

Exercise walk-through

7.6

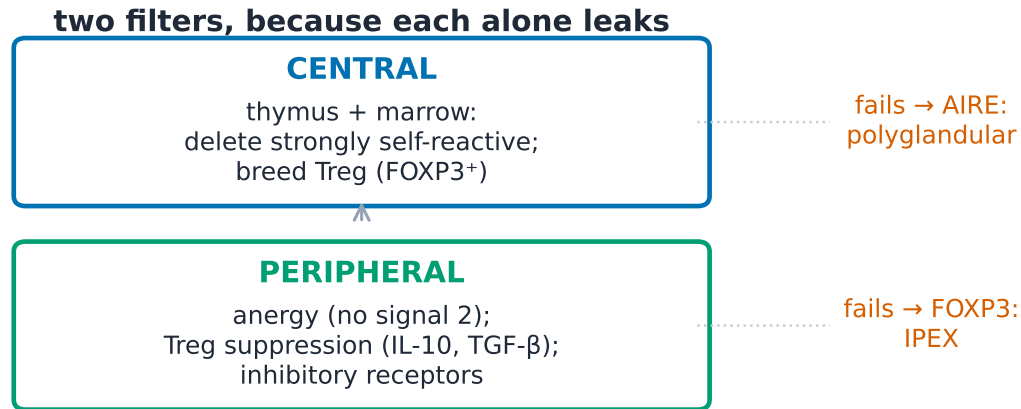
Autoimmunity and tolerance

University Medicine

Autoimmunity: two filters

- 1 **Central** Thymus/marrow delete strongly self-reactive cells and breed Treg (FOXP3⁺) - AIRE failure names polyglandular disease.
- 2 **Peripheral** Anergy (no signal 2), Treg suppression (IL-10/TGF- β) - FOXP3 failure names IPEX.
- 3 **Balance** Twin concordance 30–50% (T1D): HLA loads, environment and chance pull; mimicry (rheumatic fever) turns anti-strep onto the heart.

Autoimmunity - figure



Central and peripheral checkpoints with failure genes.

Exercises 2.1-2.3

2.1 Where does central tolerance act?

[3]

2.2 Name the Treg master gene.

[3]

2.3 What triggers molecular mimicry in rheumatic fever?

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2.1 Where does central tolerance act? [3]

2.1

- Thymus and marrow.

2.2 Name the Treg master gene. [3]

2.2

- FOXP3 ✓.

2.3 What triggers molecular mimicry in rheumatic fever? [3]

2.3

- Streptococcal infection (antibodies cross-reacting with heart and joint).

Exercise 3.1

3.1 A 4-year-old has chronic eczema, diarrhoea and early-onset diabetes (fictional IPEX picture).

Name the failed checkpoint (FOXP3 → Treg). Explain why SKIN and GUT bear the brunt (barrier surfaces need active suppression). State the inheritance and the treatment direction. [7]

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3.1

- FOXP3 failure: no functional Treg – the peripheral filter is gone.
- Barrier surfaces (skin, gut) host abundant self-reactive and commensal-reactive clones held by active suppression: they fail first ✓.
- X-linked; treatment direction = immune suppression $\pm$ bone-marrow transplant (restores Treg lineage).

Exercise 3.2

3.2 A healthy 24-year-old woman is found ANA-positive at low titer on a screening panel (fictional).

Interpret the finding (5–15 % healthy prevalence). State what would raise suspicion (high titer, specific patterns – dsDNA, anti-Sm). Explain the twin logic (30–50 % concordance) for why HLA typing is probabilistic, not deterministic. [7]

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- Low-positive ANA: 5–15 % of healthy adults – not diagnostic ✓.
- Suspicion: high titer + patterns (anti-dsDNA, anti-Sm for SLE, with corresponding clinical criteria).
- 30–50 % identical-twin concordance: HLA sets thresholds; the trigger is environmental/stochastic ✓.