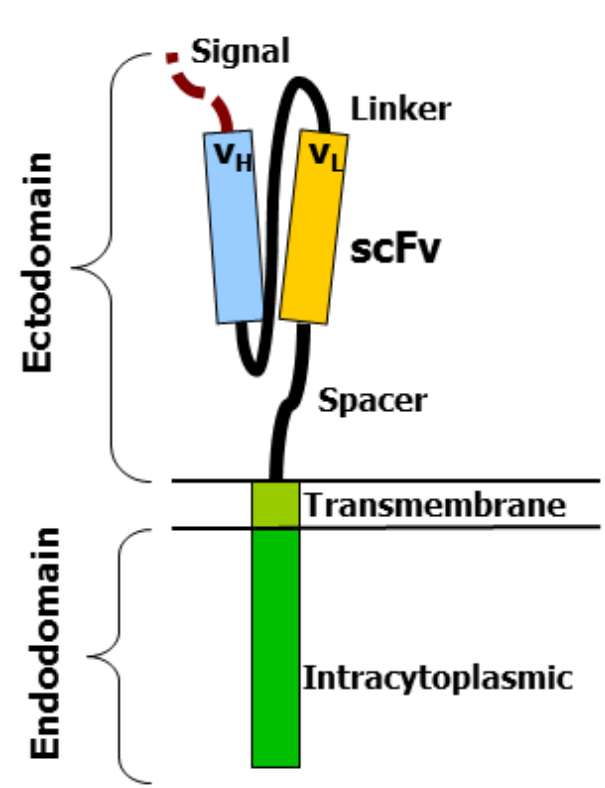


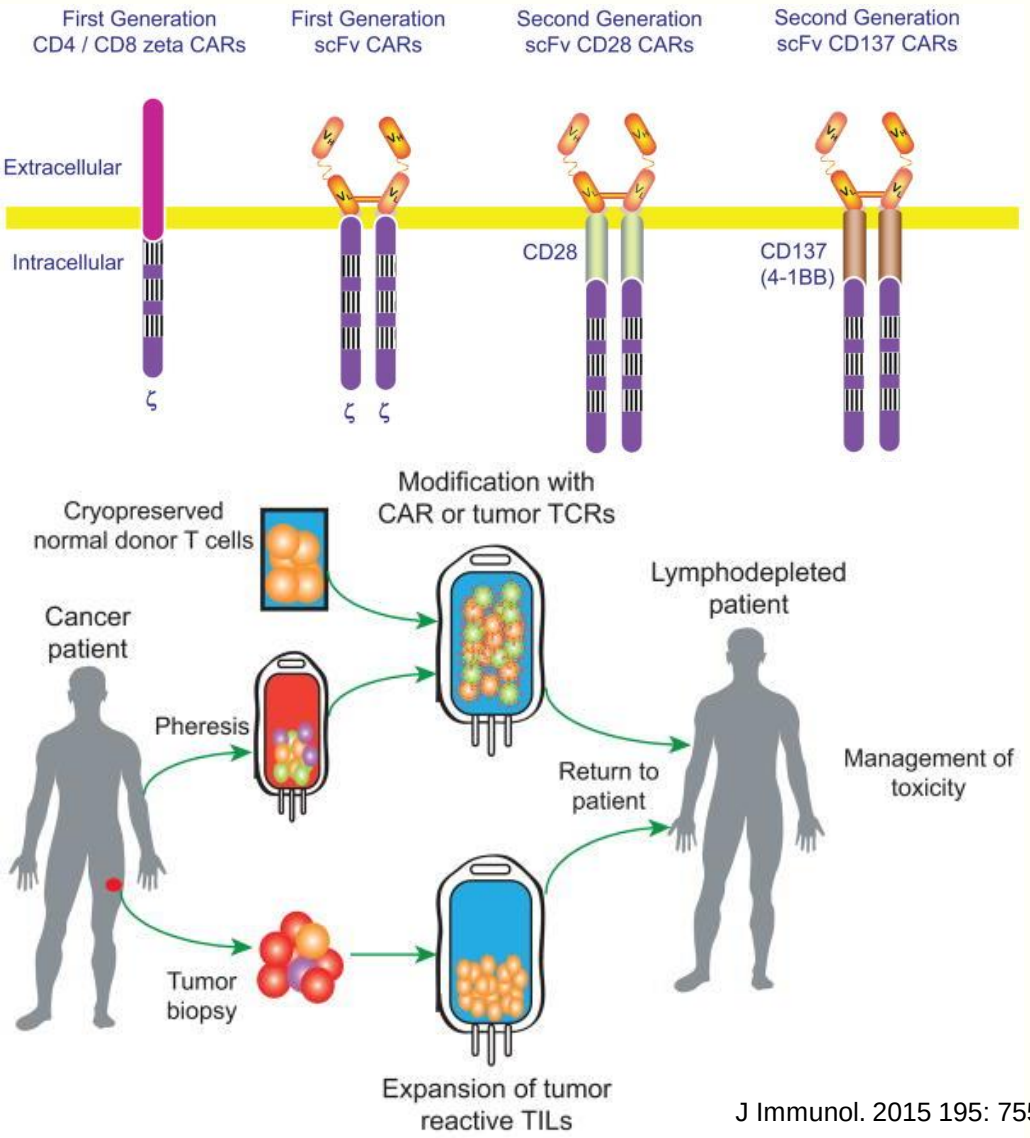
T cell receptor complex (TcR)





Between BcR and TcR – CAR (chimeric antigen receptor)





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Essentials – antigen receptors

Ig and TcR genes couple with different types of antigen recognition processes

both variable and constantregions c

Individual (clonal) & ordered rearrangement:

Intrachain order (D→J; V→DJ) as dictated by RSS/VDJ-recombinase

between receptor components (IgH or TcRβ→IgL or TcRα)

components of diversity: structural (number of V/D/J) and combinatorial (segments and subunits)

Other factors (lineage-independent):

RAG-1/2, TdT

Therapeutic application

CAR T cells combine T-cell signaling with BcR/mAb-like antigen recognition