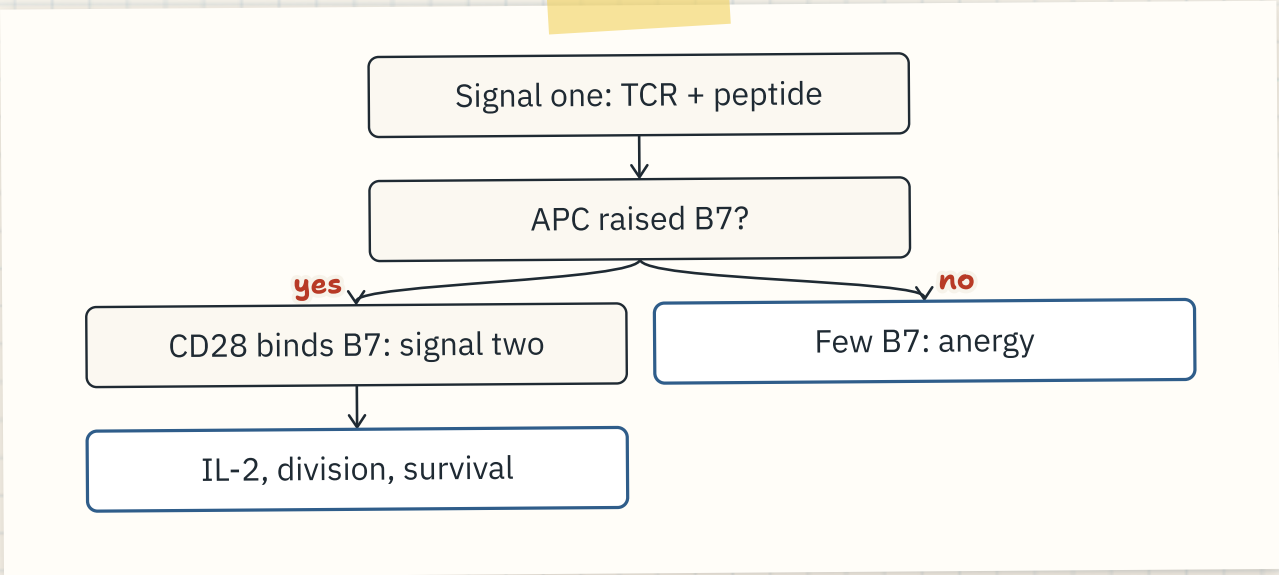
T-cell activation: two signals

Why recognition alone does not switch a T cell on



Step by step

1. APC presents peptide on MHC: signal one
2. Microbe sensed by TLRs: APC raises B7
3. CD28 binds B7: signal two
4. T cell makes IL-2, divides, survives
5. CTLA-4 later mops up B7

TWO-SIGNAL MODEL

Signal 1 + Signal 2 → activation; Signal 1 alone → anergy

Signal 1 = TCR with peptide on MHC (CD3, CD4 or CD8); Signal 2 = CD28 with B7-1 (CD80) or B7-2 (CD86)

Step	Molecules	Result
Signal 1	TCR + peptide–MHC	Specificity
Signals 1 + 2	TCR–MHC, then CD28 + B7	IL-2, division, survival
Signal 1 only	Few B7 on a resting APC	Anergy
Brake	CTLA-4 + B7 (higher affinity)	No activating signal
Brake blocked	Ipilimumab	More T-cell activity in melanoma

Signals and the brake

Rule of thumb

Signal 1 = what it is (specificity)

Signal 2 = confirmation (CD28 with B7)

Signal 1 alone = anergy

Exam traps

- Signal one alone does not activate: it causes anergy.
- CTLA-4 binds B7 with higher affinity but sends no activating signal.
- The APC decides: resting cells have few B7, microbial sensing raises B7.

T-cell activation: the two-signal model

Video, written lesson, practice question and sources: medservatory.com/usmle-step-1/immunology/t-cell-activation-costimulation-cd28-b7-anergy

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