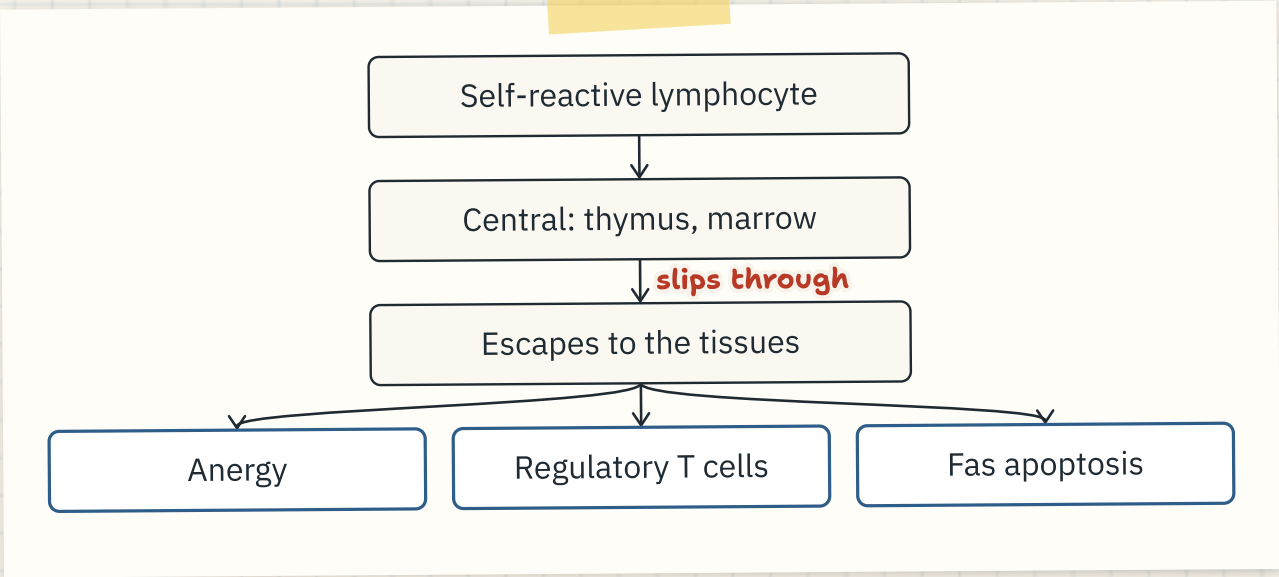
Central vs peripheral tolerance

Where self-reactive cells are removed, and what breaks



Step by step

1. Cortex: no self MHC recognition, death by neglect
2. Medulla: binds self too strongly, apoptosis
3. AIRE shows organ proteins (e.g. insulin) in the medulla
4. Periphery: anergy, regulatory T cells, Fas

Gene	Fails	Disease
AIRE	Negative selection (thymus)	APECED (APS-1)
FOXP3	Regulatory T cells	IPEX (X-linked)
Fas	Apoptosis of activated cells	ALPS

One gene, one failed checkpoint, one disease

Keep three things

Central: delete in the thymus, helped by AIRE

Peripheral: anergy, regulatory T cells, Fas

AIRE: APECED; FOXP3: IPEX; Fas: ALPS

Exam traps

- Failed positive selection is immunodeficiency, not autoimmunity.
- Less co-stimulation favours anergy; it does not prevent it.
- APECED is not X-linked; IPEX is X-linked.

Central vs peripheral tolerance: how lymphocytes learn self-tolerance

Video, written lesson, practice question and sources: medservatory.com/usmle-step-1/immunology/central-vs-peripheral-tolerance-thymic-selection-aire-tregs-fas

For exam study only, not medical advice. Follow local guidelines and your lab's ranges.
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