B-cell = Activation + Differentiation

B-cells origin and maturation occurs in bone marrow, Mature B-cells leave the bone marrow and recirculate between the blood, the Secondry lymphoid tissues and the lymph.

* when naive B-cells encounter their specific Antigens they get activated and differentiate into Antibody producing plasma cells + Memory cells

---

B cell Activation ⇒ Classification ⇒ based on the type of antigen encountered by B-cells

- T-cell Independent Activation
- T-cell Dependent Activation

Note* B-cells Signaling Require cross-linking of B-cell receptors on Antigen Recognetion, this clustering of b-cell receptors is required to Activate the accessory protcins Igα + Igβ the Antigen binding Signaling is then conveyed to the nucleous, this clustring of B-cell receptors Depend on the type of Antigen encountered

---

* The Antigen which can trigger B-cell activation <u>without</u> T-cell help called T-Independent Antigens

* Most of Antigens are proteins in their chemical nature, they form the largest group of Antigens but they don't contain Multiple rebeating units, <u>so</u> this make the cross-linking of B-cell receptors difficult so when B-cell encounters protein Antigens t-cell help required to trigger B cell activation Antigens that trigger B-cell activation with the help of T-helper cells are Know as T-dependent, and B cell activation which require T cell help is Know as T dependent B cell Activation

T-Independent B cell Activation:-

① The First Signal For T Independent Activation is ⇒ Clustering of B cell receptors triggers B-cell Activation

② To be fully Activated, B-cells Require a 2nd Signal that can be derived other molecules present on the Antigen, e.g: B cell also have Toll like receptors that can recognize the various microbial service molecules, this recognition bind to the Antigen by toll-like receptors generates 2nd Signal for T-Independent view cell activation

*After Activation this B-cells differentiate into plasma cells that mainly secrete IgM Antibodies, Memory cells aren't produced or If produced they are very less this because MC production requires t-cell help

Summry ⇒ 2 Signals process
- 1st ⇒ derived from clustering of B-cells receptors on Antigen recognation
- 2nd ⇒ " " other molecules of Antigen

↳ T-Independent B-cell activation mainly IgM Antibodies are produced and Since MC requires T-cells help no MC production occur

---

* T-Dependent B-cell Activation:-

It's a 3 Signals process

① Proteins Antigen can't cross link multiple B-cell Receptor (BCR), cuz of these Antigens repetitive and identical epitopes are absent, thus when B cell encounter protein Antigens they require T-cell help

* 1st Signal ⇒ generated on Antigen recognetion by B-cells, mature naive B-cells recognize and bind specific Antigen by it's B-cell receptor recall that the cell is also an antigen-presenting cell beside recognizing the Antigen they also process them and display them on their surfaces MHC 2 peptide complex, this B-cells also start expressing Co-stimulatory and cytokine receptors on their surface
- Most Important Co-stimulary receptor is CD40, Mean while the same Antigen is also recognize by mature naive CD4 T-cell, that this recognation by t-cell is Independent of B cell

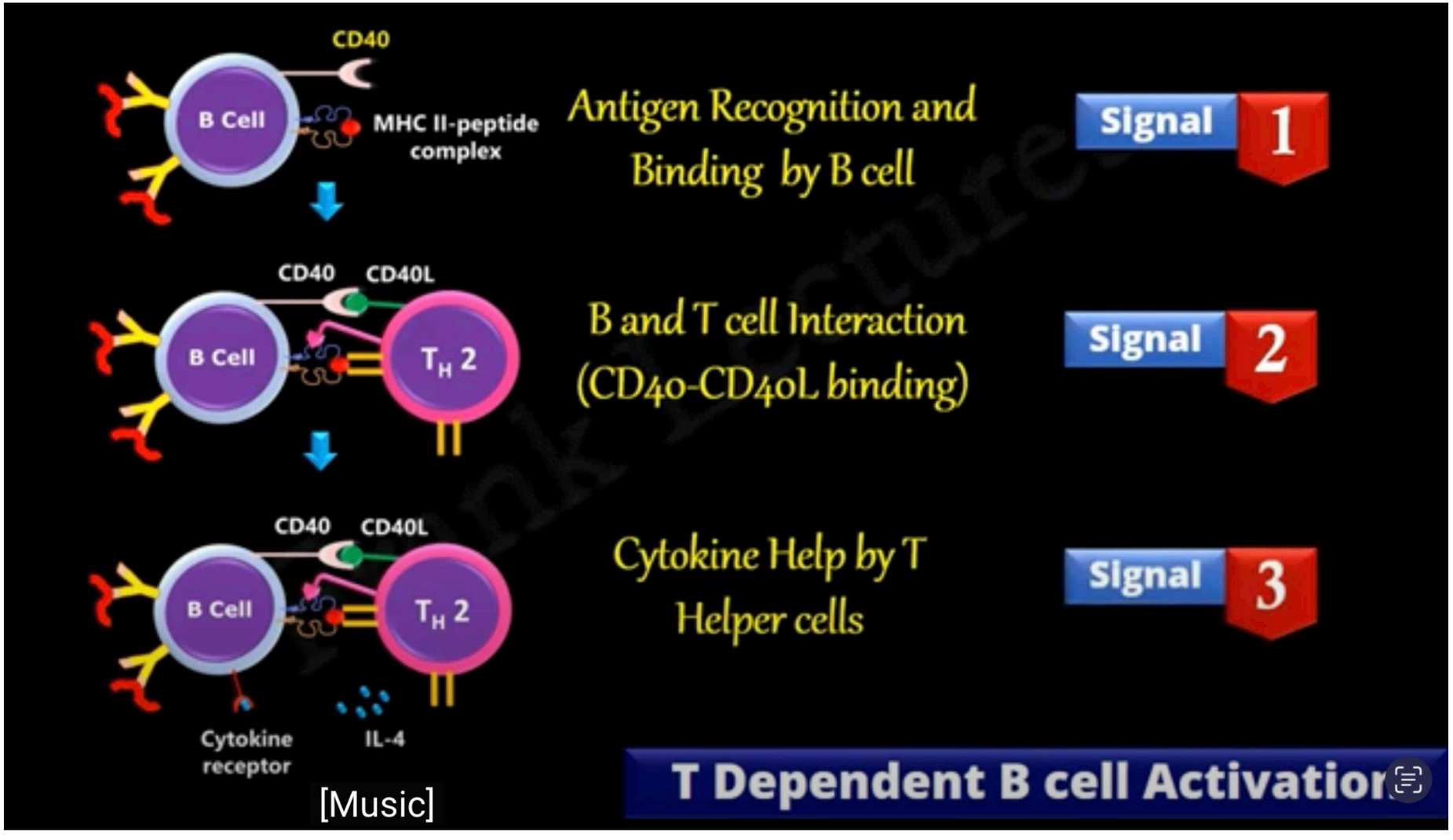
* DC are present processed Antigen in the form of MHC 2 peptide Complex, T-cell get Activated and it express T-Cell receptor capable of recognizing these Antigens

* 2nd Signal ⇒ derived from B and T cell Interactions, the B-cell in the T-helper cell come in close proximity / All that B-cell display Antigen as MHC-peptide complex on it's surface, T-helper cell recognize and bind to this MHC 2 peptide complex.

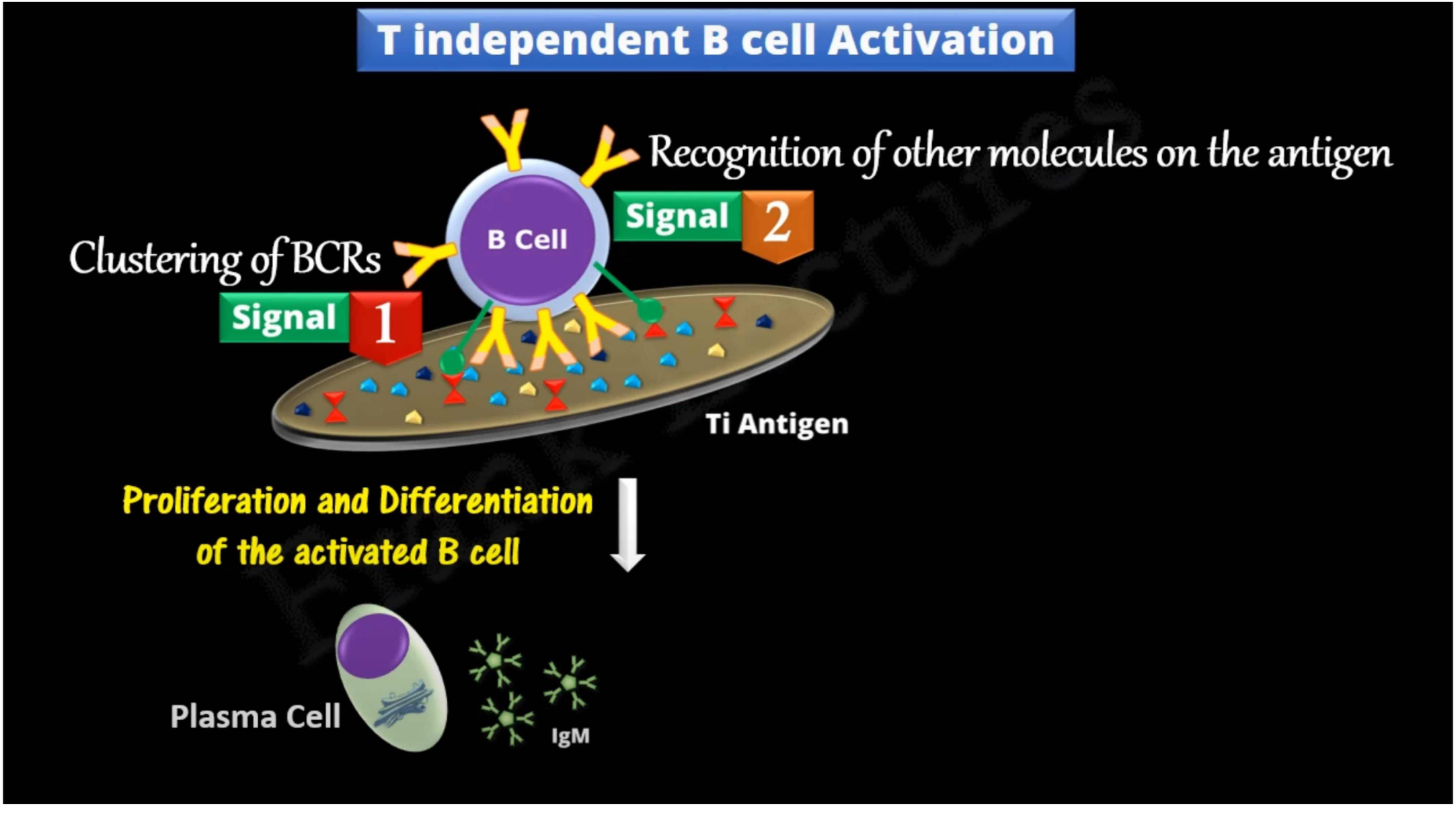
- Once Antigen recognation is Done by the T-helper cell they now Express CD 40 Ligind on their Surface.
- CD40 R present on the B-cell recognize and bind CD40 Ligind Thelper spell, these Interaction Between B and T cells, thus provide the 2nd Signal for B cell activation

* 3rd Signal ⇒ provided by realease of cytokinase by T-helper cell stimulate B-cell.

- Interaction of B and T induced the expression of New cytokine Receptor on the surface of B-cell
- T-cell release cytokines such as InterLeukin4 (IL4), that bind to the cytokines receptor present on B-cell surface.
- As a result, B cell start to proliferate and differentiated to arti body secreting plasma cells + Memory cells



T Indepent Images



* Questions :-

1. Required For isotype switching in B-cells ⇒ Activation-induced cytidine deaminase (AID).
2. plasma cells are ⇒ ① long Lived one can survive for decades, ② short lived once undergo apoptosis after a few days. ③ Sam PC migriate to Bone marrow.
3. B1 cells differ from B2 cells ⇒ B1 are primarly found in fetal life.
4. Regarding Affinity maturation ⇒ Increas the strength of Antibody binding, occurs through point mutation in the Ig V genes, Happens in germinal center, leads to selection of high Affinity B-cells.
5. Molecule that is responsible for Signal transduction in B cells ⇒ Immunoglobulin alpha and beta
6. Inovved in T-dependent B-cell activation ⇒ CD40-CD40L, class II MHC, B7 costimulators, cytokine Receptor Expression.
7. The Role of CD40L on Tcells ⇒ Induce isotype switching in B-cells
8. Regarding Memory B-cells ⇒ They have a long lifespan and quickly respond to repeat antigen exposure
9. The enzyme when deficiency Leads to hyper IgM syndrome ⇒ AID
10. B-cell receptor binds to antigen in combination with which coreceptor? ⇒ CR2 (CD21)
11. The CR2:CD19.CD81 complex on Bcells primarily helps in ⇒ Enhancing Antigen binding and signal transduction.
12. About T-cell Independent B2 cells ⇒ Respond to Non-protein Antigens, Dont undergo isotype switching, produce IgM + IgA without Tcell help, Are self-renewing and Found in mucosal tissues.
13. poly morphism in which gene is linked to SLE? FcγRIIB gene.
14. The 1st signal for B-cell activation involved? Receptor + co-receptor bind to Antigen
15. CD21 Bind to? C3d.
16. Co stimulatory Molecule bind CD28 on Th cells? B7-1 (CD80) + B7-2 (CD86)

Making Bcells Not only produce IgM.

* B cell perform Immunoglobin Isotype switching secreting types of AB.
* DNA Recombination ⇒ Molecular Mechanism of isotype switching (just change Constant genes and keep variable by allelic exclusion).
* The Key enzyme required for isotype switching + Affinity Maturation is (AID).
* Deficiancy in ((AID + CD40L)) cause X-linked hyper IgM syndrome.
* For Isotype switching to occur we need 2 things ⇒ protein Antigen (T-dependent B cell activation)
* B-cells in mucosal tissue + secretory glands switch to IgA.
* The Response of most viruses + bacteria involves production of IgG.
* " " " many helminthic parasites and allergenes by IgE.
* Selection :- B cell producing high Affinity AB profite to PC + MC, while Low Affinity Ab die.
* long-Lived plasma cells ⇒ generated in T-dependent germinal center response to protein Ag.
* Short- " " " ⇒ Rapidly formed in 2ry Lymphoid organs then go apoptosis a few days.
* Memory cells ⇒ high Level of anti-apoptotic protein BCL-2 which contributes to their long life span high in CD27 protein.
* B1 ⇒ Response to non-protein Antigens (Lipid, Carb.) Found in peritonium + Mucosal sites. and don't require T-helper lymphocytes, There response are elicted by engagment of B-cell R (Receptor) with AG and by activation of TLRs by PAMPs derived from microbes.
* Primary Response ⇒ IgM * Secondry Response ⇒ IgG
* CR2 + CD19 + CD81 ⇒ called Bcell coreceptor complex
* CD21 bind complent proteins C3d on microbe, C19 transduces the signal
* CD81 ⇒ Stabilization for molecules, Immunoglobin (α + β) do Signal transduction.
* CD40 is glycoprotein on B-cell bind to CD40L on Tcell ⇒ B-cell activation + isotype switch.
* CD32 ⇒ help in -ve Feedback Inhibition. + CD22

* Before Activation B-cell can only secrete IgM + IgD
* A polymorphism in CD3ζ gene has linked to autoimmune disease systemic Lupus erythematosus (SLE)
* T-Independent B-cell Activation ⇒ Mainly IgM AB are produced by Plasma cells, without help of T-cell, For activating B-cell :- 2 signals
- 1st ⇒ clustring of B-cell receptor on Antigen Recognation + derived from 2nd signal other molecules of Antigen.
* T-Dependent B-cell Activation ⇒ Require T-cell help / 3 signal processes
1st ⇒ Antigen Recognation and binding by B-cell = Mature naive B-cell regocnize AG, MHC II peptide complex, Co-stimulatory R (CD40), Same AG Activate T-helper cell
2nd ⇒ B (Bcell) and T (T-helper) Interactions (Antigen) (CD40 - CD40L binding)

3rd ⇒ Cytokine (Release) help by t helper cells. Cytokine e.g (IL-4) bind to Cyto-kine R present on B-cell, so B-cell start to proffereate to plasma cells + MC