B Cell activation

Types of responses

T- dependent B cell activation

① Antigen is presented to B- cells

② the receptor internalize the bound antigen into endosomal vesicle

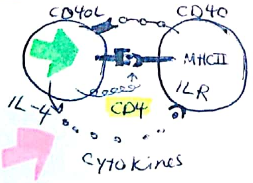
- if the antigen is protein, it will be processed into peptides then present it on the surface for recognition of helper T-cell

③ the activated lymphocytes migrate toward one another and interact at the edges of the follicles

④ Activation of B cells by Antigen .. increases the expression of

- MHC II and B7 costimulators
- CD40 which bind to CD40L on T-cells
- cytokines receptors

↳ secreted by T-cells



- So the activation of B-cells by T-cells could be direct contact or by cytokines

⑤ B-cells migrate to the germinal centers

⑥ B-cell proliferate in response to one antigen which result in one clone of cells with identicle specifics.

⑦ B cell differentiate into plasma cells by switching membrane from Ig to secretring Ig , and Ig isotype switching

proliferation + Somatic hypermutation ⟹ Differentiation

T- independent B cell activation

B_1 cells response to multivalent, non-protein antigens

- poly saccharides - lipids - nucleic acids

- Multivalent :- antigen molecule contain multiple identicle epitops.

① recognizing the antigen by membran Igs

② Signal transduction inside the cell by Ig α and Ig β

③ Recognizing of C3D on the microbe by CR2 on B cell

④ Activation of TLRs on the B cells by molecules derived from the microbe

⑤ B-cell activation and proliferation, and IGM antibody formation

*why somatic hyper mutation ?

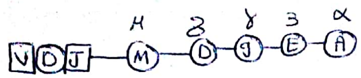
it helps the B-cells to produce a high number of antibodies

MHC ⟹ B cell engulfs the pathogen and break it down and represent it on MHC R.

- if the type of produced Antibodies is IgM .. the cell then called IgM B-cell

- Antibody response requires
1- Antigen
2- T dependent B cell activation

* Isotype switching



- It's DNA recombination
- B cell changes the isotype of the antibodies

How?

by changing the constant regions of heavy chains

* this process doesn't affect the specifity of the antibodies .. why?

because it's determined by the variable region

* AID plays a key role in class switch and somatic hyper mutation .. How?

Mechanism of AID (explaining only!)

- Creates mutation in DNA by converting C int Uracil .. so U is recognized as a T-base so C::G converted into A=T
- so the mutation occure
- mutations produce Ab diversity

→ It deficiency leads to Hyper IGM syndrome.

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when cytokines bind to it's receptors on B-cell it makes the cell undergo many changes in genetic material .. which leads to mutations.

∴ that's why cytokines regulates the isotyp switching.

Isotype determinants

① Anatomic position.
- B-cell in mucosal tissue switch to IgA

② Microbe type
- Viruses and intracellular bacteria ⇒ IgG
- helminthic parasites ⇒ IgE

③ Mutation in CD40L gene

result in X-linked hyper IgM syndrome

1- defects in antibody production and isotype switching
2- decrease affinity maturation
3- " memory B-cell generation

* Somatic hyper mutation :- (Affinity maturation)

- Increased affinity of antibodies
- mutation of Ig V genes causes this Condition.

* Selection

- we need Ab with high affinity to the Ag
- So cells with high affinity proliferate and become → plasma cells (secretory cells) / → memory cells (non secretory cells)
- Other cells with low affinity die.

* plasma cells :

① - short lived
- found in 2ry lymphoid organs, and peripheral non lymphoid tissues
- generated in both dependent and independent B- cell Activation

② - long lived
- produced in T-dependent response

* generation of plasma cells by : B cell antigen receptor + IL-21

mature B-cells doesn't express CD20 → marker..

** Some B-cells enter the circulation and home into the BM where they differentiate into long-lived plasma cells

** Some stay in the medulla in 2ry LN

* Memory cells

Source : B-cells activated in T-dependent manner

- It mounts rapid responses with subsequent encounters with Ag
- High level of anti-apoptotic protein (BcL-2) contribute to their long life span

* Co-receptors

- they facilitate intracellular transduction.

① T- cells coreceptors

- they are CD4 and CD8
- they interact with MHCII and MHCI

② B- cell coreceptors

- CD21 is expressed on mature B cells with ⟹ bind complement protein C3D on microbe
- CD19 ⟹ transduce the signal
- CD81 (TAPI-1) ⟹ Stabilises both molecules