

Which of the following events occurs first during T and B lymphocyte maturation?

- A) Differentiation into subpopulations
- B) Antigen receptor rearrangement
- C) Commitment to B or T lineage
- D) Negative selection
- E) Positive selection

Answer

- Correct answer: C) Commitment to B or T lineage
- Explanation: Progenitor cells first commit to a lymphoid fate before undergoing receptor rearrangements or selection processes.

Which enzyme complex is directly responsible for initiating V(D)J recombination?

- A) Ku70/80
- B) Artemis
- C) RAG1/RAG2 complex
- D) TdT
- E) DNA ligase IV

Answer

- Correct answer: C) RAG1/RAG2 complex
- Explanation: The RAG1/RAG2 heterodimer is the lymphocyte-specific recombinase that mediates cleavage at recombination signal sequences.

The diversity of antigen receptors is primarily generated through:

- A) Somatic hypermutation
- B) Junctional diversity
- C) Class switch recombination
- D) Affinity maturation
- E) Allelic exclusion

Answer

- Correct answer: B) Junctional diversity
- Explanation: Addition and deletion of nucleotides at V(D)J junctions create immense receptor diversity beyond combinatorial rearrangement.

In the TCR complex, signaling after antigen binding is mediated by:

- A) The α and β chains
- B) CD3 and ζ chains
- C) Co-receptors CD4/CD8 only
- D) ITIM-containing receptors
- E) Cytokine receptors

Answer

- Correct answer: B) CD3 and ζ chains
- Explanation: These non-covalently associated chains contain ITAM motifs essential for signal transduction upon TCR engagement.

Which statement best describes positive selection in the thymus?

- A) Eliminates autoreactive T cells
- B) Selects T cells recognizing self-MHC
- C) Deletes T cells lacking receptors
- D) Occurs in the bone marrow
- E) Promotes NK cell differentiation

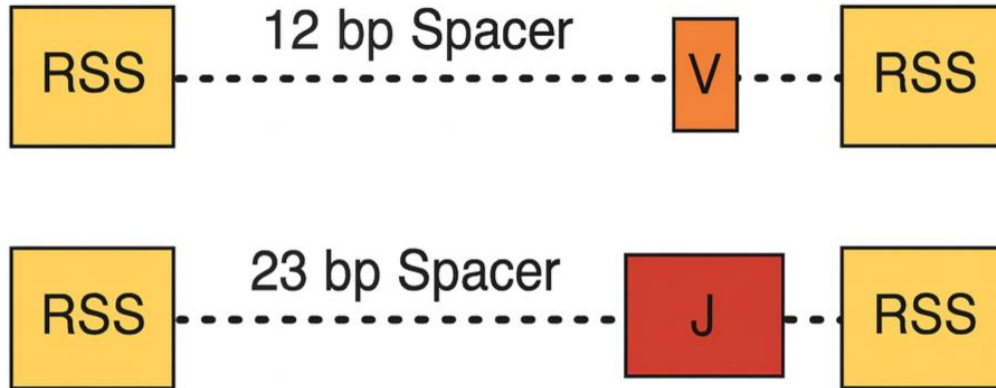
Answer

- Correct answer: B) Selects T cells recognizing self-MHC
- Explanation: Positive selection ensures that only T cells capable of recognizing self-MHC molecules survive.

The 12/23 rule in V(D)J recombination refers to:

- A) The number of exons in the V and J genes
- B) The base-pair length of RSS spacers
- C) The cytokines controlling recombination
- D) The ratio of heavy to light chains
- E) The number of gene loci

Answer



Correct Answer B) The base-pair length of RSS spacers

Explanation: Recombination occurs only between gene segments flanked by 12 bp and 23 bp spacers in RSS sequences.

Which lymphocyte developmental stage expresses a pre-antigen receptor complex?

- A) Stem cell
- B) Pro-B/T cell
- C) Pre-B/T cell
- D) Immature lymphocyte
- E) Mature lymphocyte

Answer

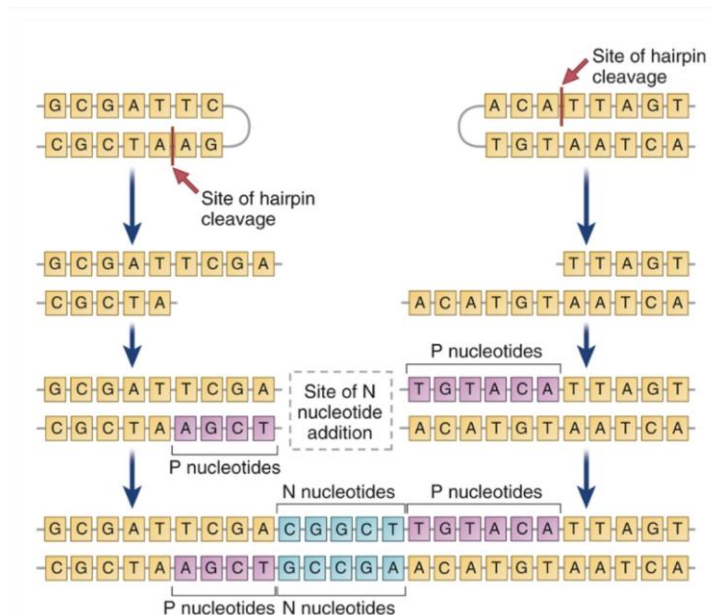
- Correct answer: C) Pre-B/T cell
- Explanation: At this stage, only one chain (heavy or β) is expressed to form a pre-receptor complex, testing successful rearrangement.

What is the main role of TdT during recombination?

- A) Cut DNA at RSS sites
- B) Ligate DNA ends
- C) Add non-templated nucleotides
- D) Repair double-strand breaks
- E) Open chromatin

Answer

- Correct answer: C) Add non-templated nucleotides
- Explanation: TdT adds random nucleotides to junctions, creating N-region diversity crucial for receptor variability.



CD8 co-receptor binds to:

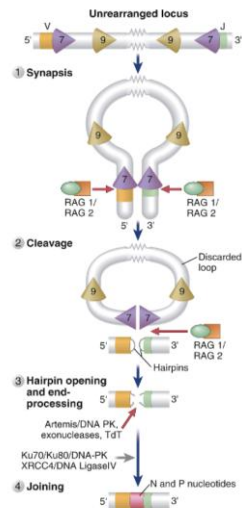
- A) MHC class II β 2 domain
- B) MHC class I α 3 domain and β 2-microglobulin
- C) Peptide antigen directly
- D) TCR β chain
- E) CD3 ζ chain

Which of the following enzymes opens DNA hairpins formed during recombination?

- A) RAG1
- B) Artemis
- C) Ku70
- D) DNA ligase IV
- E) TdT

Answer

- Correct answer: B) Artemis
- Explanation: Artemis endonuclease opens hairpin loops, enabling junctional diversity by modifying coding ends.



Enzymes involved in recombination

- V(D)J recombinase = RAG1/RAG2 heterodimeric complex that orchestrates the V(D)J recombination
- RAG-1, RAG-2 = *lymphocyte-specific* enzymes (only expressed in developing lymphocytes)
- Ku70/80, DNA-PK (DNA-dependent protein kinase), Artemis (nuclease), DNA ligase IV, XRCC4, DNA pol μ = *DNA-modifying* enzymes

Which process ensures that each lymphocyte expresses only one receptor specificity?

- A) Allelic exclusion
- B) Junctional diversity
- C) Isotype switching
- D) Receptor editing
- E) Class switching

Answer

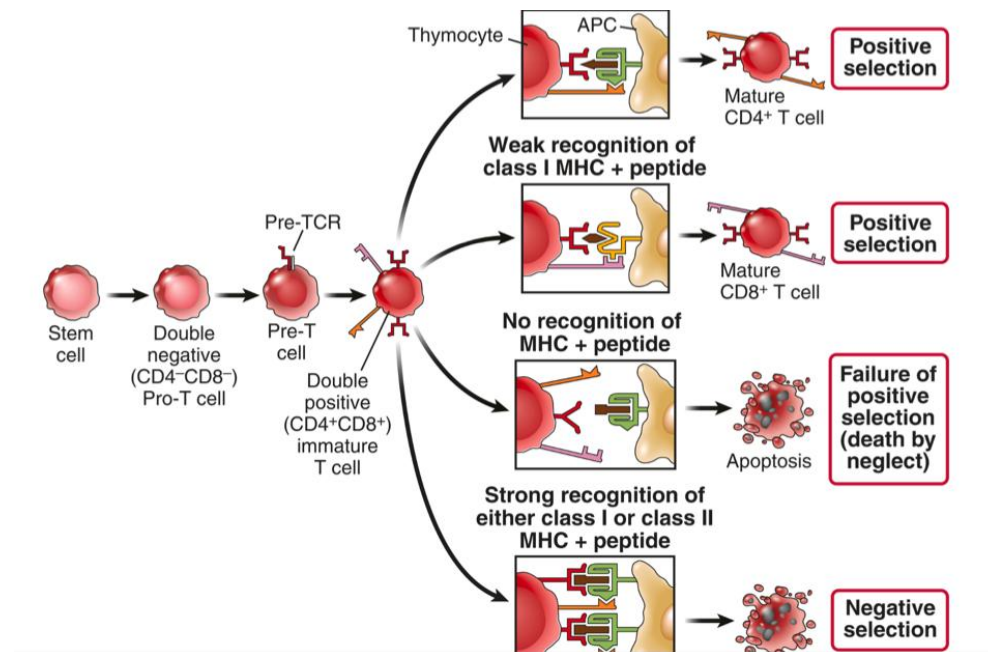
- Correct answer: A) Allelic exclusion
- Explanation: The pre-TCR complex delivers intracellular signals once it is assembled, similar to the signals from the pre-BCR complex in developing B cells. These signals promote survival, proliferation, and TCR α gene recombination and inhibit VDJ recombination in the second β chain locus (allelic exclusion).

Where does T cell positive selection occur?

- A) Bone marrow
- B) Thymic cortex
- C) Thymic medulla
- D) Lymph node
- E) Spleen

Answer

- Correct answer: B) Thymic cortex
- Explanation: Positive selection occurs in the thymic cortex, mediated by cortical epithelial cells presenting self-MHC.



What is the function of LFA-1 in the immunological synapse?

- A) Kinase recruitment
- B) Cytokine secretion
- C) Adhesion and cytoskeletal linkage
- D) Peptide presentation
- E) Signal amplification

Answer

- Correct answer: C) Adhesion and cytoskeletal linkage
- Explanation: LFA-1 binds to ICAM and connects to talin to stabilize the T cell–APC interaction.

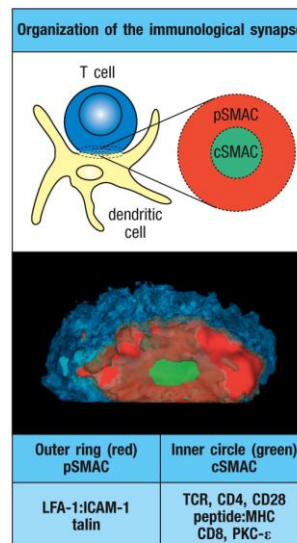


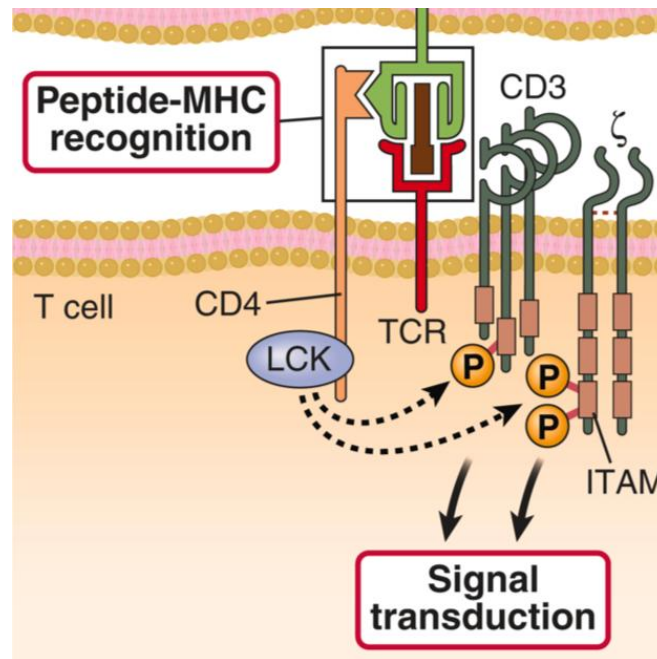
Figure 9.37 Janeway's Immunobiology, 9th ed. (© Garland Science 2017)

Which molecule phosphorylates ITAM motifs upon TCR activation?

- A) ZAP-70
- B) LCK
- C) FYN
- D) CD3 γ
- E) PKC

Answer

- Correct answer: B) LCK
- Explanation: LCK, associated with CD4/CD8, phosphorylates ITAMs on CD3 and ζ chains to initiate signaling.



Which component defines the cSMAC region of the immunological synapse?

- A) LFA-1/talin
- B) TCR and signaling molecules
- C) Actin filaments
- D) Cytokines
- E) Adhesion molecules

Answer

- Correct answer: B) TCR and signaling molecules
- Explanation: The central SMAC (cSMAC) concentrates TCR complexes and signaling components.

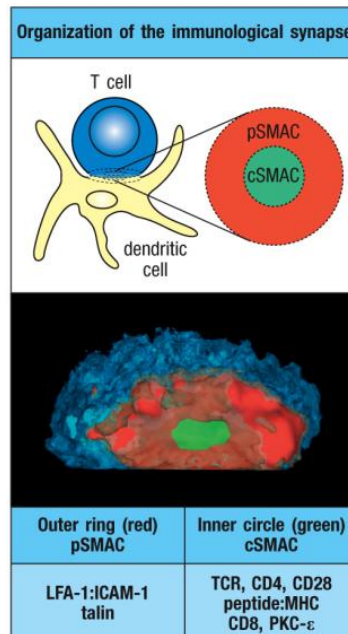


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The $\alpha\beta$ TCR complex differs from $\gamma\delta$ TCR mainly in:

- A) Location of expression
- B) Association with CD3
- C) MHC restriction
- D) Presence of ITAMs
- E) Signal transduction mechanisms

Answer

- Correct answer: C) MHC restriction
- Explanation: $\alpha\beta$ T cells recognize peptide–MHC complexes, whereas $\gamma\delta$ T cells are generally MHC-independent.

Where do hematopoietic stem cells (HSCs) reside?

- A. Thymus
- B. Spleen
- C. Fetal liver and bone marrow
- D. Lymph nodes

Answer & Explanation

Correct Answer: C. Fetal liver and bone marrow

HSCs originate in the fetal liver and later reside in the bone marrow, where they generate all blood lineages.

What is the main consequence of X-linked severe combined immunodeficiency (SCID)?

- A. Impaired T and NK cell development
- B. Defective antigen presentation
- C. Overproduction of antibodies
- D. Increased MHC expression

Answer & Explanation

Correct Answer: A. Impaired T and NK cell development

Caused by a mutation in the common γ chain shared by the receptors for IL-2, IL-7, and IL-15, leading to defective signaling and failed maturation of T and NK cells.

What are the main checkpoints during lymphocyte development?

- A. Random elimination and cytokine release
- B. Pre-antigen receptor expression and complete receptor expression followed by positive/negative selection
- C. MHC expression and antibody secretion
- D. Cell migration and apoptosis

Answer & Explanation

Correct Answer: B. Pre-antigen receptor expression and complete receptor expression followed by positive/negative selection

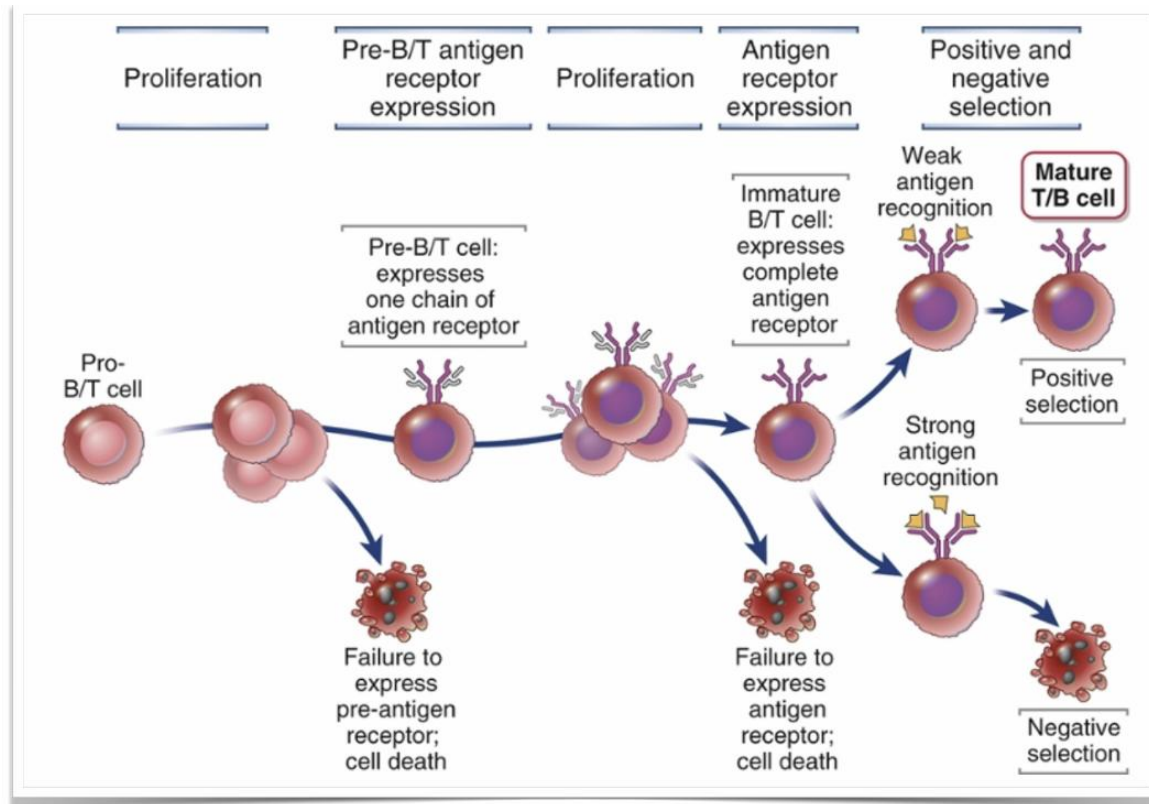
These checkpoints ensure that developing B and T cells express functional antigen receptors and that self-reactive clones are deleted or edited..

Correct order of key events in B/T cell development:

- A. Pre-B/T receptor expression → positive and negative selection → proliferation → antigen receptor expression
- B. Proliferation → pre-B/T receptor expression → proliferation → antigen receptor expression → positive and negative selection
- C. Antigen receptor expression → pre-B/T receptor expression → positive and negative selection → proliferation
- D. Proliferation → antigen receptor expression → allelic exclusion → selection → recombination

Answer & Explanation

Correct Answer: B.



What is gene rearrangement in lymphocytes?

- A. Post-translational modification
- B. Chromosomal translocation
- C. Somatic recombination of V(D)J segments
- D. RNA splicing of cytokine genes

Answer & Explanation

Correct Answer: C . Somatic recombination of V(D)J segments

Gene rearrangement is a DNA-level process that joins variable (V), diversity (D), and joining (J) gene segments to form a functional antigen receptor gene. This mechanism occurs only in developing B and T cells and generates the enormous diversity of antibodies and TCRs before antigen exposure.

Which are the three immunoglobulin gene loci?

- A. Heavy, κ , and λ chains
- B. α , β , and γ chains
- C. CD4, CD8, and CD3
- D. Light, heavy, and δ chains

Answer & Explanation

Correct Answer: A. Heavy, κ , and λ chains

Immunoglobulin genes are organized into three separate loci: one for the heavy chain and two for the light chains (κ and λ), each located on different chromosomes. These loci undergo independent V(D)J recombination to generate diverse antibody molecules with unique antigen-binding sites.

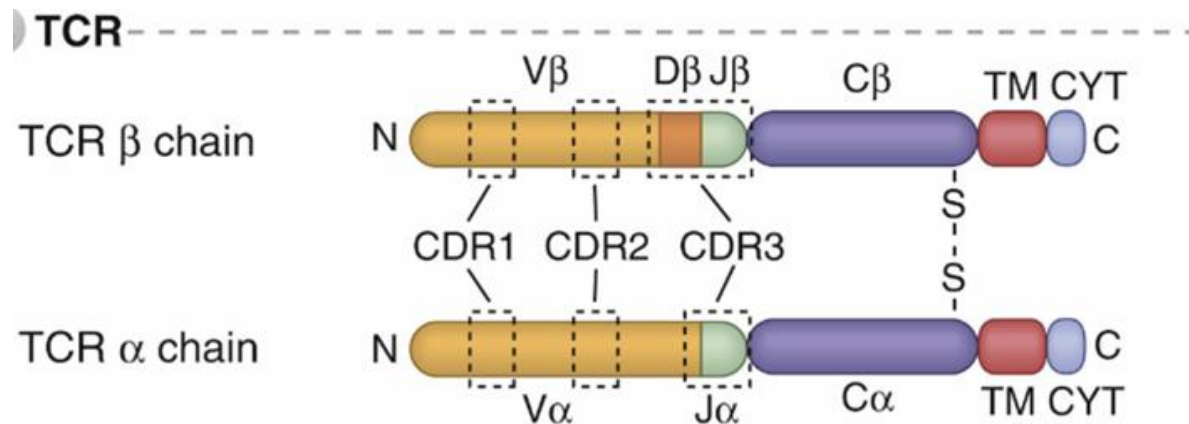
Which domains does the T cell receptor (TCR) have?

- A. One α and one β chain, each with variable and constant domains
- B. Three γ chains
- C. Two heavy chains only
- D. Only cytoplasmic domains

Answer & Explanation

Correct Answer: A. One α and one β chain, each with variable and constant domains

TCR is a heterodimer composed of two transmembrane polypeptide chains an α chain and a β chain. Each chain contains one variable (V) domain that binds antigen–MHC complexes and one constant (C) domain that maintains structural stability.



Correct sequence of V(D)J rearrangement steps:

- A. Gene expression → DNA cleavage → hairpin opening → ligation
- B. Chromatin opening → gene segments brought together → DNA double-strand break → nucleotide modification → ligation
- C. Chromatin condensation → DNA cleavage → transcription → nucleotide addition
- D. Chromatin opening → transcription → translation → recombination

Answer & Explanation

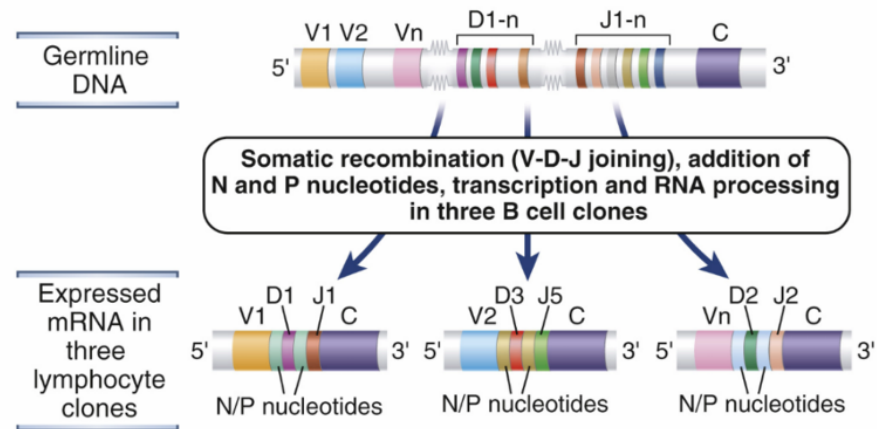
Correct Answer: B.

V(D)J rearrangement

Functional antigen receptor genes are only generated in developing lymphocytes.

Steps needed to generate a function AR gene:

- 1) Opening of chromatin
- 2) Gene segments are brought together
- 3) DS DNA break
- 4) Addition/deletion of nucleotides at the break
- 5) Ligation
- 6) RNA splicing



Tremendous diversity arising from:

- Different *combination*
- addition/removal *nucleotides* at junctions

Combinatorial diversity arises from:

- A. Addition and deletion of nucleotides at coding junctions by TdT and Artemis
- B. Somatic hypermutation in variable regions after antigen exposure
- C. Differential RNA splicing of constant region exons into mature mRNA
- D. Random pairing of variable (V), diversity (D), and joining (J) gene segments within and between heavy/light or α/β chains

Answer & Explanation

Correct Answer: D. Random pairing of variable (V), diversity (D), and joining (J) gene segments within and between heavy/light or α/β chains

Combinatorial diversity results from the vast number of possible combinations of V, D, and J segments and from the pairing of different heavy/light or α/β chains, before antigen exposure.

What is junctional diversity caused by?

- A. Random addition or deletion of nucleotides
- B. Rearrangement of whole chromosomes
- C. Alternative splicing
- D. Cytokine binding

Answer & Explanation

Correct Answer: : A. Random addition or deletion of nucleotides

Mediated by TdT and Artemis, this generates maximal variability at V–J and V–D junctions.

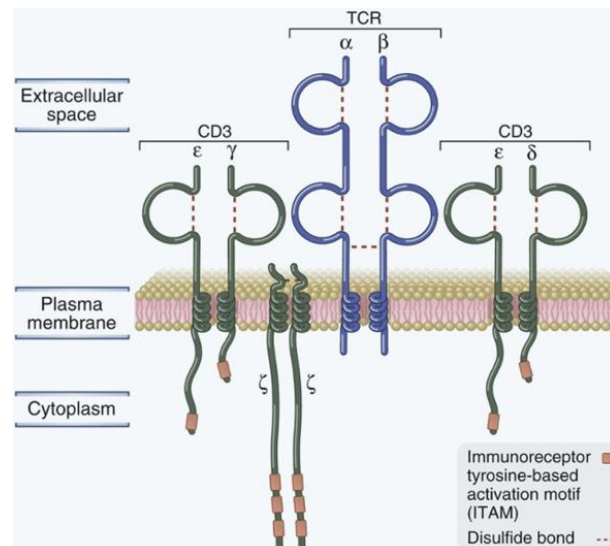
The TCR complex structure includes:

- A. TCR $\alpha\beta$ + CD3 + ζ chain
- B. Ig α + Ig β
- C. TCR $\gamma\delta$ + CD19
- D. Only TCR $\alpha\beta$

Answer & Explanation

Correct Answer: A. TCR $\alpha\beta$ + CD3 + ζ chain

The T cell receptor (TCR) complex is composed of the antigen-recognizing α and β chains, associated non-covalently with CD3 proteins and the ζ (zeta) chain. CD3 and ζ contain ITAM motifs that transduce intracellular signals when the TCR binds to peptide–MHC complexes.



Which of the following are T cell co-receptors?

- A. CD19 and CD21
- B. B7 and CD40
- C. ICAM and LFA
- D. CD4 and CD8

Answer & Explanation

Correct Answer: D. CD4 and CD8

CD4 is a transmembrane protein that recognizes non-polymorphic regions on MHC class II molecules, existing as a monomer with extracellular Ig domains.

CD8 is a heterodimer that binds to constant regions of MHC class I molecules and $\beta 2$ microglobulin.

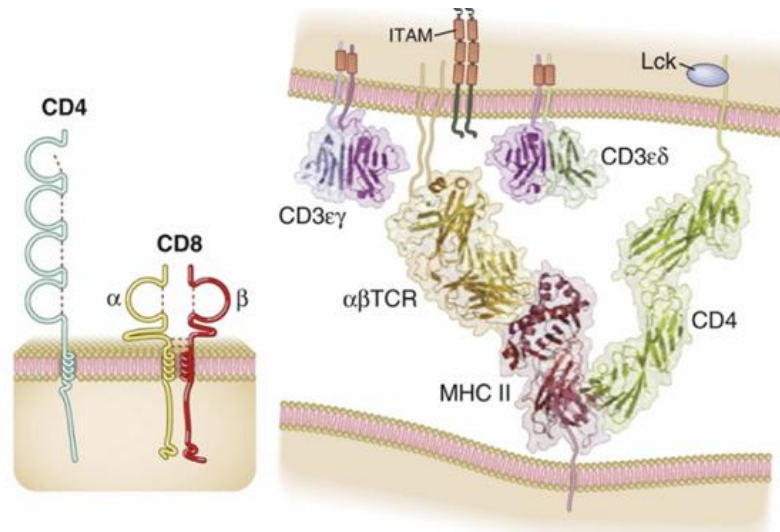
Function of CD4 and CD8 co-receptors:

- A. Bind MHC and bring LCK to TCR complex
- B. Activate macrophages directly
- C. Produce antibodies
- D. Degrade antigen

Answer & Explanation

Correct Answer: A. Bind MHC and bring LCK to TCR complex

Caused the co-receptors are constitutively associated with a signalling kinase (LCK). Upon binding to MHC molecules, the coreceptors are brought into close proximity of the TCR complex and the associated kinase can phosphorylate the ITAM regions and, thus, initiate downstream signalling



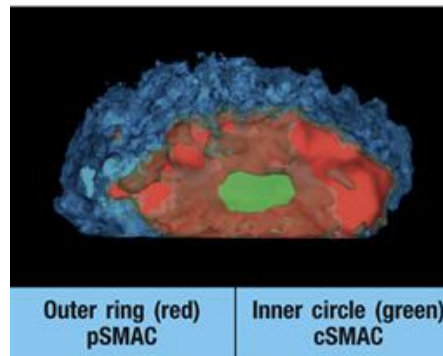
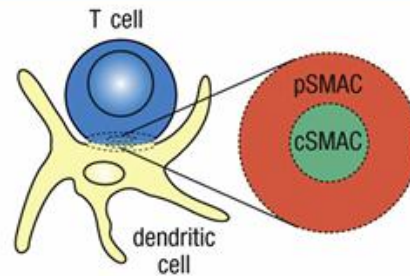
What happens to the cytoskeleton at the immunological synapse?

- A. It disassembles
- B. It polarizes and reorients to direct secretion
- C. It is degraded
- D. It remains static

Answer & Explanation

Correct Answer: B. It polarizes and reorients to direct secretion

Organization of the immunological synapse



During synapse formation:

- A. LFA-1/talin form tight seals in the peripheral zone
- B. CD3 moves to pSMAC
- C. Cytokines bind outside SMAC
- D. Antigens diffuse away

Answer & Explanation

Correct Answer: A. LFA-1/talin form tight seals in the peripheral zone

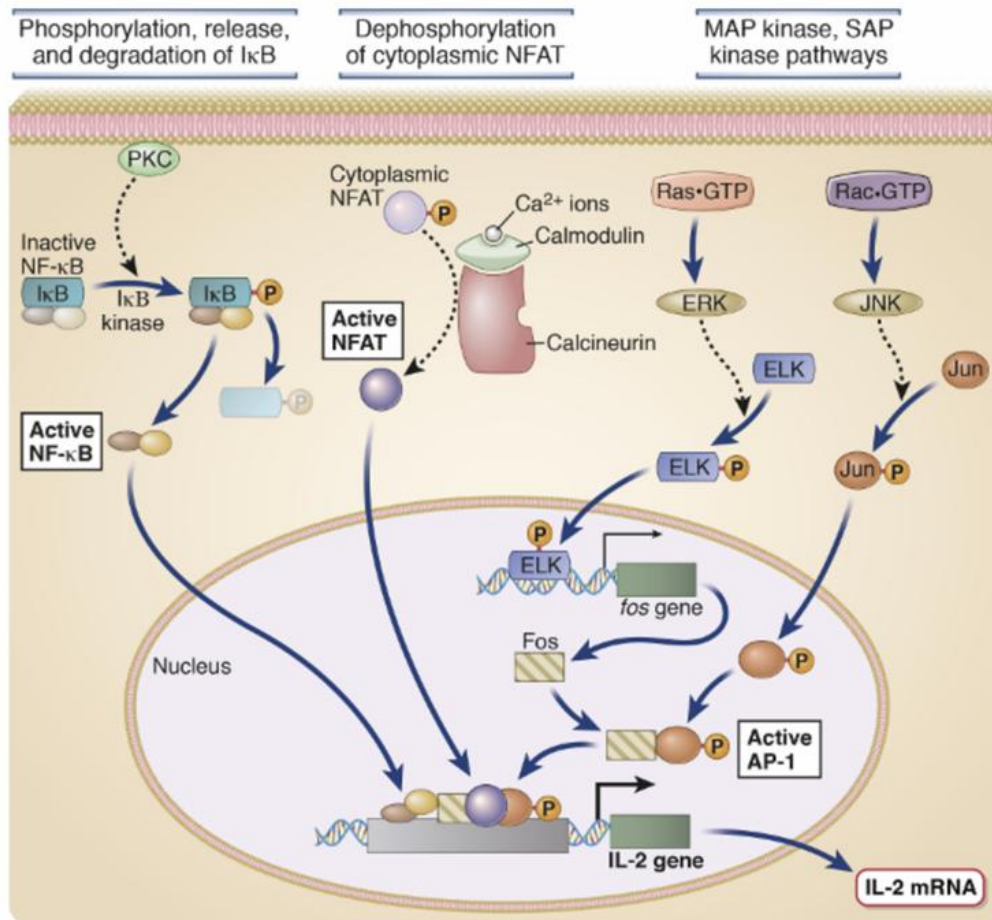
LFA-1 (on the T cell) and talin (on the APC) interact to form a tight adhesion in the peripheral zone of the immunological synapse, stabilizing the T cell-APC contact for effective signaling.

Final key cytokine induced by TCR signaling:

- A. IL-10
- B. IL-17
- C. IFN- γ
- D. IL-2

Answer & Explanation

Correct Answer: D. IL-2



Structure of the BCR complex:

- A. Membrane-bound IgG associated with CD3 and ζ chains
- B. Cytoplasmic IgM associated with Fc γ RIIB inhibitory receptor
- C. Membrane-bound IgM/IgD associated with Ig α and Ig β signaling chains
- D. Secreted IgM coupled with CD19 and CD21 co-receptors

Answer & Explanation

Correct Answer: C. Membrane-bound IgM/IgD associated with Ig α and Ig β signaling chains

The BCR of naïve B cells is a membrane-bound immunoglobulin (IgM or IgD) that binds antigen and signals through the associated Ig α /Ig β heterodimer containing ITAM motifs.

Why does a B cell require multiple antigen molecules for activation?

- A. To bind both chains
- B. To activate macrophages
- C. To crosslink multiple BCRs and trigger signaling
- D. To switch isotype

Answer & Explanation

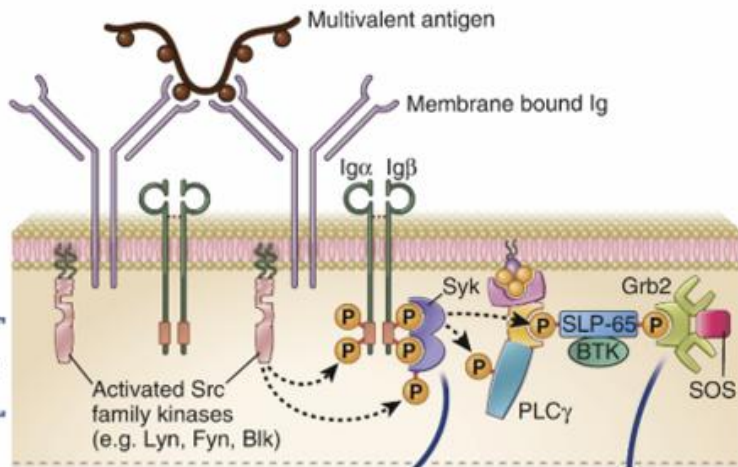
Correct Answer: C. To crosslink multiple BCRs and trigger signaling

B cell activation requires antigen-mediated crosslinking of several B cell receptors (BCRs), which brings together the $Ig\alpha/Ig\beta$ signaling subunits and initiates phosphorylation of ITAM motifs. This clustering is essential to reach the activation threshold for downstream signaling.

Initiation of signal transduction

Activation of multivalent antigens

Cross-linking of membrane Ig by antigen

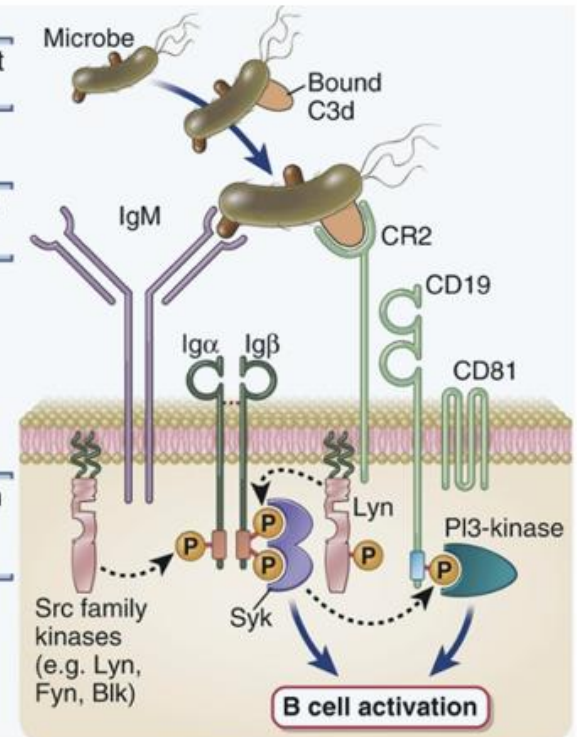


Activation of antigens and co-factors

Complement activation

Recognition by B cells

Signals from Ig and CR2 complex



Which transcription factor is activated downstream of calcineurin?

- A) NF- κ B
- B) NFAT
- C) AP-1
- D) STAT5
- E) CREB

Answer

- Correct answer: B) NFAT
- Explanation: Calcineurin dephosphorylates NFAT, allowing its nuclear translocation and activation of IL-2 gene expression.

