**T cell activation**

- 2 signal model: antigen (TCR)
- Plus co-stimulation (CD28)
- Ligands for CD28 are CD80 and CD86 (B7 molecules)
- Without this the interaction between APC and T-cell can be non-productive
  - Can even lead to T cell anergy
    - A lack of reaction by the body’s defense mechanisms to foreign substances, and consists of a direct induction of peripheral lymphocyte tolerance
- Co-stimulatory ligands are unregulated as APC gets activated
- Phenotype of APC is important in deciding whether T-cell response will go ahead or not
- Up regulation of co-stimulatory are molecules derived from microbes or inflammatory cytokines (danger signals)
- Linking T cell activation to co-stimulation ensures T cells respond in right context when microbes present as as opposed to responding to harmless antigen

**CD28 has a homologue called CTLA-4**

- CTLA-4 binds to the same ligands as CD28 but with higher affinity
- CTLA-4 is constitutively expressed at high levels in regulatory T cells (Treg)
  - Treg suppress immune responses
  - CTLA-4 stop signal to down regulate immunity
- CTLA-4/- mice die of a lethal lymph proliferative syndrome (non-self control)
- Critical inhibitor of immune responses of both mice and humans

**How does CTLA-4 work?**

- CTLA-4 can capture and internalize the co-stimulatory ligands (CD80, CD86) from the surface of APCs
  - many mechanisms proposed...
    - Negative signaling
    - Ligand competition
    - Influence adhesion/motility
    - Reverse signaling through ligands

**T-cell activation and regulation**

- 2 signal model: antigen (TCR) plus co-stimulation (CD28)
- CTLA-4 can deplete co-stimulatory ligands from APC

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Which of the following are correct about regulatory T cells

- [ ] They are responsible for negative selection of T cells in the thymus
- [ ] They do not express TCR or CTLA-4
- [x] Lack of regulatory T cells lead to autoimmune disease
- [ ] They are cytotoxic cells that kill normal cells
- [ ] The suppress immune response to self antigens