T-cell precursors travel from the bone marrow to develop in the thymus

Mature T cells leave the thymus and travel to secondary lymphoid tissues

Figure 7.1 The Immune System, 3ed. (© Garland Science 2009)
Figure 7.2 The Immune System, Jed. (© Garland Science 2009)
Figure 7.4 The Immune System, 3ed. (© Garland Science 2009)
Flow cytometry of thymocytes
A common double-negative T-cell progenitor gives rise to α:β and γ:δ T cells

Figure 7.7 The Immune System, 3ed. (© Garland Science 2009)
Double-negative T cells start to rearrange their $\beta$, $\gamma$, and $\delta$ loci

$\gamma$- and $\delta$-chain genes rearrange. A $\gamma$:8 receptor assembles. Signals through $\gamma$:8 TCR stop further rearrangements and commit cell to $\gamma$:8 lineage

$\beta$-chain gene rearranges. A pre-TCR assembles. Signals through pre-TCR stop rearrangement, and induce proliferation and expression of CD4 and CD8

The $\gamma$:8 T cell matures, leaves the thymus and migrates to peripheral tissues

Pre-T cell resumes rearrangement of $\alpha$, $\gamma$, and $\delta$ genes

Figure 7.9 The Immune System, 3rd ed. (© Garland Science 2009)
Two attempts can be made to achieve a productive rearrangement of the β-chain locus

Unproductive rearrangement to C1

Productive rearrangement to C2

Transcription of functional β-chain mRNA

Synthesis of T-cell receptor β chain

Figure 7.11 The Immune System, 3ed. (© Garland Science 2009)
The \( \alpha \)-chain locus can sustain many attempts at a functional rearrangement

First unproductive rearrangement

Second unproductive rearrangement

Third rearrangement is productive

Transcription of functional \( \alpha \)-chain mRNA

Synthesis of T-cell receptor \( \alpha \)-chain

Figure 7.12 The Immune System, 3ed. (© Garland Science 2009)
Figure 7.10 The Immune System, 3ed. (© Garland Science 2009)
### Rearrangement

<table>
<thead>
<tr>
<th>Surface Molecule</th>
<th>Function</th>
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<tr>
<td>Kit</td>
<td>Signaling</td>
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<tr>
<td>Notch</td>
<td>Signaling</td>
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<tr>
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<td>IL-2 receptor</td>
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<tr>
<td>CD4, CD8</td>
<td>Co-receptor</td>
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<td>RAG-1</td>
<td>Lymphoid-specific recombinase</td>
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<td>RAG-2</td>
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<td>N-nucleotide addition</td>
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<td>Surrogate α chain</td>
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<tr>
<td>ZAP-70</td>
<td>Signal transduction</td>
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<td>GATA-3</td>
<td>Transcription factor</td>
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<td>Th-Pok</td>
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</tr>
</tbody>
</table>

### Double-negative

- Committed T-cell progenitor
- Re-arranges β, γ, δ
- First checkpoint
- Proliferating pre-T cells

### Double-positive

- Re-arranges α, γ, δ
- Second checkpoint
- CD8
- TCR
The early development of α:β T cells in the thymus

- **Checkpoint for pre-TCR**
- **Checkpoint for TCR**
- **Rearrange β genes**
- **Rearrange α genes**
- **Double-negative pre-T cells**
- **Immature double-positive cells**
- **Proliferating double-negative pre-T cells**
- **Double-negative T cells commit to T lineage**
- **Proliferation**
- **Venule**
- **Progenitor cells**

Figure 7.15 The Immune System, 3ed. (© Garland Science 2009)
Figure 5.22 The Immune System, 3ed. (© Garland Science 2009)
Positive selection of $\alpha:\beta$ T cells by cortical epithelial cells in the thymus

- Weak or no binding: TCR on thymocyte dies
- Moderate or strong binding: TCR on thymocyte lives

TCR: T-cell receptor
MHC: Major Histocompatibility Complex

Figure 7.16 The Immune System, 3rd ed. (© Garland Science 2009)
Double-positive thymocytes

Receptor binds self-peptide:self-MHC class I

[Diagram showing receptor binding and cell interaction]

Receptor binds self-peptide:self-MHC class II

[Diagram showing receptor binding and cell interaction]

Single-positive thymocytes

CD8 T cell

[Diagram showing CD8 T cell with TCR and CD8]

CD4 T cell

[Diagram showing CD4 T cell with TCR and CD4]

Figure 7.17 The Immune System, 3ed. (© Garland Science 2009)