T Cell Supplementary Material Contents:

CD28 versus CTLA-4 in T cell activation. Helper T cells regulate themselves with an elegant switch. When first encountering antigen-presenting cells the T cell expresses CD28, which engages CD80 and CD86 on the APC. CD28 transmits activation signals so the Th begins to divide and differentiate. With time, the T cell upregulates CTLA-4 on its surface. CTLA-4 transmits *inhibitory* signals into the T cell. Its affinity for CD80/CD86 is higher that that of CD28, so the inhibitory message predominates and the T cell shuts down.

So naturally, several groups have taken advantage of the T cell's natural "turn-off" mechanism to develop therapeutic reagents. A fusion between CTLA-4 and the Fc of IgG (for good solubility and pharmacodynamics) can bind CD80/CD86 on APC, making these molecules unavailable to the costimulatory CD28 on T cells, and thus suppressing T cell activation. The product is **abatacept**, made by Bristol-Meyers Squibb. It is recently approved for self-administration at home for rheumatoid arthritis.
Manufacturer's site: www.Orencia.com

Th17 (T_H17) cells are the newest Th subset. They were recognized as a separate type of Th cell in 2005. They make the proinflammatory cytokines IL-17 and IL-23, and have been shown to play a part in certain mouse autoimmunity models. They can also be found in lesions of human psoriasis and inflammatory bowel disease (*see* Autoimmunity). A monoclonal antibody against IL-23 (unfortunately also against IL-12, which shares a p40 chain with IL-23) is claimed to have some efficacy in psoriasis. Since Th17 are generally studied under conditions artificially manipulated to enhance their numbers, their true role and importance in human biology is not yet established. However, recent reports suggest a role for Th17 cells in resistance to infection by *Mycobacterium tuberculosis*, *Klebsiella pneumoniae*, and *Bordetella pertussis*.
Review: http://www.ncbi.nlm.nih.gov/pubmed/20044948

About their development: Th0 cells exposed to high concentrations of TGFβ upregulate the transcription factor FoxP3 and develop into Treg. If a high concentration of IL-6 is also present, FoxP3 is suppressed and the "orphan relation to retinoic acid receptors" gene ROR-γt is expressed instead, resulting in a Th17 cell. Like other Th, Th17 is self-stimulating, using autocrine IL-21.

SUMMARY: T_H CELL SUBSETS

T cell	Induced by	Cytokines made	Surface markers	Transcription factors	Competitive actions
Th1	"DC1" IL-12	IL-2 IFN-γ (TNF-β)	CD4	T-bet Stat4	IFN-γ promotes Th1, suppresses Th2
Th2	"DC2" IL-4	IL-4, IL-5, IL-6, IL-10, IL-13	CD4	GATA-3	IL-4 promotes Th2, suppress Th1
Th17	TGFβ + IL-6 IL-21 IL-23	IL-17 IL-21 IL-23	CD4	ROR-γt	IL-21 promotes Th17, ? suppresses Th1, Th2
Tfh	?	A variety of Th1 and Th2 cytokines	CD4; CXCR5 for homing to follicles	BCL-6	Suppressed by Treg
Treg	"Natural" TGFβ	TGF-β IL-10	CD4 CD25 $CD127^{low}$	Foxp3	Suppresses Th1, Th2, Th17, Tfh by contact and soluble factors (IL-10, TGF-β)

"DC1" and "DC2" refer to dendritic cells polarized by exposure to the appropriate cytokine/chemokine soup to favor differentiation of Th0 into Th1 or Th2, respectively. Not everyone uses this terminology.