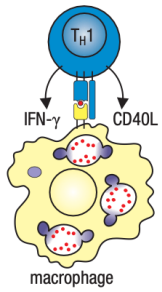
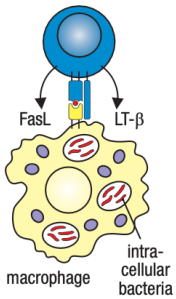
T_H1 effector functions in infections by intracellular bacteria

T_H1 cells produce IFN-γ and CD40L, which induce and activate M1 macrophages



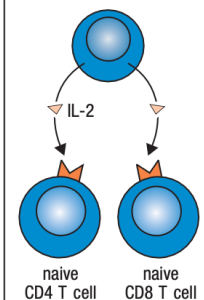
Enhances macrophage killing of engulfed bacteria

Fas ligand and LT-β produced by T_H1 cells induce apoptosis of bacteria-laden macrophages



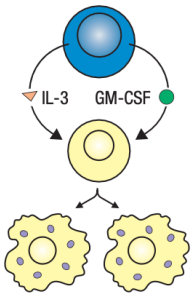
Kills chronically infected cells, releasing bacteria to be destroyed by fresh macrophages

IL-2 produced by T_H1 cells acts on naive CD4 and CD8 T cells



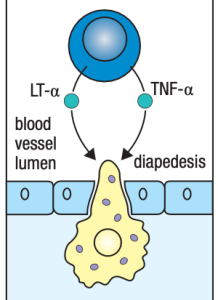
Alters balance of T_H1 versus T_{FH} differentiation to favor T_H1; supports expansion of CD8 CTLs

IL-3 and GM-CSF produced by T_H1 cells stimulate production of monocytes by bone marrow



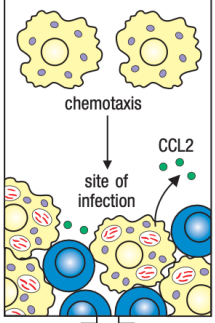
Induces monocyte differentiation in the bone marrow

T_H1 cells produce TNF-α and LT-α which act on local blood vessels



Activates endothelium to induce macrophage binding and exit from blood vessel at site of infection

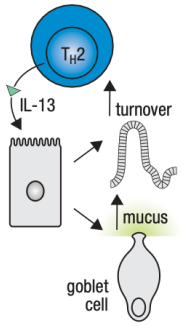
CCL2 induced by T_H1 cells is a chemoattractant for monocytes



Causes macrophages to accumulate at site of infection

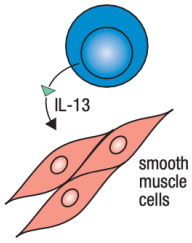
T_H2 cell effector functions in helminth infections

T_H2 cells produce IL-13, which induces epithelial cell repair and mucus



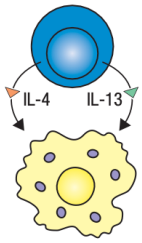
Increased cell turnover and movement helps shedding of parasitized epithelial cells. Mucus prevents adherence and accelerates loss of parasite

IL-13 produced by T_H2 cells increases smooth muscle contractility that enhances worm expulsion



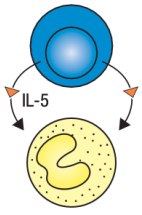
Increased contractility of mucosal smooth muscle enhances worm expulsion

T_H2 cells recruit and activate M2 macrophages via IL-4 and IL-13



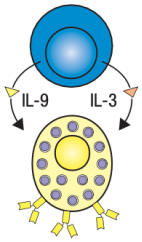
Products of arginase-1 expressed by M2 macrophages increase smooth muscle contraction and enhance tissue remodeling and repair

IL-5 produced by T_H2 cells recruits and activates eosinophils



Eosinophils produce MBP, which kills parasites. They can also mediate ADCC using parasite-specific Ig

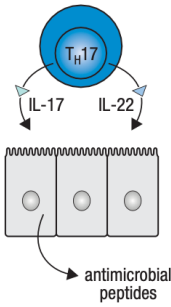
T_H2 cells drive mast cell recruitment via IL-3, IL-9. Specific IgE arms mast cells against helminths



Mast cells produce mediators such as histamine, TNF-α, and MMCP. These recruit inflammatory cells and remodel the mucosa

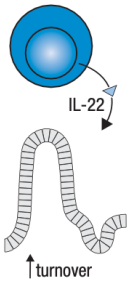
T_H17 effector functions in infections by extracellular bacteria

IL-17 and IL-22 produced by T_H17 cells induce the production of antimicrobial peptides by epithelial cells



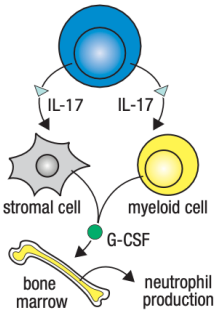
Direct killing or growth inhibition of bacteria attached to the epithelium

IL-22 produced by T_H17 increases epithelial cell turnover



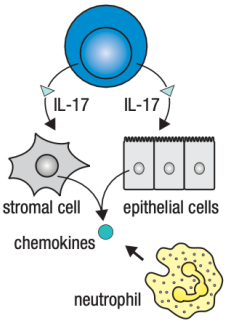
Increased epithelial cell division and shedding impairs bacterial colonization

IL-17 produced by T_H17 cells activates stromal cells and myeloid cells to produce G-CSF, which stimulates neutrophil production in bone marrow



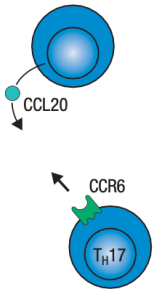
Increases numbers of circulating neutrophils to sustain supply of short-lived innate effectors at infection site

IL-17 produced by T_H17 cells activates stromal cells and epithelial cells to produce chemokines that recruit neutrophils



Recruitment of neutrophils to the site of infection

CCL20 produced by T_H17 cells is a chemoattractant for other T_H17 cells



Increased recruitment of T_H17 cells to site of infection

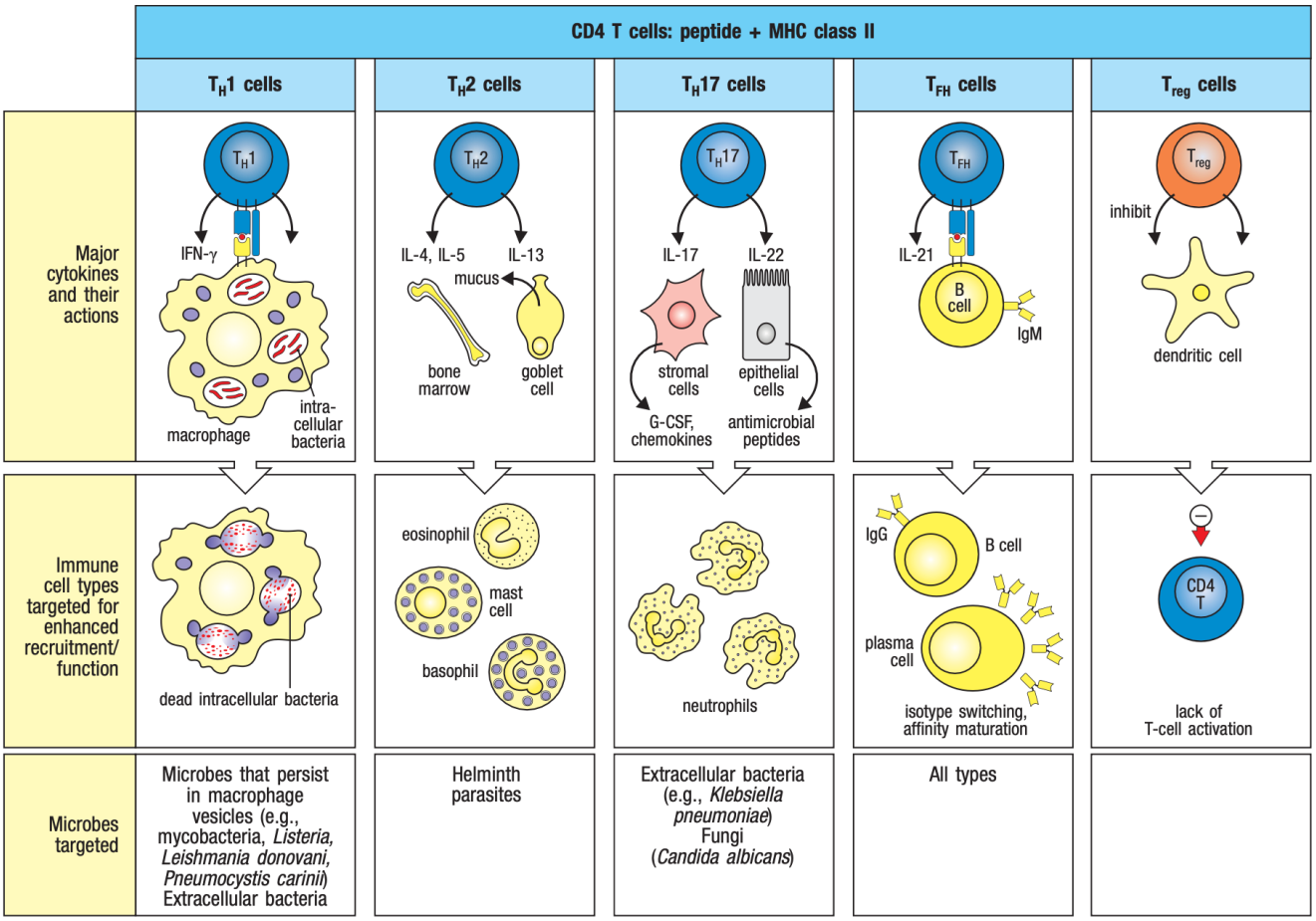


Fig. 9.30 Subsets of CD4 effector T cells are specialized to provide help to different target cells for the eradication of different classes of pathogens. Unlike CD8 T cells, which act directly on infected target cells to eliminate pathogens, CD4 T cells typically enhance the effector functions of other cells that eradicate pathogens—whether cells of the innate immune system, or, in the case of T_{FH} cells, antigen-specific B cells. T_H1 cells (first panels) produce cytokines, such as IFN-γ, which activate macrophages, enabling them to destroy intracellular microorganisms more efficiently. T_H2 cells (second panels) produce cytokines that recruit and activate eosinophils (IL-5) and mast cells and basophils (IL-4), and promote enhanced barrier immunity at mucosal surfaces (IL-13) to eradicate helminths. T_H17 cells (third panels) secrete IL-17-family cytokines that induce local epithelial and stromal cells to produce chemokines that recruit neutrophils to sites of infection. T_H17 cells also produce IL-22, which along with IL-17 can activate epithelial cells at the barrier site to produce antimicrobial peptides that kill bacteria. T_{FH} cells (fourth panels) form cognate interactions with naive B cells through linked recognition of antigen and traffic to B-cell follicles, where they promote the germinal center response. T_{FH} cells produce cytokines characteristic of other subsets and participate in type 1, 2, and 3 responses that are recruited against different types of pathogens. T_{FH} cells producing IFN-γ activate B cells to produce strongly opsonizing antibodies belonging to certain IgG subclasses (IgG1 and IgG3 in humans, and their homologs, IgG2a and IgG2b, in the mouse) in type 1 responses. Those T_{FH} cells producing IL-4 drive B cells to differentiate and produce immunoglobulin IgE, which arms mast cells and basophils for granule release in type 2 responses. T_{FH} cells that produce IL-17 appear to be important for generating opsonizing antibodies directed against extracellular pathogens in the context of type 3/T_H17 immunity. Regulatory T cells (right panels) generally suppress T-cell and innate immune cell activity and help prevent the development of autoimmunity during immune responses.