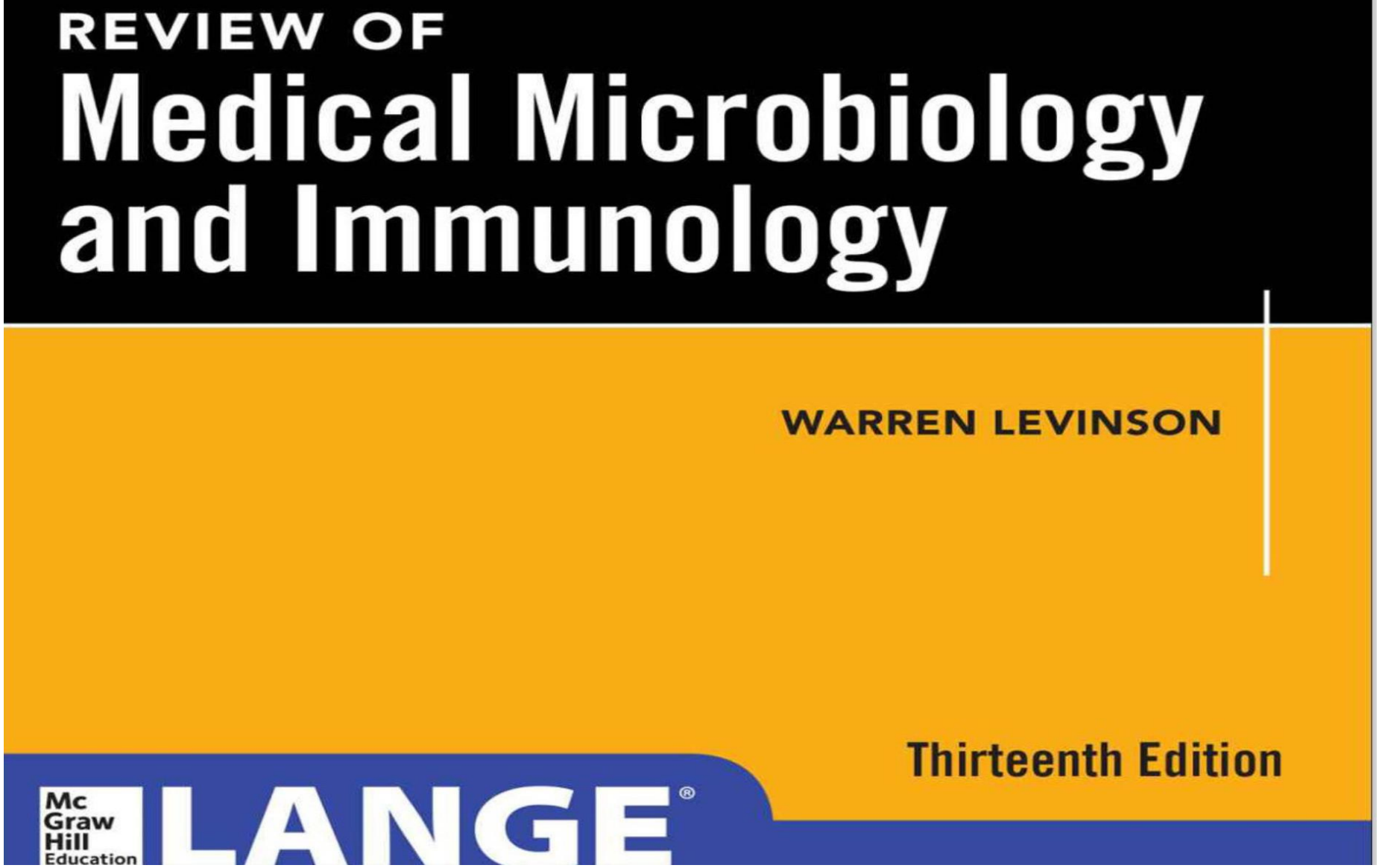
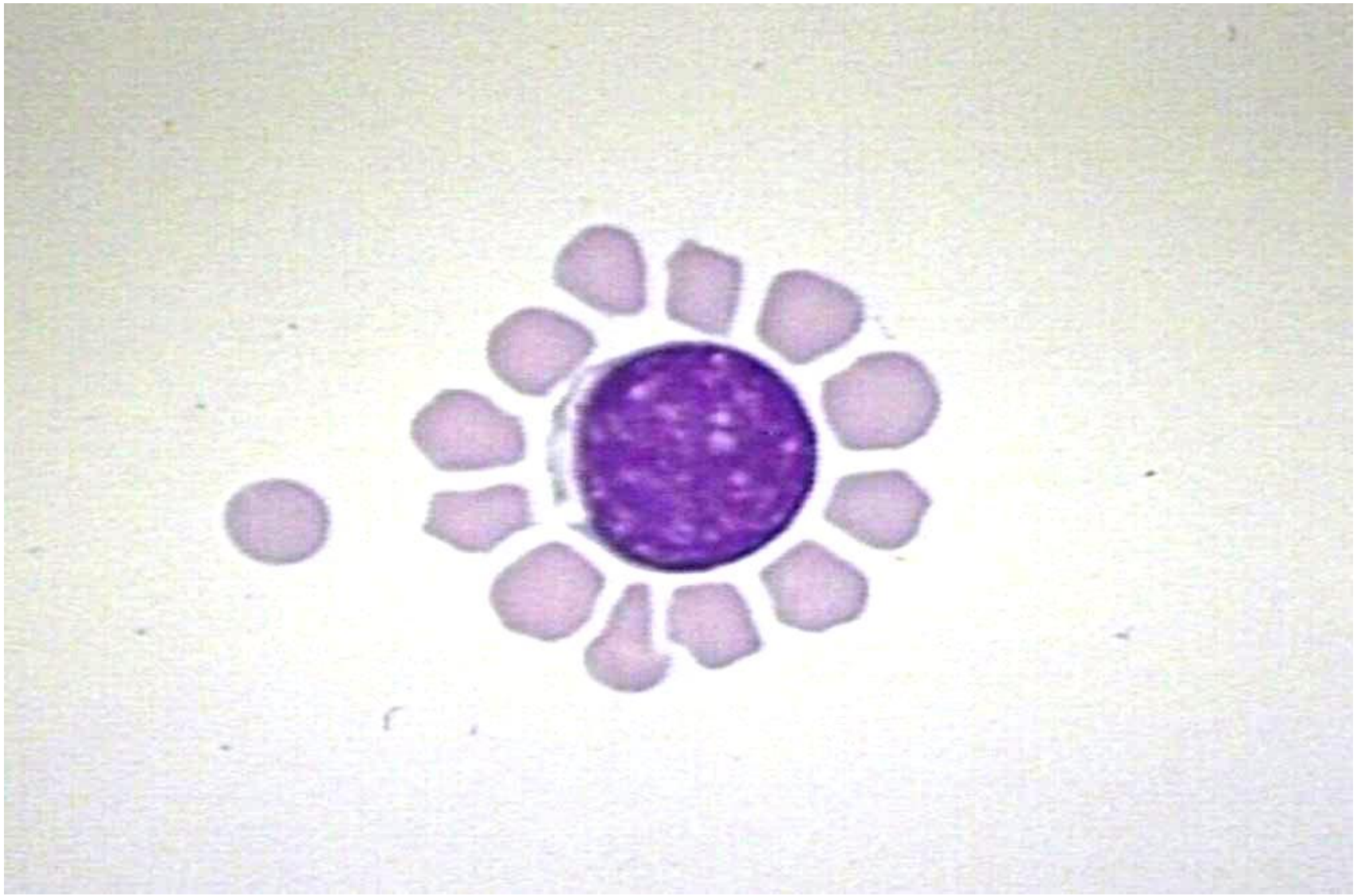


Levinson, W., Review of medical microbiology and immunology. Fourteenth edition. ed. 2016, New York: McGraw-Hill Education. ix, 821 pages.

Chapter 58, all tables and figures taken from this chapter

Features of T Cells

- T cells make up about 65% to 80% of the recirculating pool of small lymphocytes, the rest are B cells.
- Within lymph nodes, T cells are found in the inner and subcortical regions, whereas B cells are located primarily in the germinal centers of the lymph node.
- T cells have a very long half life, they can survive for months or even years.
- These cells can be stimulated to proliferate by using mitogens (mitosis generating molecules) – IL-2 producing signals are mitogens, since they will activate them and cause clonal proliferation-.
- mitogens for T cells include: phytohemagglutinin or concanavalin A [endotoxin, a lipopolysaccharide found on the surface of gram-negative bacteria, is a mitogen for B cells but not T cells]).
- T cells are detected in blood by using sheep blood, this is because all T cells have receptors on their surface that reacts with sheep RBCs, and form a unique structure seen by the eye “rosettes”.



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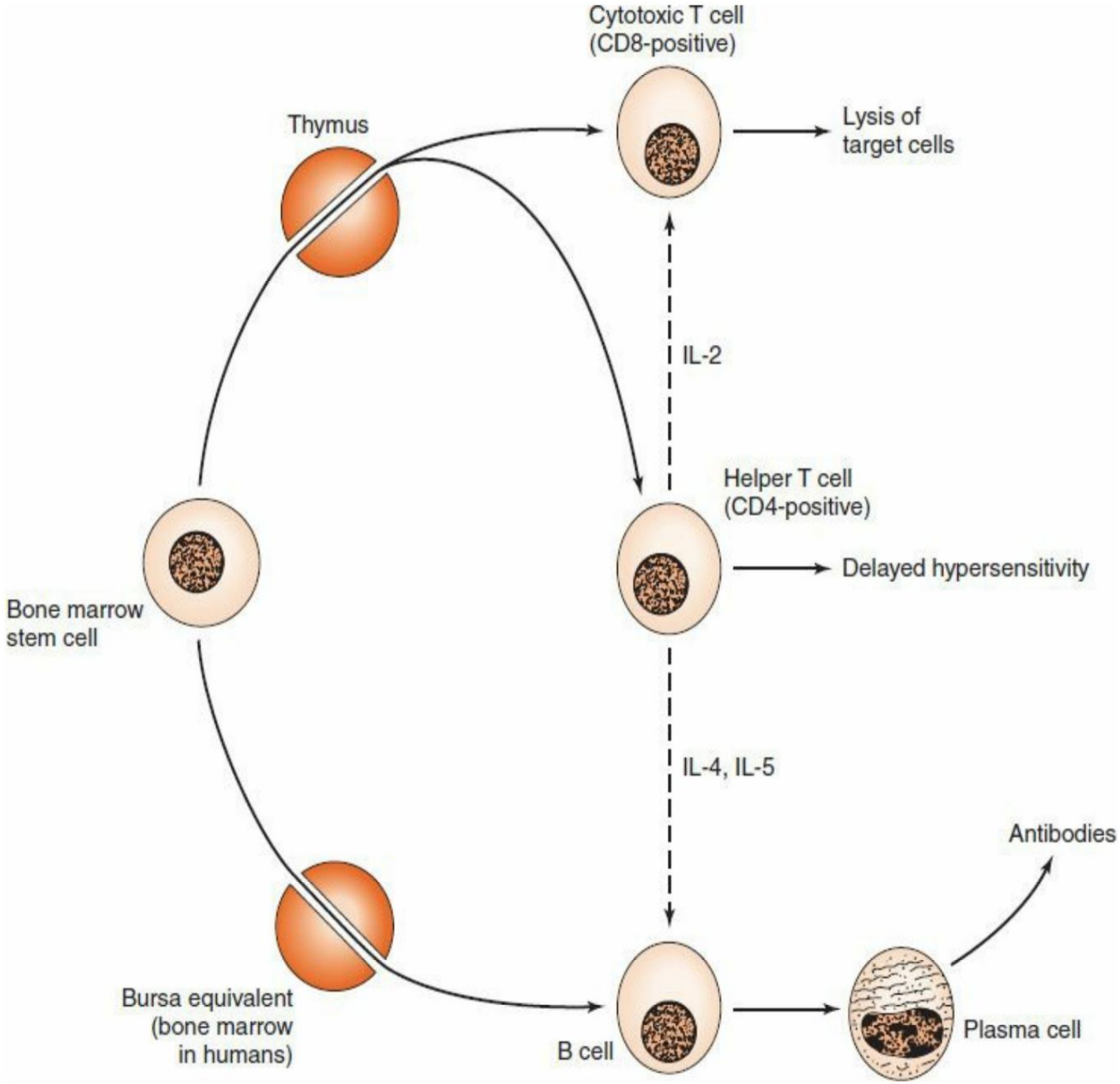
Effector Functions of T Cells- recap

- The four types of T cells (Th-1, Th-2, and Th-17 types of CD4 cells, and CD8 cells) mediate different aspects of our host defenses.
- Th-1 cells mediate delayed hypersensitivity reactions against intracellular organisms.
- Th-2 cells mediate protection against helminths (worms).
- Th-17 cells protect against the spread of bacterial infections by recruiting neutrophils to the site of infection.
- CD8 cells protect against viral infection by killing virus-infected cells.


Cytotoxic T cell
(CD8-positive)
Thymus
Lysis of
target cells
IL-2
Helper T cell
(CD4-positive)
Delayed hypersensitivity
Bone marrow
stem cell
IL-4, IL-5
Antibodies
Bursa equivalent
(bone marrow
in humans)
B cell
Plasma cell

Th-1 Cells

- **Th-1 cells and macrophages** are the main effectors of cell mediated (also called delayed hypersensitivity reactions, type IV hypersensitivity reaction).
- This type of reaction is aimed to protect against :
- 1) intracellular pathogens (fungi Histoplasma and Coccidioides) and (bacteria such as *M. tuberculosis*) and some viruses
- the main signaling molecule in this type of reaction is GAMMA INTERFERON, with other signals (IL-2, TNF-beta) that help recruit or exclude macrophages (macrophage activation factor and macrophage migration inhibition factor (MIF)) also play a role.
- The actual function of destroying these intracellular pathogens is performed by macrophages, however Th-1 cells direct macrophages (recruit them to the site and tell them what to look for) by the production of interleukins.
- If one has a diminished delayed hyprsensitivity reaction, they will of course be unable to clear these pathogens.
- *The clincher: Th1 cells perform cellular immunity by producing Gamma Interferon and kill some intracellular pathogens by directly orchestrating macrophages to kill the target cells.*

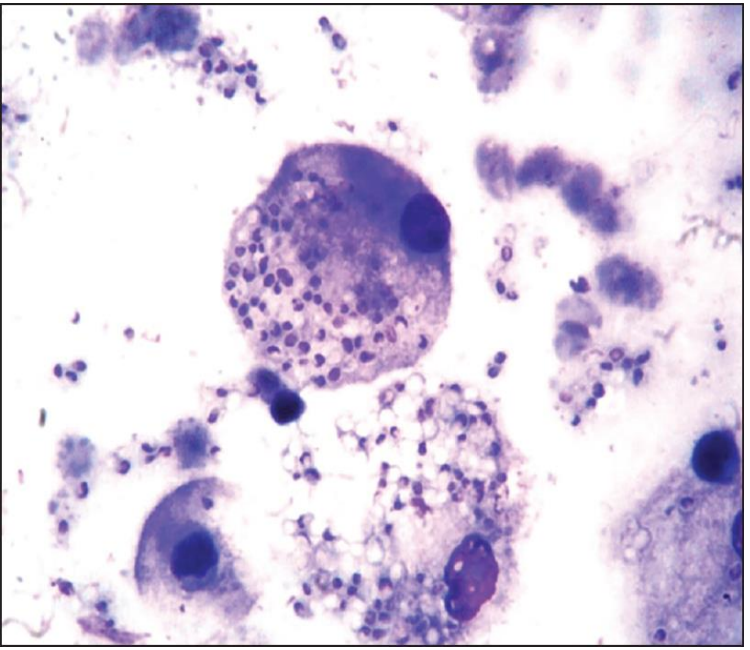
- There is a balance between Th1 cells and Th1 cells.
- This balance is is provided by the production of IL-12 from macrophages. IL-12 increases the number of Th-1 cells (cell mediated), enhancing host defenses against organisms that are controlled by a delayed hypersensitivity response.
- Moreover, Interferon from Th1 cells also inhibits the production of Th2 cells, tipping the scale further towards Th1 response). Th1 = IL-12 (stimulatory to Th1) + Interferon (inhibitory to Th2)
- IL-10 produced by Th-2 cells inhibits IL-12 production by macrophages and drives the system toward an antibody response and away from a cell-mediated response (towards Th2).
- CD4 cells make up about 65% of peripheral T cells and predominate in the thymic medulla, tonsils, and blood. Th2 = IL-4 (stimulatory to Th2) + IL10 (inhibitory to Th1)

TABLE 58–4 Comparison of Th-1 Cells and Th-2 Cells

Property	Th-1 Cells	Th-2 Cells
Produces IL-2 and gamma interferon	Yes	No
Produces IL-4, IL-5, IL-6, and IL-10	No	Yes
Enhances cell-mediated immunity and delayed hypersensitivity primarily	Yes	No
Enhances antibody production primarily	No	Yes
Stimulated by IL-12	Yes	No
Stimulated by IL-4	No	Yes

IL = interleukin.

- The well studied case of *M. tuberculosis*, a specific lipoprotein of the bacterium is picked up and then stimulates a specific Toll-like receptor on the macrophage, which signals the cell to synthesize IL-12 (indicating that a foreign object was encountered).
- IL-12 is an inducer of the correct type of response to this lipoprotein (cellular Th1 response), thus IL-12 induces naïve helper T cells to differentiate into the Th-1 type of helper CD4 T cells to start the delayed hypersensitivity response, at this point Th-1 cells produce gamma interferon, which activates macrophages, thereby enhancing their ability to kill *M. tuberculosis*.
- This IL-12–gamma interferon axis is very important in the ability of our host defenses to control infections by intracellular pathogens, such as *M. tuberculosis* and *Listeria monocytogenes*.
- recap: Macrophage found a foreign protein→ IL-12→ activate Th1 CD4 cells →G-INF →activate macrophages



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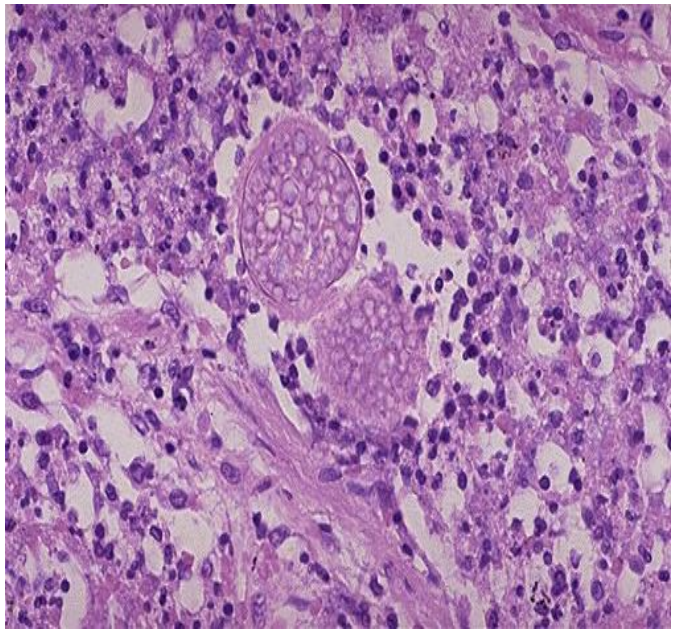
Histoplasmosis



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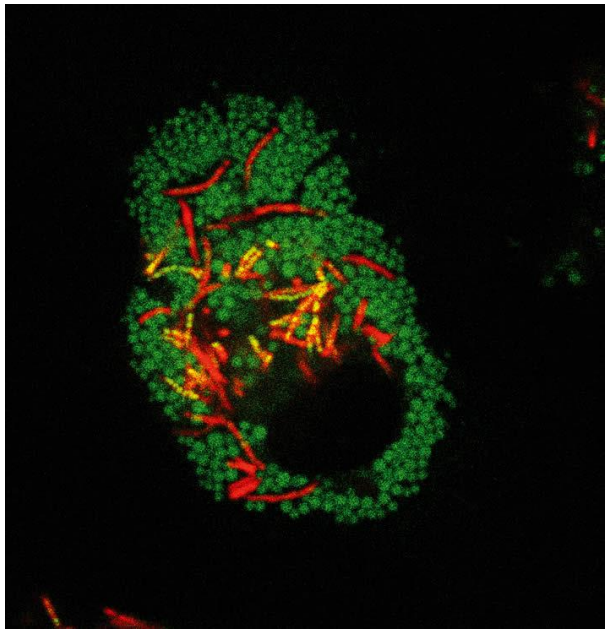
coccidosis



http://www.vet.cornell.edu/news/Images/tuberculosisbacteria.jpg

TB

Th-2 Cells

- *Th-2 CD4 cells along with **eosinophils*** constitute the main effectors of reactions that are protective against helminths (worms) such as Schistosoma and Strongyloides (**remember IgE and eosinophils**).
- The most important interleukins for these reactions are IL-4 (why? Because we need Th2 response to produce IL-4),
- IL-4 increases the production of IgE, and IL-5, which activates eosinophils.
- IgE binds to the surface of the worm. Eosinophils then bind to the heavy chain of IgE and secrete their enzymes that destroy the worm.
- **Th-17 Cells**
- Th-17 cells protect against the spread of bacterial infections at mucosal surfaces by producing IL-17. →IL-17 attracts neutrophils to the site of infection whereupon the bacteria are ingested and destroyed.

CD8 Cells

- CD8 cells mediate the cytotoxic response that is concerned primarily with destroying **virus-infected cells and tumor cells** but also play an important role in graft rejection(MHC-I).
- In response to virus-infected cells, the CD8 lymphocytes must recognize both viral antigens and class I molecules on the surface of infected cells.
- To kill the virus-infected cell, **the cytotoxic T cell must be activated by IL-2 produced by a helper (CD4-positive) T cell, whereas a NK cell doesn't**.
- To become activated to produce IL-2, helper T cells recognize viral antigens bound to class II molecules on an APC (e.g., a dendritic cell or macrophage).
- The activated helper T cell, once it has recognized the MHC-II with viral epitope, will secrete IL-2 that will stimulate the CD8 cell that is specific to that virus- which then will form a clone of that now **activated cytotoxic T cells.**

- Activated cytotoxic T cells kill virus-infected cells primarily by inserting perforins and degradative enzymes called granzymes into the infected cell.
- 1- Perforins form a channel through the membrane, the cell contents are lost, and the cell dies.
- 2- Granzymes are proteases (enzymes that degrade proteins) and work against the proteins in the cell membrane, which also leads to the loss of cell contents.
- 3- Granzymes also activate caspases (a type of protease) that initiate apoptosis, resulting in cell death.
- After killing the virus-infected cell, the cytotoxic T cell itself is not damaged and can continue to kill other cells infected with the same virus.
- **Cytotoxic T cells have no effect on free virus, only on virus-infected cells.**

- The main Apoptotic mechanisn, by which cytotoxic T cells kill target cells is activation of apoptosis through the the Fas-Fas ligand (FasL) interaction.
- This apoptosis mechanism happens when Fas (which is a protein displayed on the surface of many cells) and cytotoxic TCR recognizes an epitope on the surface of a target cell (MHC-I), FasL (Fas Ligand) is induced in the cytotoxic T cell.
- Once FasL and Fas interact, apoptosis (death) of the target cell occurs.
- **NK cells can also kill target cells by Fas-FasL–induced apoptosis**.

- To eliminate virus infected cell, an antibody mediated mechanism is employed as well (In addition to direct killing by cytotoxic T cells) this is done by a combination of **IgG** and phagocytic cells.
- In this **antibody-dependent cellular cytotoxicity (ADCC),** the antibody directed at the virus, is bound to the surface of the infected cell. The bound Antibody is then recognized by phagocytic cells (macrophages or NK cells) by an IgG receptor on their surface → the infected cell is killed.
- The ADCC process is the mechanism of killing helminths (worms).
- However, in this case, ADCC is mediated by IgE, and eosinophils (not phagocytes) are the effector (does the function, in this case killing) cells.
- The mechanism is quite similar, IgE binds to surface proteins on the worm, and eosinophils have a receptor on their surface for the epsilon heavy chain (IgE).
- The actual killing is mediated by granules inside the eosinophils that are released after they are activated by IgE, the major basic protein in these granules damages the surface of the worm. worm.

- In tumors, new antigens (not self) will be displayed on their MHC-I surface protein → CD8 cells will recognize this (and will stimulated to proliferate by IL-2) and target these tumor cells for destruction (either direct or by inducing apoptosis)
- IL-2 produced means that this clone of CD8 cell will proliferate, which will mean that this **CD8 clonal expansion is now able to kill this type of tumor cells** (this phenomenon is called immune surveillance).
- In allografts, cytotoxic (CD8) cells recognize the class I MHC molecules on the surface of the foreign cells (and depending on how similar it is to the self, they will either reject or accept).
- But what activates these CD8 cells in the allograft rejection? They need IL-2, produced by helper (CD4), they will recognize the foreign class II molecules on certain cells in the graft (APCs from the allograft, macrophages and lymphocytes).
- The activated helper cells secrete IL-2, which stimulates the cytotoxic cell to form a clone of cells that will function to kill the allograft cells (this means now the body has memory against this allograft and there is very little that we can do to help, this also means that if we aim to reduce allograft rejection we must work on having the CD4 cells not activating clones of CD8 cells that target the graft.

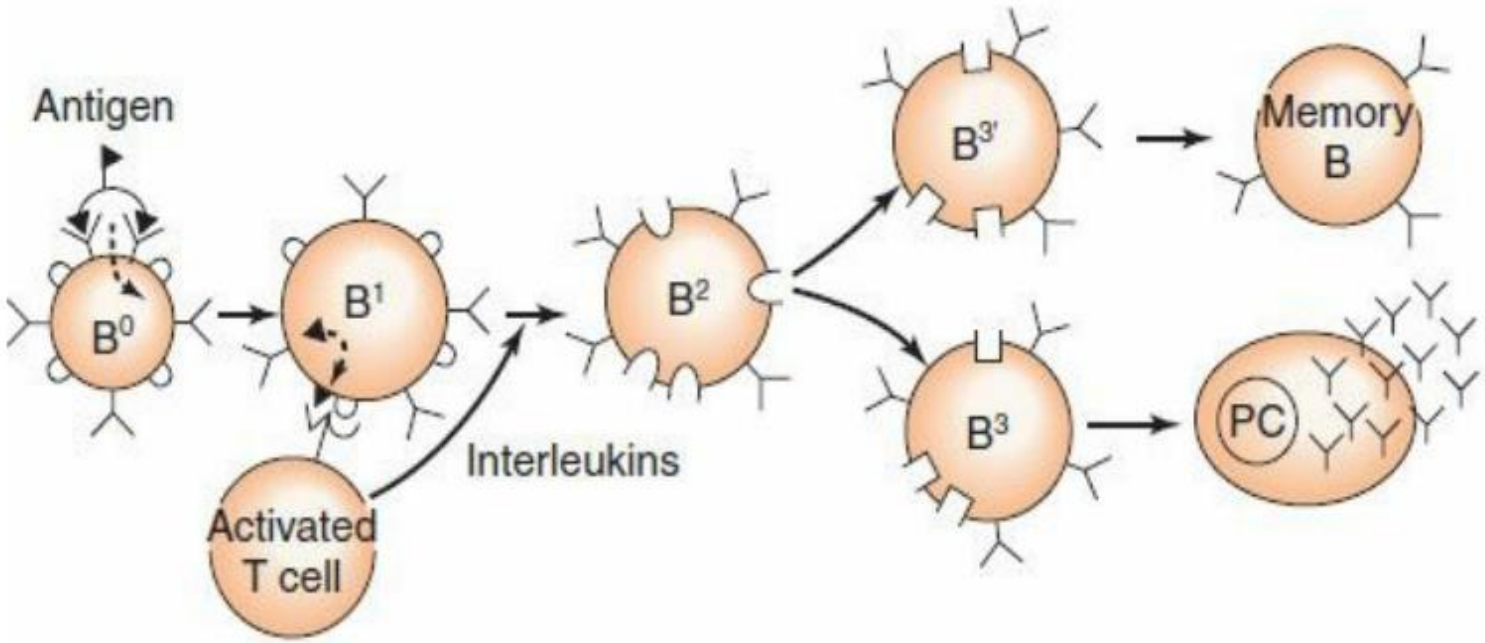
Regulatory T cell function, B cells and APCs

Regulatory Functions of T Cells

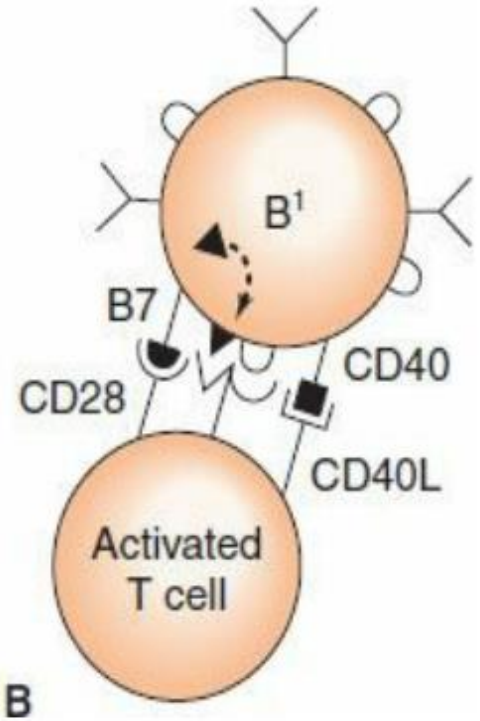
- →The T cell is the main player in the regulation of adaptive immune response, in both its arms (Humoral and cell mediated).
- In humoral (Antibody production), helper T cells are required to **directly** activate the specific B cell to differentiate into a plasma (AB producing cell) this is called the (**T-cell–dependent response).**
- However, to produce antibodies to certain atypical antigens (**large molecules such as bacterial capsular polysaccharides** that are multivalent – can attach to antibodies at more than one side and thus cause cross linking) such antigens (along with haptens, although with a slightly different mechanism) are **T cell–independent producers of antibodies.**
- Macromolecules: (Polysaccharides, sometimes DNA or RNA) are made up of long repeating chains of subunits of several sugars (or nucleotides).
- The repeating nature of their structure (being multivalent) cross-links the IgM antigen receptors on the B cell **surface** and activates it **without needing activation from a helper T-cell**. Other macromolecules, such as DNA, RNA, and many lipids, also elicit a T-cell–independent response (see later of subtypes).

1- T cell dependent Antibody production

- This is the direct activation (next slide) -B cells are used as the APC-.
- In this direct method, the antigen is processed by an APC (in the next slide the APC is the B cell itself) and is presented to the helper T cell on following its interaction with the IgM or IgD on the surface of the B cell.
- Once the antigen is internalized within the B cell, the epitope is the linked to the MHC-II complex and presented on the surface of the APC.
- Similar to what explained before, the interaction with the receptor on the helper T cell, (along with a costimulatory signal is given by the B7 protein with T cell CD28 protein) the helper T cell is then stimulated to produce interleukins (e.g., IL-2, IL4, and IL-5).
- IL-4 and IL-5 induce “class switching” from IgM (IgM is the first class of immunoglobulins produced in the ACUTE phase) to other classes, namely, IgG, IgA, and IgE.
- These interleukins (IL2, IL4,IL5) stimulate the B cell to divide and differentiate into many antibody-producing plasma cells.



A



B

FIGURE 58–7 **A:** B-cell activation by helper T cells. B^0 is a resting B cell to which a multivalent antigen is attaching to monomer IgM receptors (Y). The antigen is internalized, and a fragment (▲) is returned to the surface in conjunction with a class II molecule (□). A receptor on an activated T cell recognizes the complex on the B-cell surface, and the T cell produces interleukins that induce the B^1 cell to form B^2 and B^3 cells, which then differentiate into antibody-producing (e.g., pentamer IgM) plasma cells (PC). Memory B cells are also produced. **B:** Inducible protein B7 (◒) on the B cell must interact with CD28 protein on the helper T cell in order for the helper T cell to be fully activated, and CD40L (CD40 ligand) on the helper T cell must interact with CD40 on the B cell for the B cell to be activated and synthesize the full range of antibodies. (Modified and reproduced with permission

- **There is a 3rd signal** (similar to co activation with B7 CD28) between a now fully activated T cell (CD40 Ligand), this protein interacts with RESTING B cells, which helps them differentiate into antibody producing plasma cells.
- Other proteins on the surface of B and T cells serve to strengthen the interaction between them helper T cell and the antigen-presenting B cell (CD28 and B7 protein in last figure and others).
- There are a few differences now being seen between T cell dependent and independent responses:
- 1- In T-cell–dependent response, all classes of antibody are produced at first (IgG, IgM, IgA, etc.), this is different in T-cell–independent response, where primarily IgM is produced. This is because T cells are responsible for Ig class switching through their lymphokines (which they will produce with the T cell dependent response).
- 2- only the T-cell–dependent response generates memory B cells , therefor there is no secondary antibody production in T cell independent response (which mean it is usually faster responding, but keeps no memory Antibody production).
- The T-cell–independent response is the main response to bacterial capsular polysaccharides, because these molecules are not processed and presented by APCs and hence do not activate helper T cells. The reason for this is that polysaccharides do not bind to class II MHC proteins, whereas peptide antigens do (see later).

2- T cell independent Antibody production

- This is in part similar to hapten and the hypersensitivity reaction following it in that it bypasses the need for T cell, and cause activation for **non peptide** molecules however, unlike the hypersensitivity reaction to haptens, T cell independent activation of these molecules comes with two main differences:
- 1) these molecules are not usually small, but instead are large molecules that are not peptide based (cant be presented on MHC-II to B cells) and thus they must CROSS LINK the IgM on the B cells to activate them, once they are active
- 2) they cause full activation and antibody production without the need to present the antigen to the T cell and cause a loop of activation, but rather start producing antibodies right away (remember carrier protein in haptens causes T cells to activate the B cell to produce Antibodies).

Two types of antigens produce a T cell independent B cell activation

- 1) B cell mitogens: molecules that cause proliferation of B cells and production of polyclonal (and sometimes monoclonal at low concentrations) antibodies. The activation occurs due to reaction between these molecules and toll like receptors on these B cells. (do you notice the link between innate immunity?) **Bacterial DNA and LPS –the endotoxin- (no peptides here) are of this type**
- 2) Large macromolecules **that cause cross link**ing of a critical number of IgM on the B cell surface of only MATURE B cells, immature B cells (those in young children) produce an anergy response and this is why UNCONJUGATED vaccines do not elicit a response in children or why children are more susceptible to infections with capsulated bacteria
- Bacterial capsules are the classic example of this type – remember they are made of the same molecule cross linked over and over to form a macromolecule

So why do we conjugate vaccines? Why are children less able to produce antibodies for capsulated organisms?

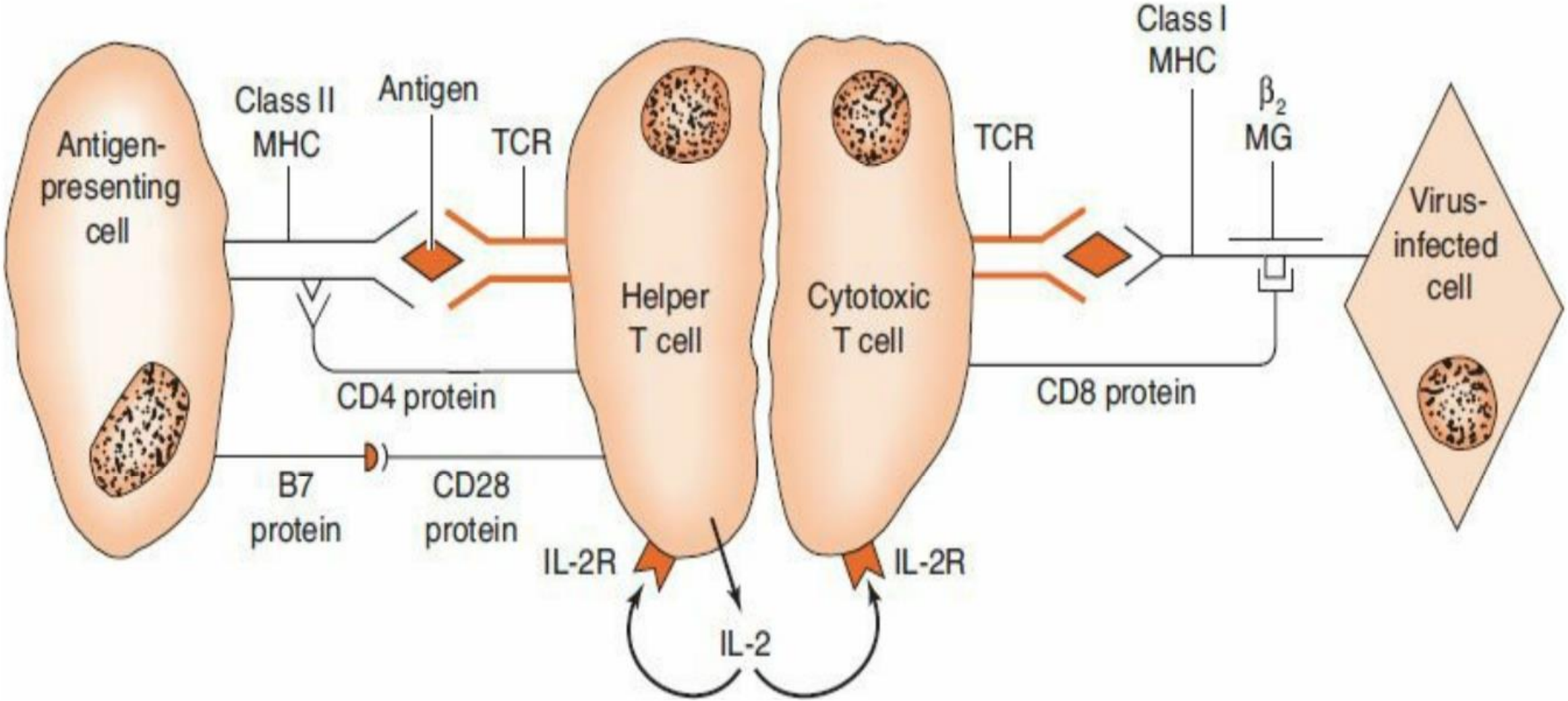
- We conjugate a weak immunogen protein (capsule) to a known strong immunogen (typhoid toxoid).
- Children have less mature IgM on the surface of their B cells, we need to help them by including the T cell independent loop (to present the antigen to T cells to help activate the B cells faster)

- Discussion point: will there be any T cell DEPENDANT activation here? Can it be responsible for side effects of vaccines? Or improve its efficacy?

2- Cell-Mediated Immunity

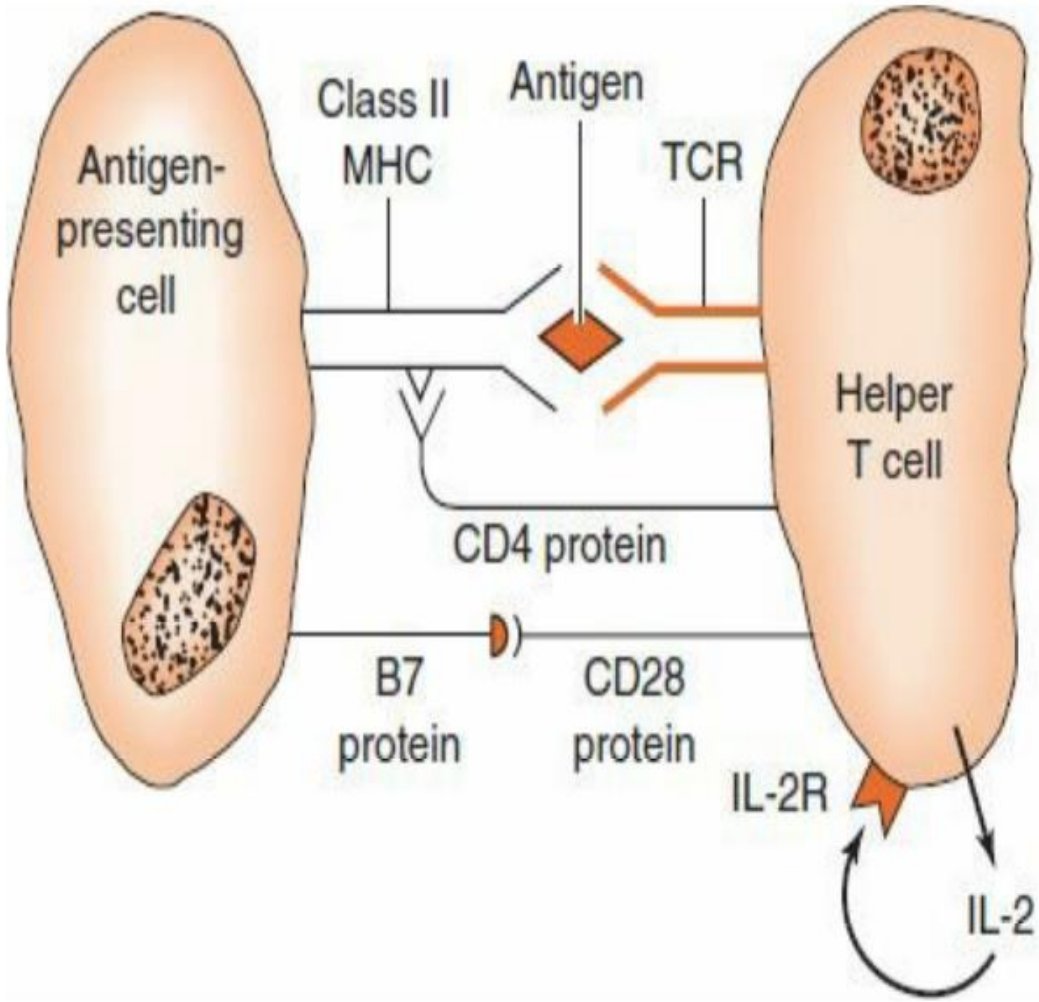
- Reminder, the regulatory function for cell mediated immunity is similar to direct T cell dependent activation:

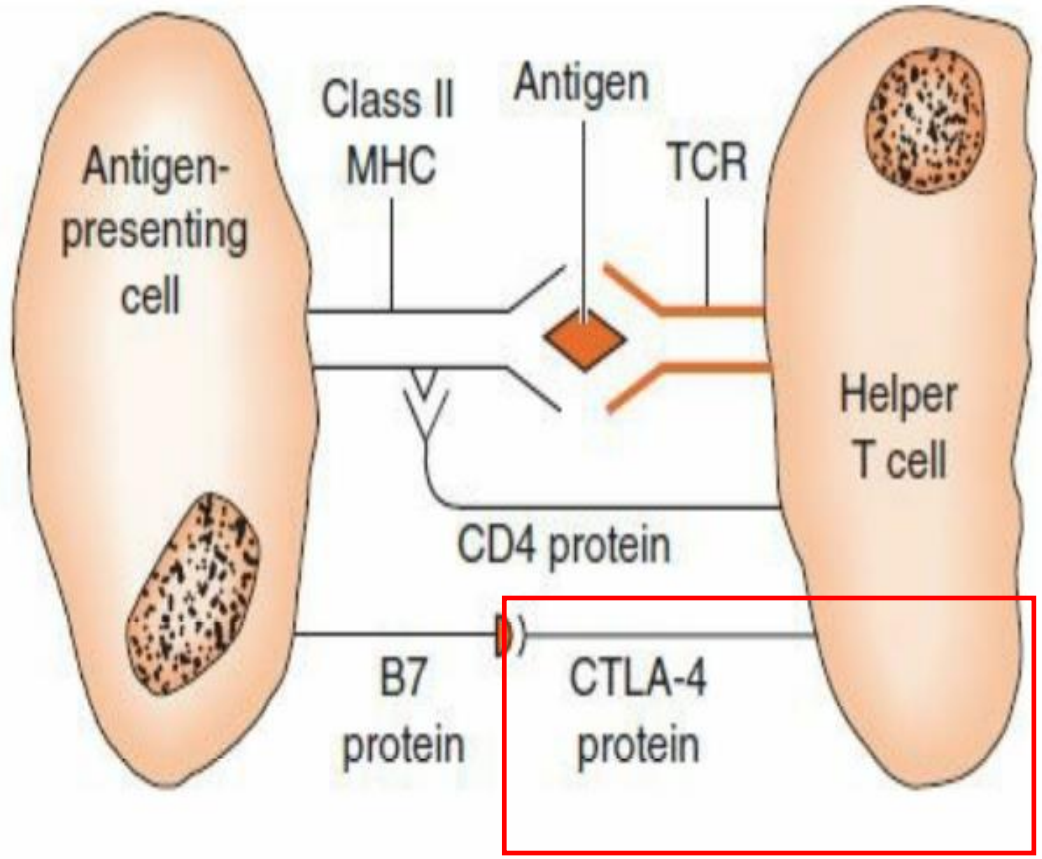
- *APC process antigen, present it on MHC-2 and then bind to helper CD4 T cell, this is followed by co stimulation and then IL-2 production form the CD4 helper T cell which stimulates the specific helper and cytotoxic T cells to grow.*


Antigen-presenting cell
Class II MHC
Antigen
TCR
Helper T cell
Cytotoxic T cell
TCR
Class I MHC
β_2 MG
Virus-infected cell
CD4 protein
CD8 protein
B7 protein
CD28 protein
IL-2R
IL-2R
IL-2

3- Suppression of Certain Immune Responses

- Regulatory T cells (a subset of T cells) (TR) act as inhibitors for effector functions of CD4 (helper) and CD8 (cytotoxic) T cells.
- (These cells are also called suppressor T cells.)
- TR cells are 5% to 10% of the CD4-positive cells and are characterized by possessing the CD25 marker.
- These TR cells also produce a protein that regulates transcription of other various genes (called FoxP3).
- Inhibitory TR cells (which express FoxP3) are the ones that produce CTLA-4.
- In people where TR cells do not express FoxP3, those individuals are predisposed to autoimmune diseases such as SLE (Systemic lupus) and a rare X-linked disease characterized by polyendocrinopathy and enteropathy (IPEX).


Antigen-
presenting
cell
Class II
MHC
Antigen
TCR
Helper
T cell
CD4 protein
B7
protein
CD28
protein
IL-2R
IL-2


Antigen-
presenting
cell
Class II
MHC
Antigen
TCR
Helper
T cell
CD4 protein
B7
protein
CTLA-4
protein

- Regulation of T cells is extremely important, if an imbalance in numbers or ratio/activity between CD4 and CD8 cells happens, normal immune response is impaired (suppressed) as seen in three examples below:
- Example 1: In lepromatous leprosy there is uncontrolled multiplication of *Mycobacterium leprae* (intracellular organism, similar to *Mycobacterium tuberculosis* it needs a delayed hypersensitivity reaction and recruitment of macrophages), but a lack of delayed hypersensitivity (Type 4) to *M. leprae* antigen and a lack of cellular immunity to that organism plus an excess of CD8 cells in lesions, all contribute to the uncontrolled growth.
- → Removal of some CD8 cells can restore cellular immunity in such patients and limit *M. leprae* multiplication.
- Example 2: in normal individuals the ratio of CD4: CD8 cells is (>1.5), however in acquired immunodeficiency syndrome (AIDS), the normal ratio of CD4: CD8 is greatly reduced (CD4 cell count falls below 200 = from HIV to AIDS, so as CD4 cells are targeted and destroyed by HIV, CD8 cells numbers increase, creating further imbalance- loss of T helper activity and increase in suppressor activity).
- This imbalance is the cause of the susceptibility to opportunistic infections and certain tumors in AIDS patients.

- Example 3:
- An important mechanism of the host response to infection is the increased expression of class I and class II MHC proteins which is induced by various cytokines (gamma interferon especially).
- Having more MHC means more antigen presentation and more vigorous (highly controlled) immune reaction.
- Some viruses (HBV Adenovirus and CMV) suppress this increase in MHC (MHC-I to be exact, why?) during infection, making the control mechanism more loose and allowing them to escape more easily.

B CELLS

- B cells perform two important functions:

- (1) They differentiate into plasma cells and produce antibodies
- (2) They can present antigens to helper T cells

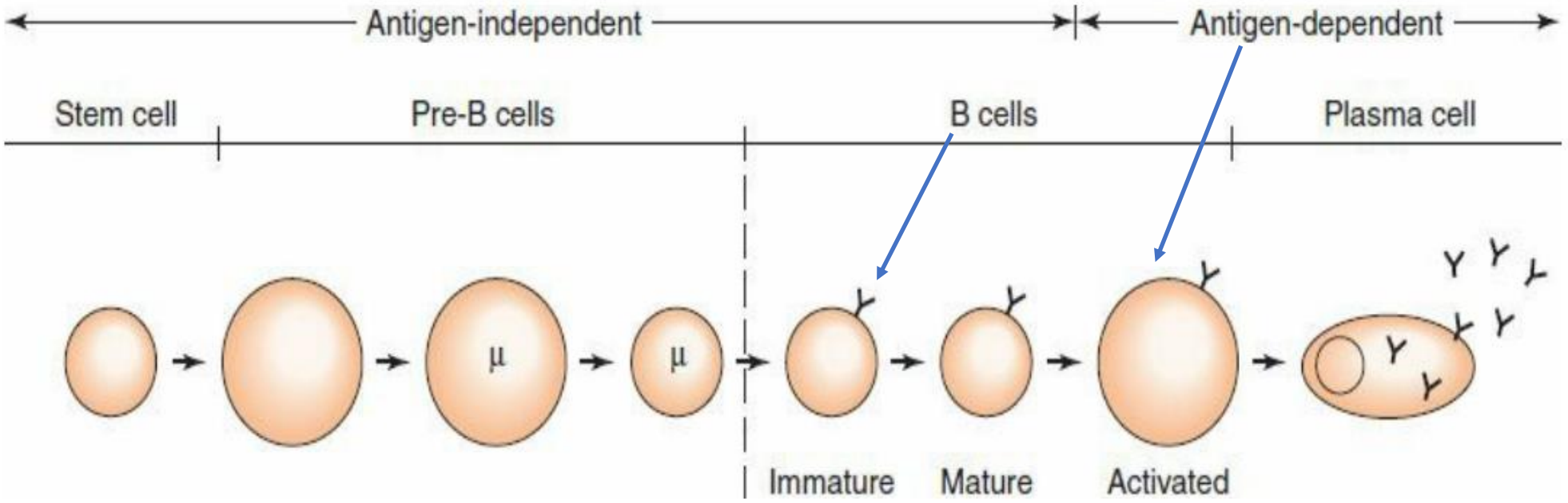


FIGURE 58–8 Maturation of B cells. B cells arise from stem cells and differentiate into pre–B cells expressing μ heavy chains in the cytoplasm and then into B cells expressing monomer IgM on the surface. This occurs independent of antigen. Activation of B cells and differentiation into plasma cells is dependent on antigen. Cells to the left of the vertical dotted line do not have IgM on their surface, whereas B cells, to the right of the vertical line, do have IgM. μ, mu heavy chains in cytoplasm; Y, IgM. (Modified and reproduced with permission from Stites DP, Terr A, eds. *Basic & Clinical Immunology*. 7th ed. Originally published by Appleton & Lange. Copyright 1991 McGraw-Hill.)

- Pre B cells differentiate into immature B cells (with IgM on the surface without the need of antigen presentation) , they even mature to naïve mature B cells, without the need of antigen presentation, they only proliferate and become **active** once antigen is presented to them (or through T cell independent activation).
- HOWEVER, you do need a certain protein for pre–B cells to differentiate into B cells(immature), a signal transduction protein called Bruton's tyrosine kinase is required.
- If Bruton's kinase is mutated this causes X-linked agammaglobulinemia in which immunoglobulins (e.g., IgM, IgG) are not made and B cells are absent.
- Severe infections caused by pyogenic bacteria (this bacteria usually needs antibody production to be cleared, like capsulated bacteria) occur in these patients.
- B cells display surface IgM, which serves as a receptor for antigens.
- This surface IgM is a monomer (1 piece or 1 molecule), in contrast to circulating IgM, which is a pentamer (5 IgMs in one), a pentamer is too large and doesn't cross the placenta, thus the baby is usually protected by IgG.

- The monomeric IgM on the surface has an extra transmembrane domain that anchors the protein (basically IgM with a membrane attachment module) in the cell membrane that is not present in the circulating pentameric form of IgM.
- Surface IgD on some B cells may also be an antigen receptor.
- Pre–B cells are found in the bone marrow, whereas B cells circulate in the bloodstream. The mature lymphocytes have a relatively short lifespan (weeks at most), this is compensated by high production of B lymphocytes about 10^{9} B cells are produced each day - about 30% of the recirculating pool of small lymphocytes- (remember these aren't necessarily active yet).
- Within lymph nodes, they are located in germinal centers; within the spleen, they are found in the white pulp. They are also found in the gut-associated lymphoid tissue (GALT) such as Peyer's patches.

Clonal Selection

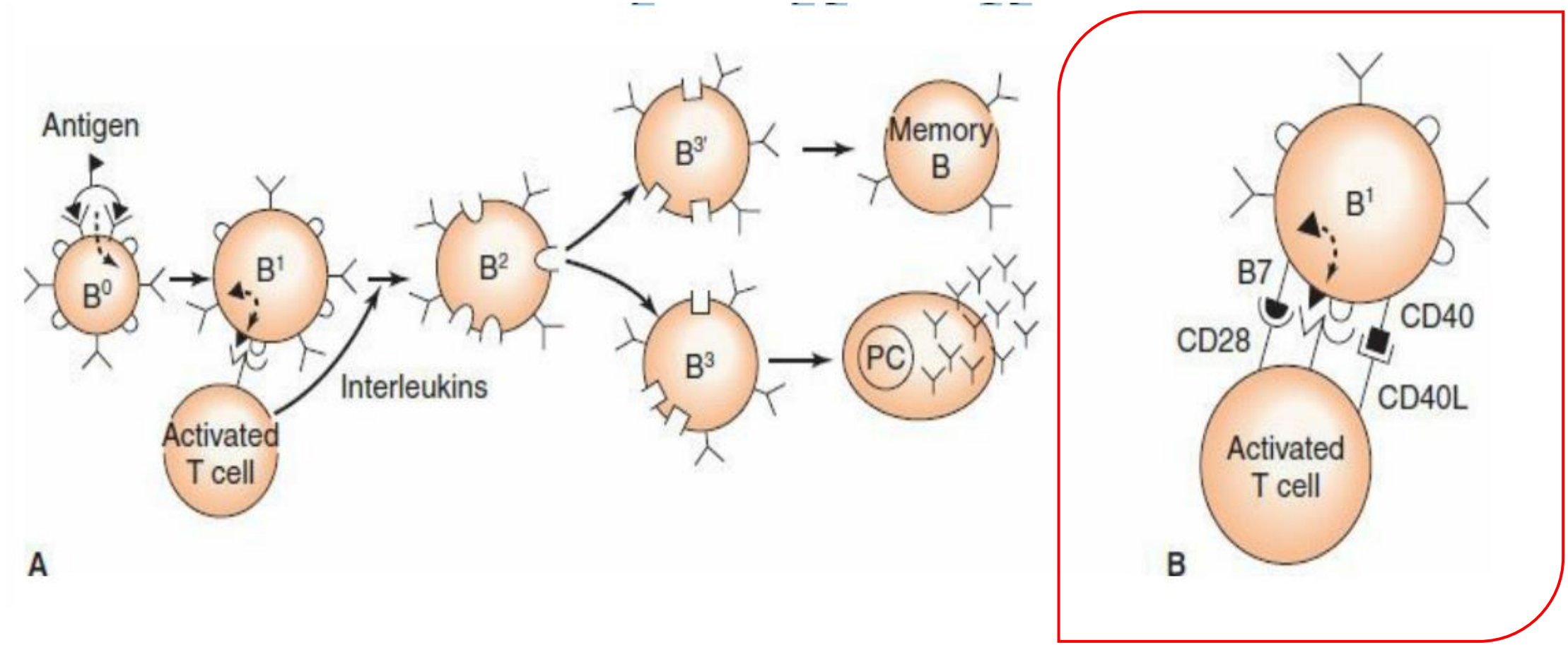
- How are antibodies made (selectively for each antigen?) the current theory which is most accepted is what we mentioned so far (an antigen basically waits to be picked up by a B cell that is already selected a variability in its IgM receptor that accepts this antigen (this is called clonal selection, the clone of that IgM carrying B cell will be selected since it has the correct IgM and thus it proliferates-sort of like positive selection)-.
- Each individual has a large pool of B lymphocytes (about 10^7).
- Each immunologically responsive B cell bears a surface receptor (either IgM or IgD) that can react with one antigen (or closely related group of antigens- this is basically how cross reactivity occurs, when an antigen of a bacteria like GAS is similar to a self antigen).
- It is estimated that there are at least 10 million different specificities.

- So basically →An antigen “key” will interact (lock and key in a sense) with the B lymphocyte that shows the best “fit” or “lock” with its immunoglobulin surface receptor.
- After the antigen binds, the B cell is stimulated to proliferate and form a clone of cells, this is similar to T cell activation with end result of gene activation to produce IL-2.
- Once these B cells are selected , they will become plasma cells and secrete the antibody specific for the antigen.
- Plasma cells synthesize the immunoglobulins with the same antigenic specificity (i.e., they have the same heavy chain and the same light chain) as those carried by the selected B cell.
- If class switching from IgM to IgG for example is to occur, only the heavy chain is changed and the specificity remains the same.
- This is all similar to clonal selection with T cell → *The antigen that interacts with the specific TCR on the surface of either a CD4-positive or a CD8-positive* T cell will select this specificity of the antigen and produce clones of the T cell that are specific to this antigen.

Activation of B Cells

- The process of activation of B cells, occurs in the following manner: a *multivalent antigen binds to surface IgM (or IgD) and cross link a critical number of those surface antigen*.
- The Ig aggregate (combine together in a clump) and form patches which they further combine together to form a cap on one pole of the B cell.
- Endocytosis of the capped Ig material ensues and the antigen on these Ig is then processed within the B cell to reveal epitopes which then appear on the surface of the B cell in conjunction with class II MHC proteins.
- This complex is recognized by a helper T cell with a receptor for the antigen on its surface (so now I need a B cell specific to that antigen and then a T cell as well)→ The T cell now produces various interleukins (IL-2, IL-4, and IL-5) that stimulate the growth and differentiation of the B cell.

- As mentioned, now the only thing remaining is to have the two other co stimulatory signals
- (1) CD28 on the T cell must interact with B7 on the B cell
- (2) CD40L on the T cell must interact with CD40 on the B cell.
- The CD28-B7 interaction is required for activation of the T cell to produce interleukins- prevent anergy which will prevent IL-4 and IL-5 production and thus no activation of the B cell, and the CD40L-CD40 interaction is required for class switching from IgM to other immunoglobulin classes, such as IgG and IgA, to occur.
- A syndrome called: Hyper-IgM syndrome is caused when CD40L is mutated and no class switching occurs → high IgM , no IgA or IgG→ severe PYOGENIC infections.


Antigen
B0
B1
Activated
T cell
Interleukins
B2
B3'
B3
Memory
B
PC
A
B1
B7
CD28
CD40
CD40L
Activated
T cell
B

Effector Functions of B Cells/Plasma Cells

- The end result of the activation process is the production of many plasma cells that produce large amounts of immunoglobulins specific for the epitope.
- Plasma cells secrete thousands of IDENTICAL antibody molecules per second for a few days and then die.
- Some activated B cells form memory cells, which can remain quiescent for long periods but are capable of being activated rapidly upon reexposure to antigen.
- Most memory B cells have surface IgG that serves as the antigen receptor, but some have IgM.
- Memory T cells secrete interleukins that enhance antibody production by the memory B cells.
- The presence of these cells explains the rapid appearance of antibody in the secondary response