B cell activation

The activation of B cells results in their proliferation and differentiation into antibody-secreting plasma cells and memory cells

Overview of B cell activation

① T-dependent

CD4+ T cell help required

Class switch and SHM

② T-independent (Special cases)

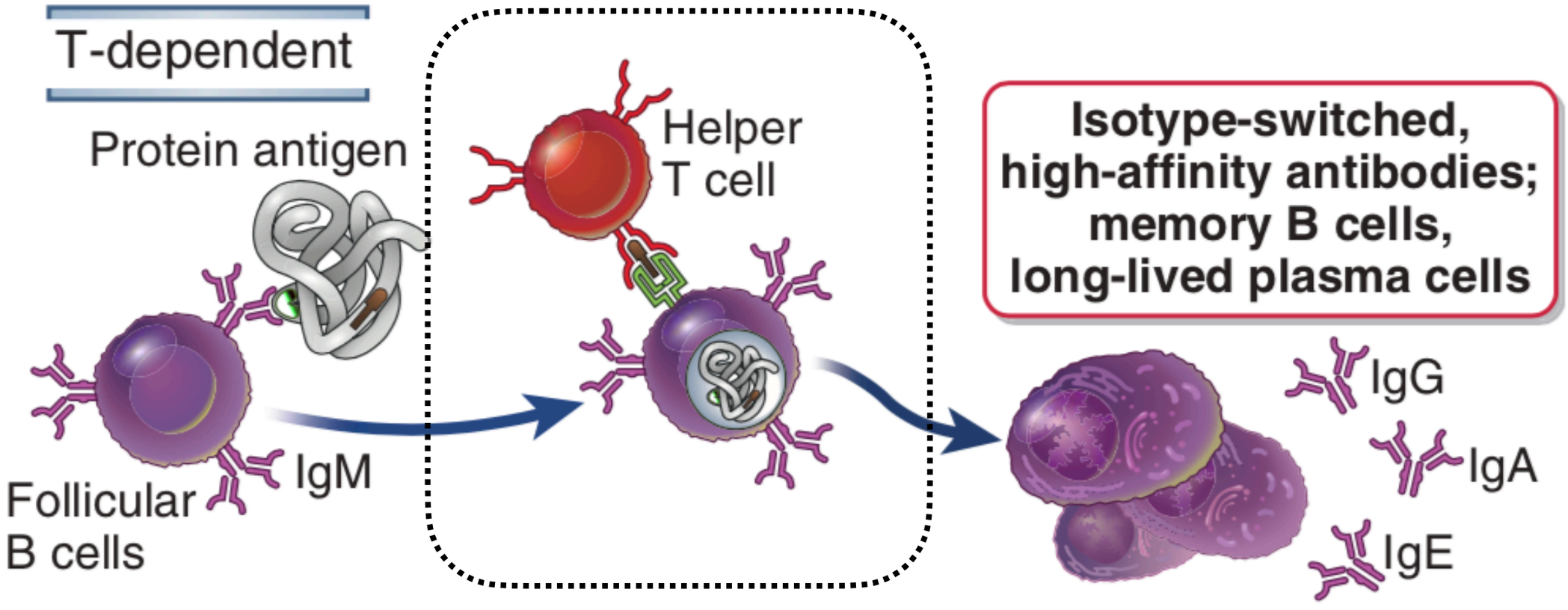
No need of T cell help

No class switch or SHM

T-dependent B cell responses

Follicular B cells (lymphoid organs and blood) - <u>protein antigens</u>

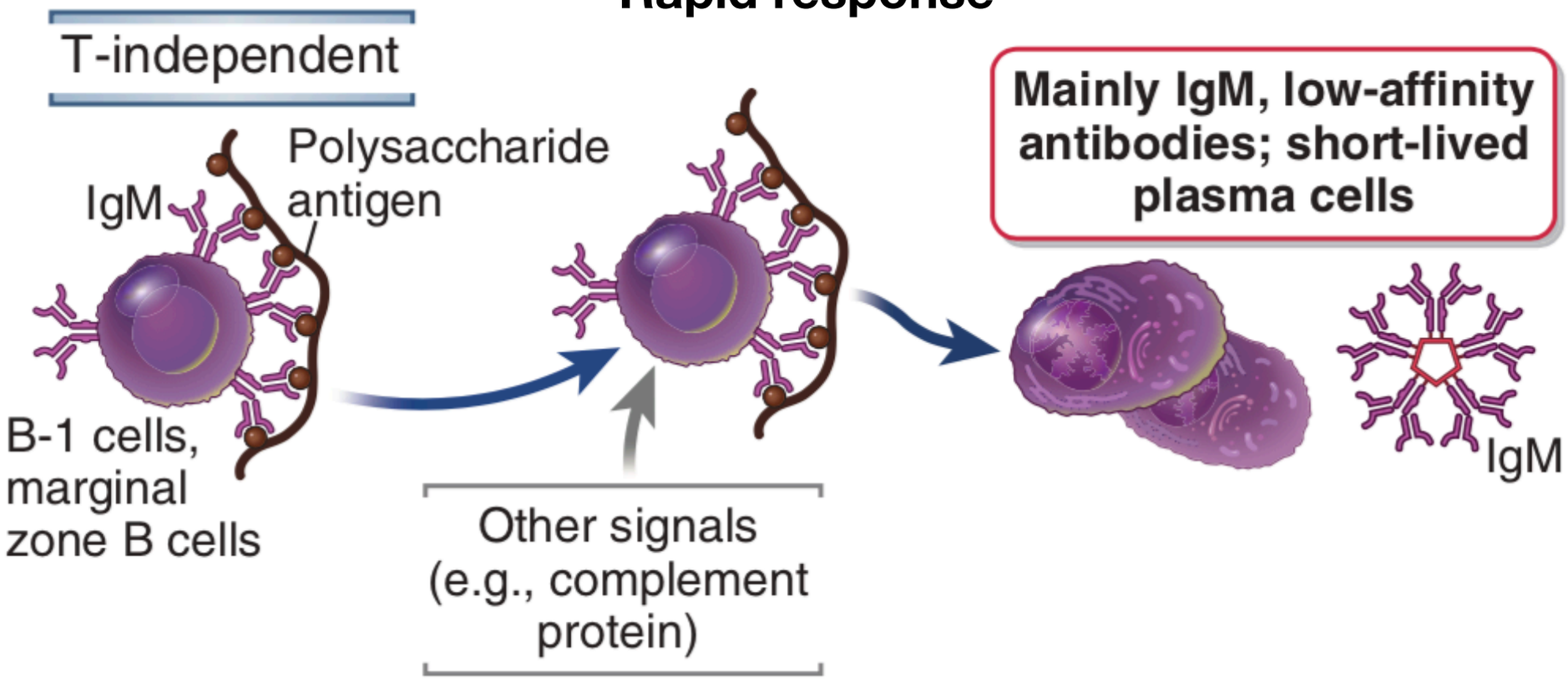
$CD4^+$ T cell help



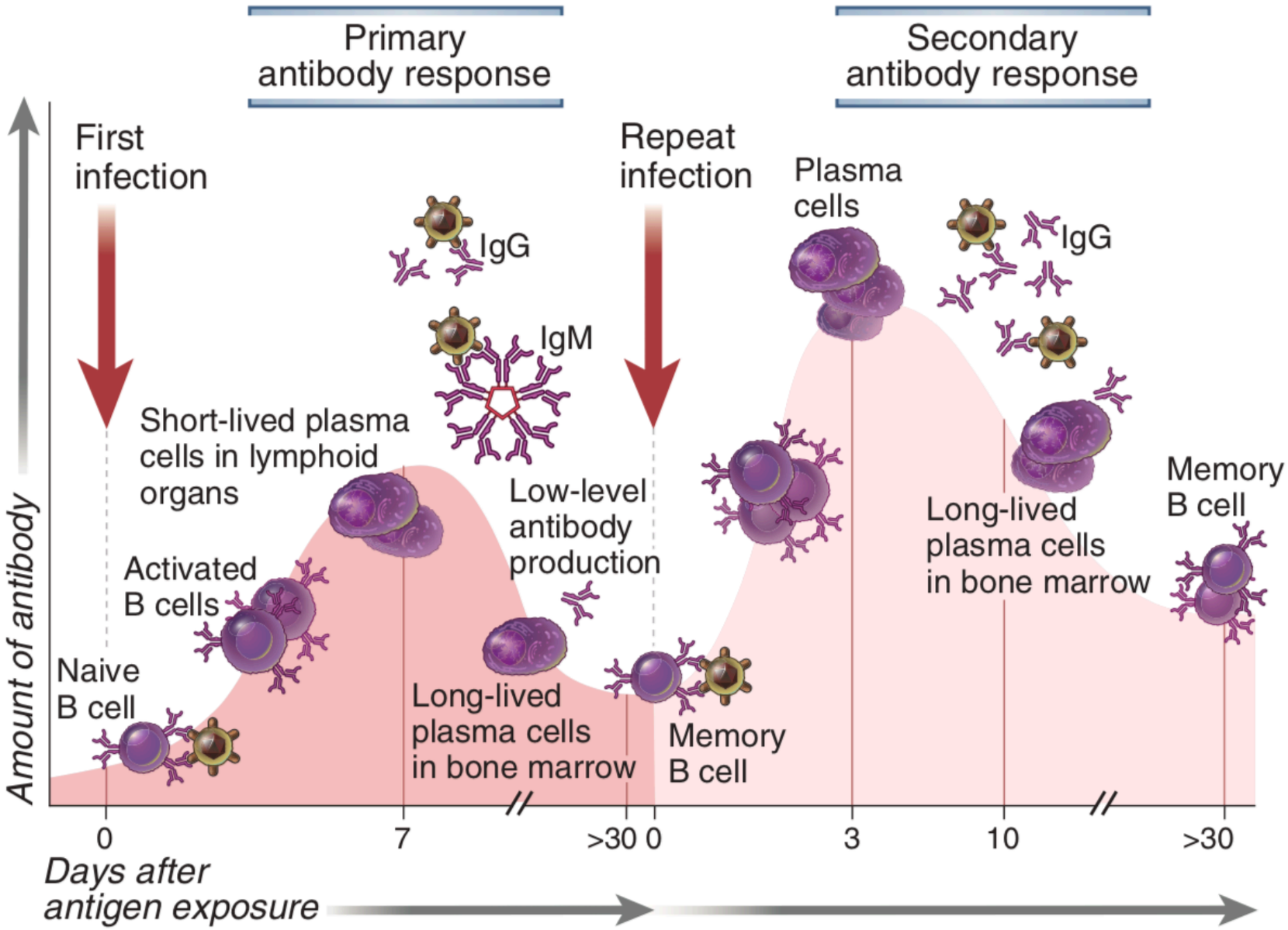
T-independent B cell responses

B1(peritoneal and pelvic cavity) and marginal zone B cells (spleen) - <u>multivalent antigens</u>

Rapid response



Primary and secondary T-dependent B cell responses are different



Primary and secondary T-dependent B cell responses are different

Feature	Primary response	Secondary response
Magnitude	Smaller	Larger
Antibody isotype	Usually IgM > IgG	Relative increase in IgG and, under certain situations, in IgA or IgE
Antibody affinity	Lower average affinity, more variable	Higher average affinity (affinity maturation)
Induced by	All immunogens	Only protein antigens

Antigen capture and delivery

Antigens can reach B cells in lymphoid organs via many routes, depending on their **size** and **complement binding**:

With the lymph, via the afferent lymphatic vessels

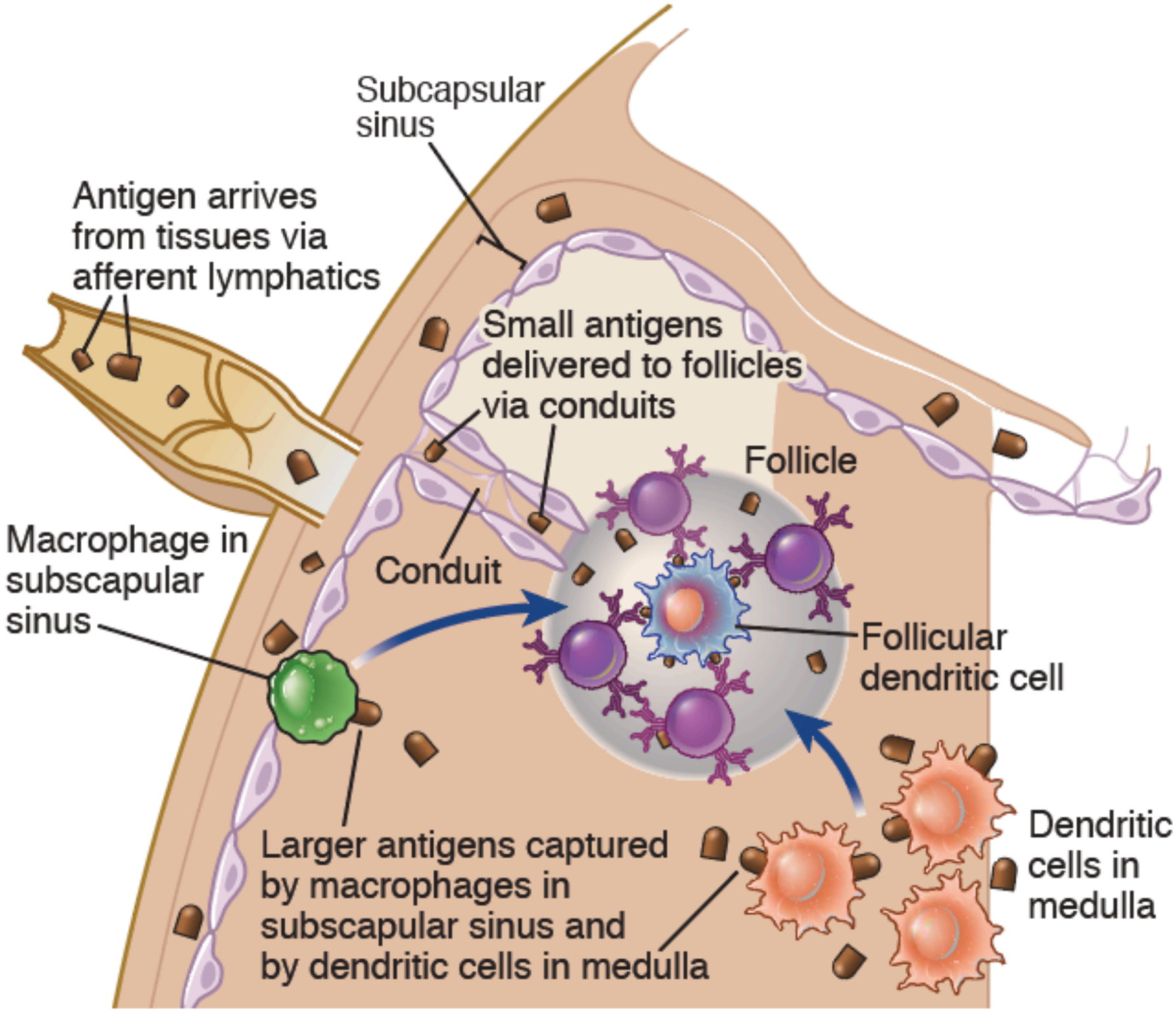
- Small antigens (<70 KDa) enter conduits and reach the follicle

- Larger antigens are captured by subcapsular sinus macrophages

- Antigen is captured by medullary dendritic cells in the medulla, and then transported to follicles

- Antigen in immune complexes bind to complement receptors (CR2 expressed on FDCs, and marginal zone B)

Antigen capture and delivery

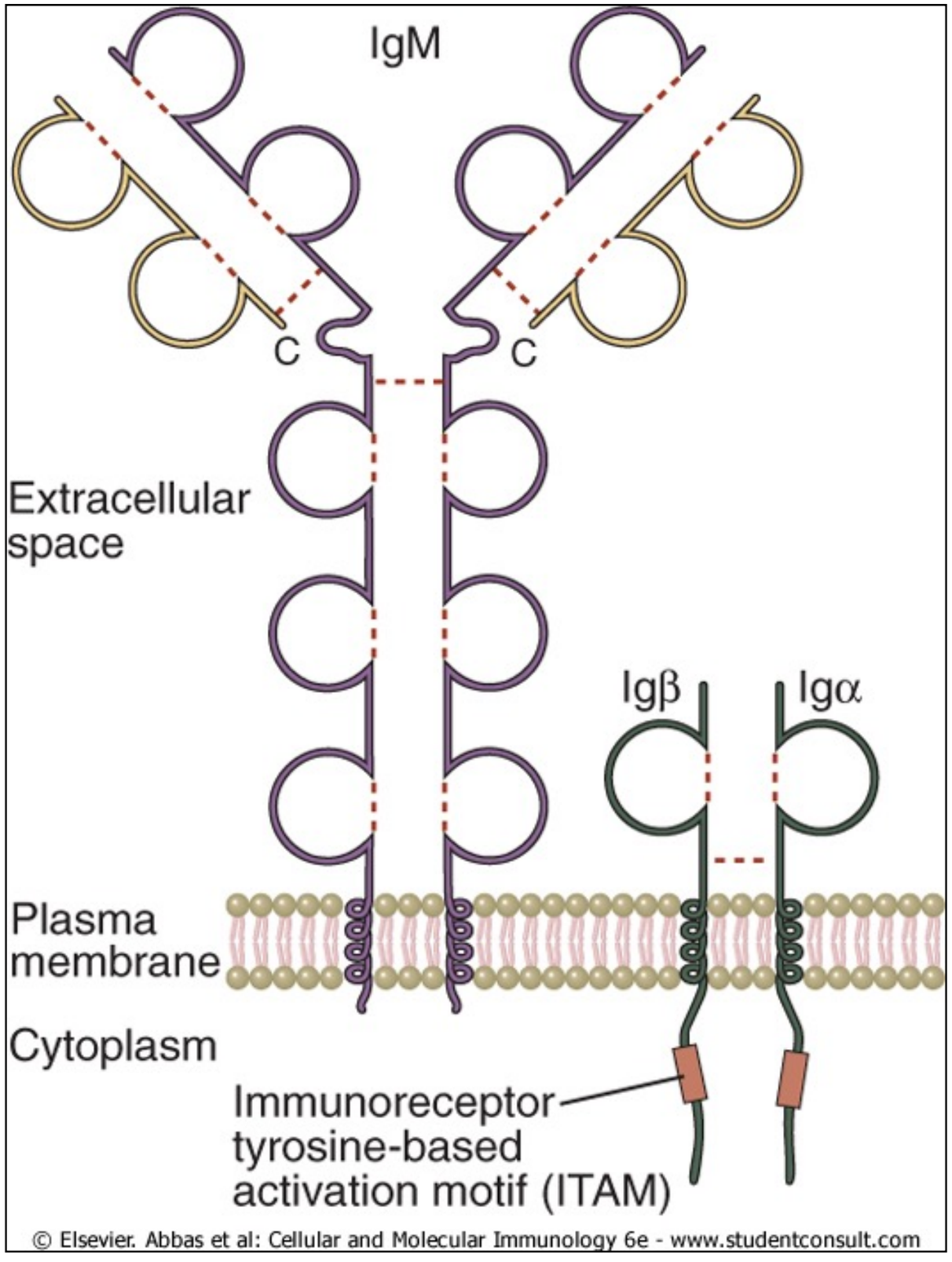


Antigen capture and delivery

Regardless of the route of antigen delivery, B cells recognize - thanks to their BCRs - antigens that are NOT processed

? subcapsular sinus macrophages ? medullary DCs?
Why not????

BCR



B cell activation

Antigen binding to the BCR leads to:

1. Intracellular signaling that initiates B cell activation

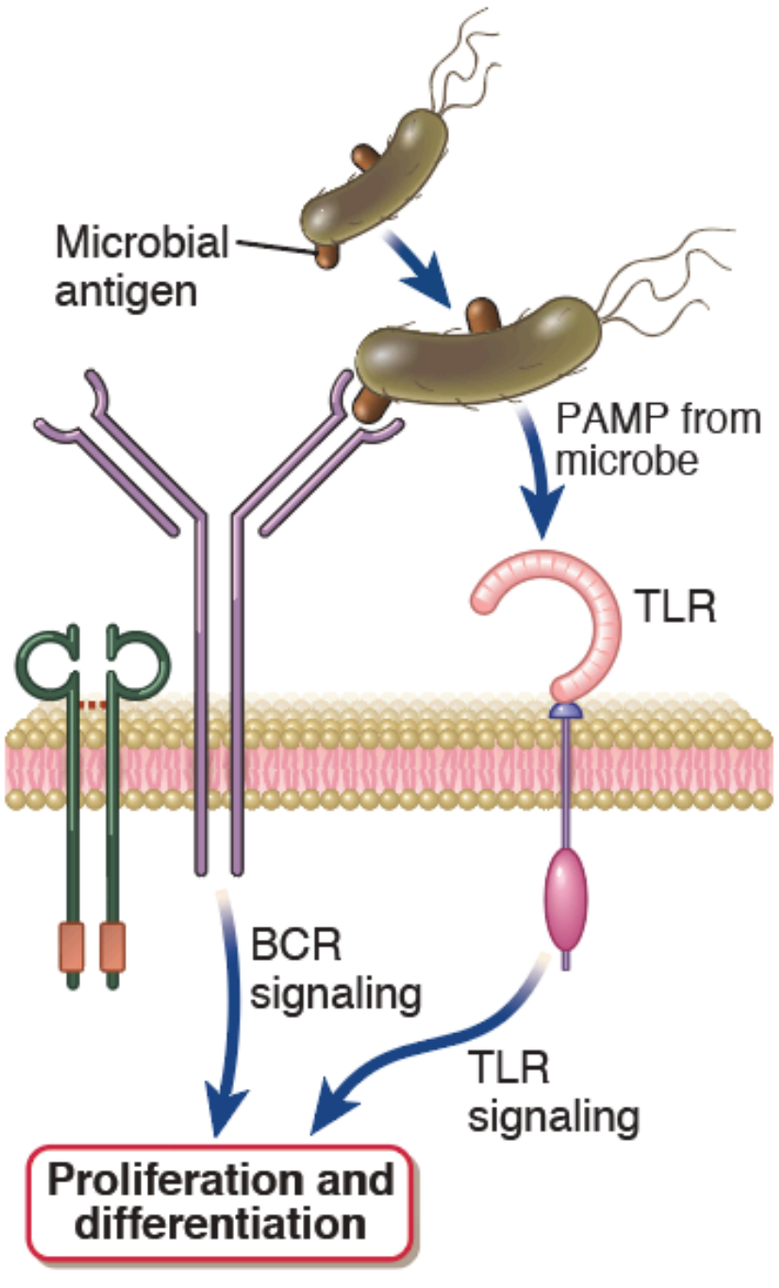
if signal strong enough, T cell help is not needed, more strong for T independent

2. Antigen internalization and presentation on MHC-II

Not sufficient

⇨ Potential recognition by PRRs

BCR signaling is enhanced by PRR activation



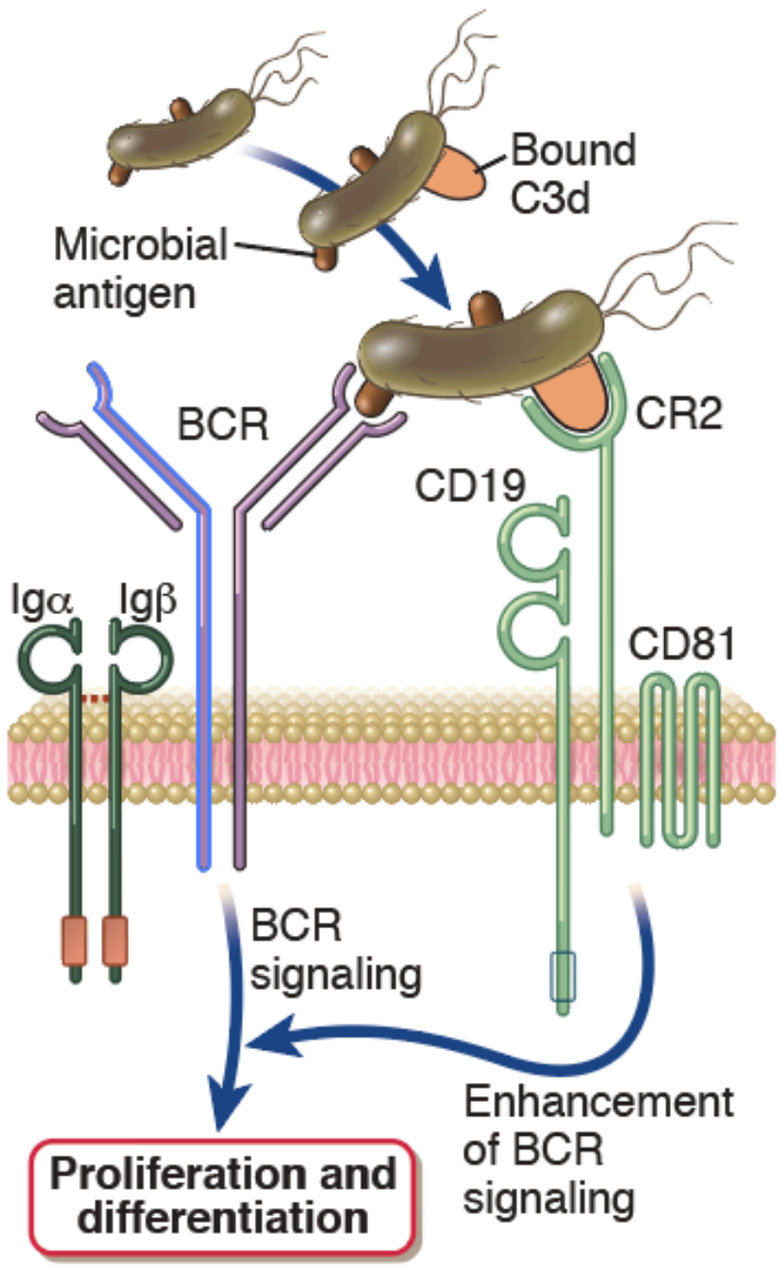
BCR does not signal by itself

BCR associated with **Igα** and **Igβ**, which are responsible for signaling upon BCR crosslinking

Crosslinking = both antigen binding sites engaged in interaction

Simultaneous PRRs signaling (e.g. TLRs) enhances B cell stimulation

BCR signaling is enhanced by complement recognition via CR2



CR2 expressed by B cells (higher expression in marginal zone B cells) also leads to activation signaling when C3 is recognized

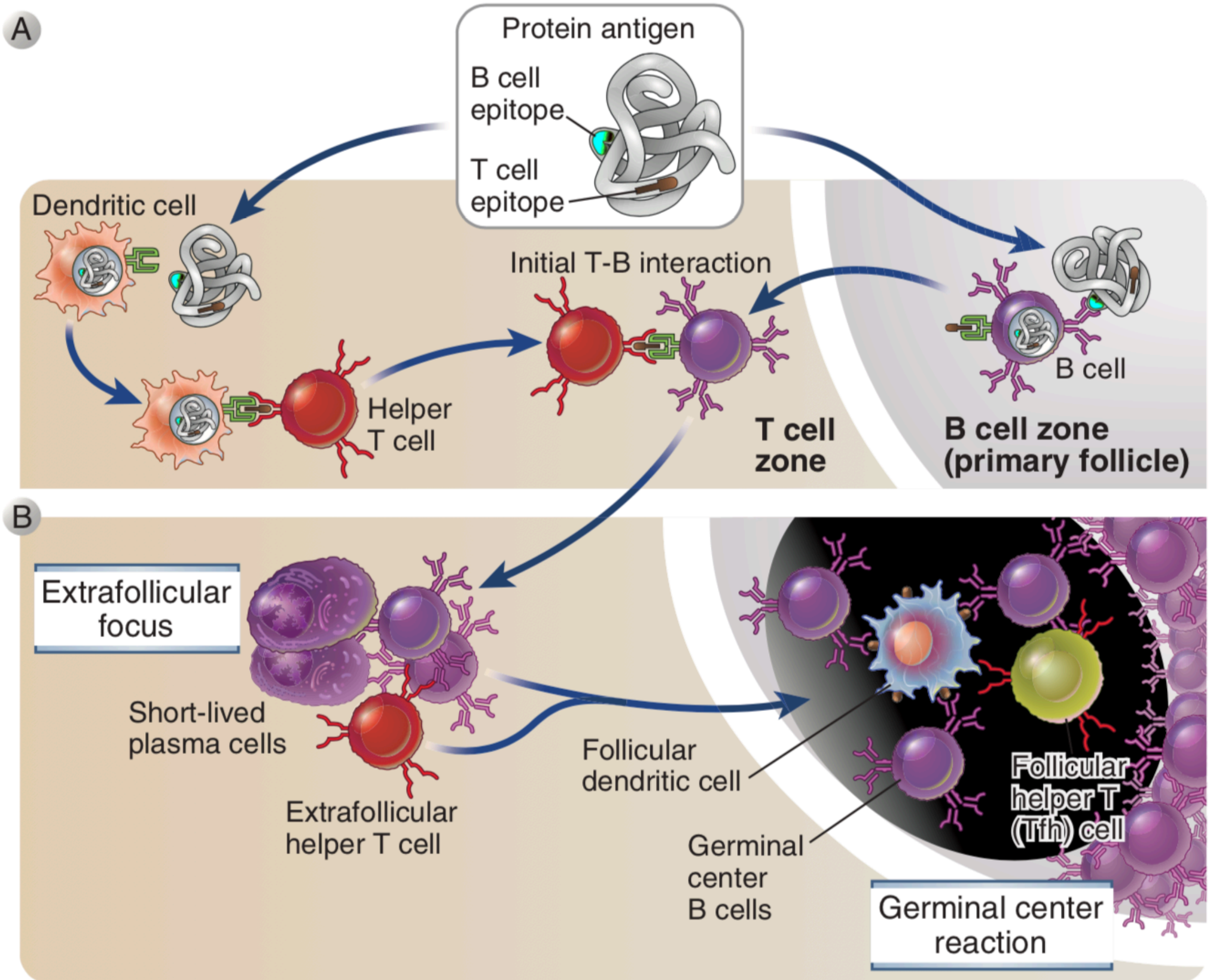
If these signals are strong enough, B cells proliferate

T-independent responses are induced by

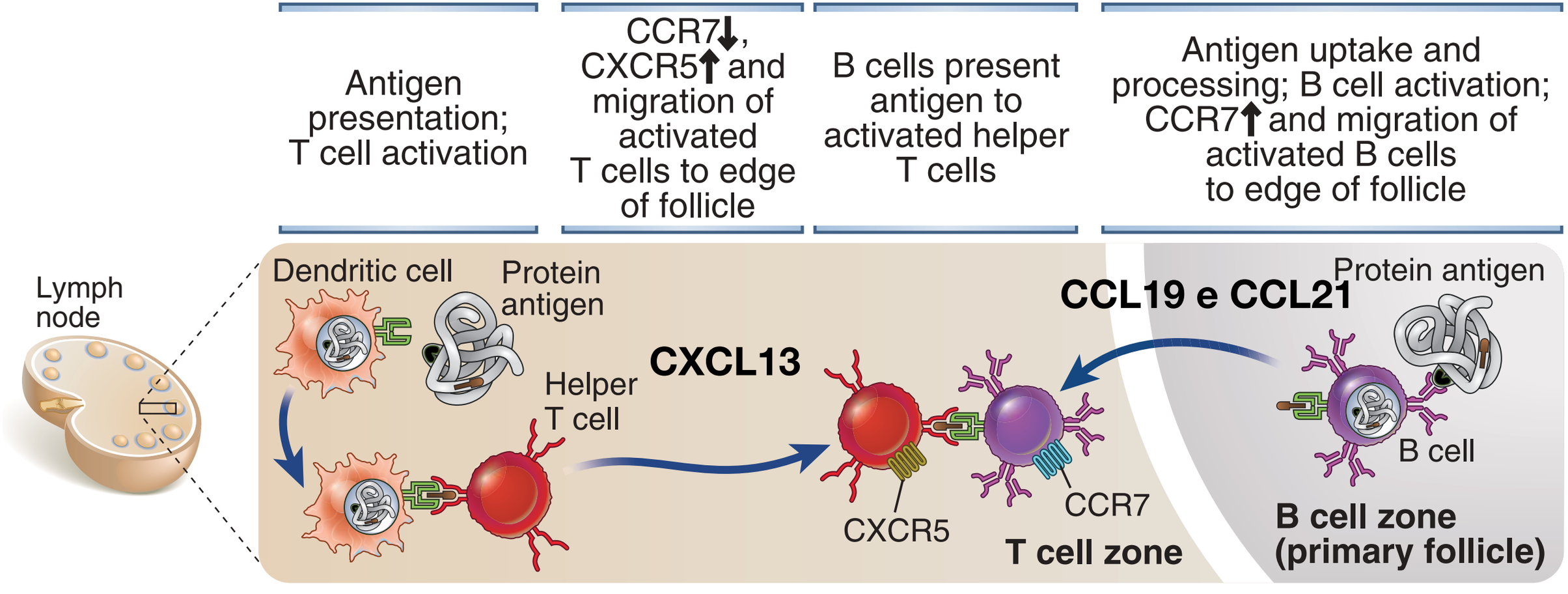
- Strong TLR agonist as LPS

- Multivalent antigens, e.g. polysaccharides

SEQUENCE OF EVENTS IN HUMORAL IMMUNE RESPONSES TO T CELL-DEPENDENT PROTEIN ANTIGENS

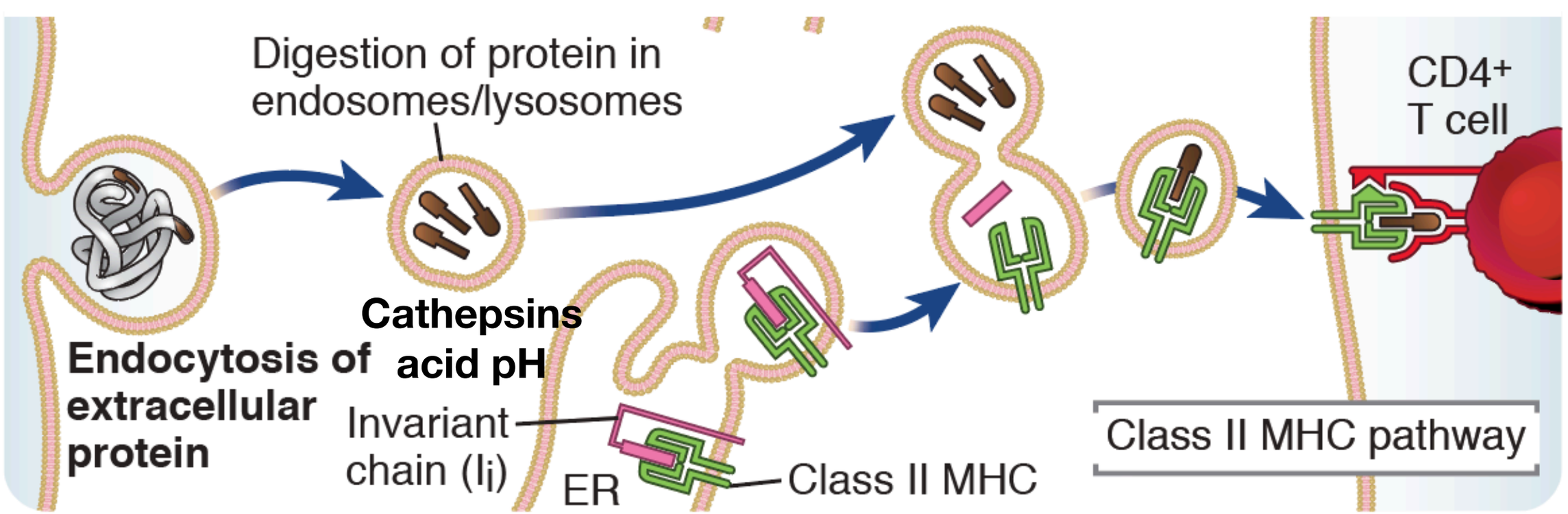


Migration of B cells and helper T cells and T-B interaction



MHC-II: peptide processing and loading

Antigen uptake	Antigen processing	MHC biosynthesis	Peptide-MHC association

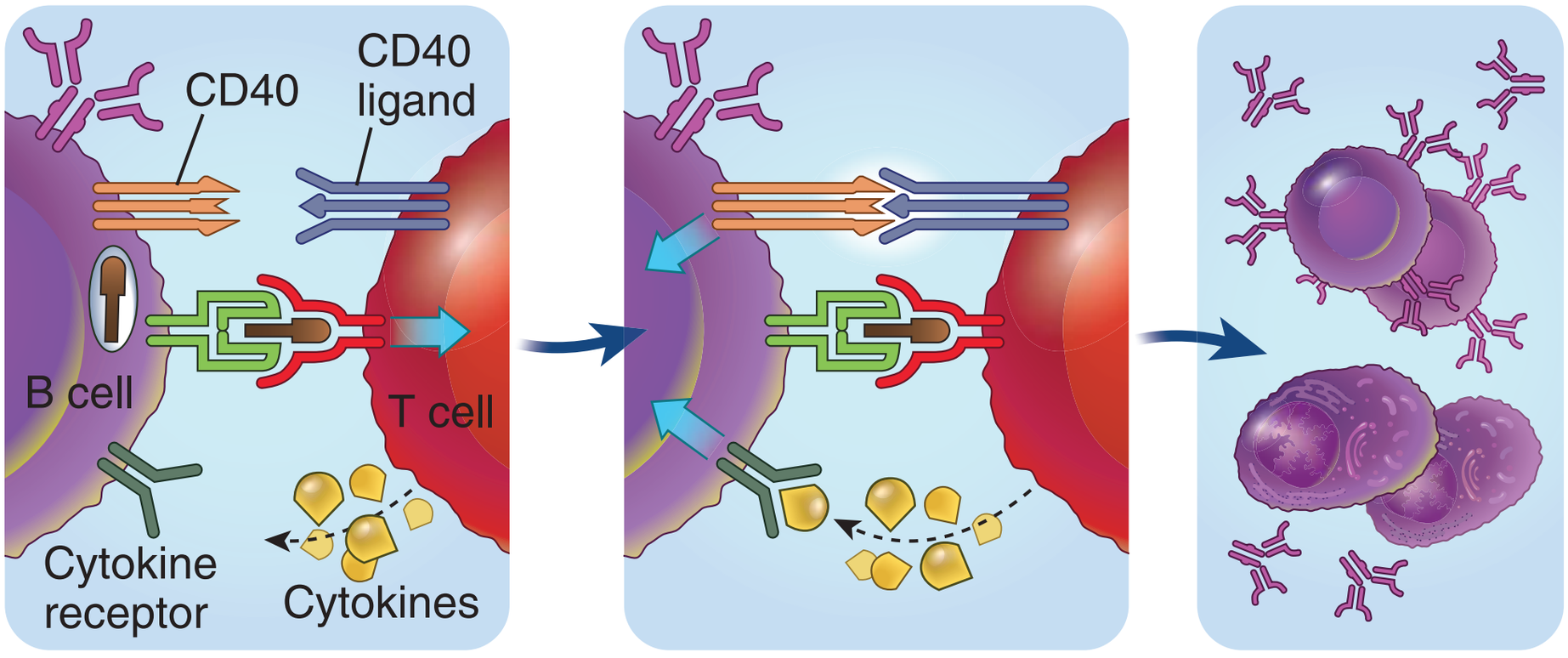


Mechanism of helper T cell mediated B cell activation

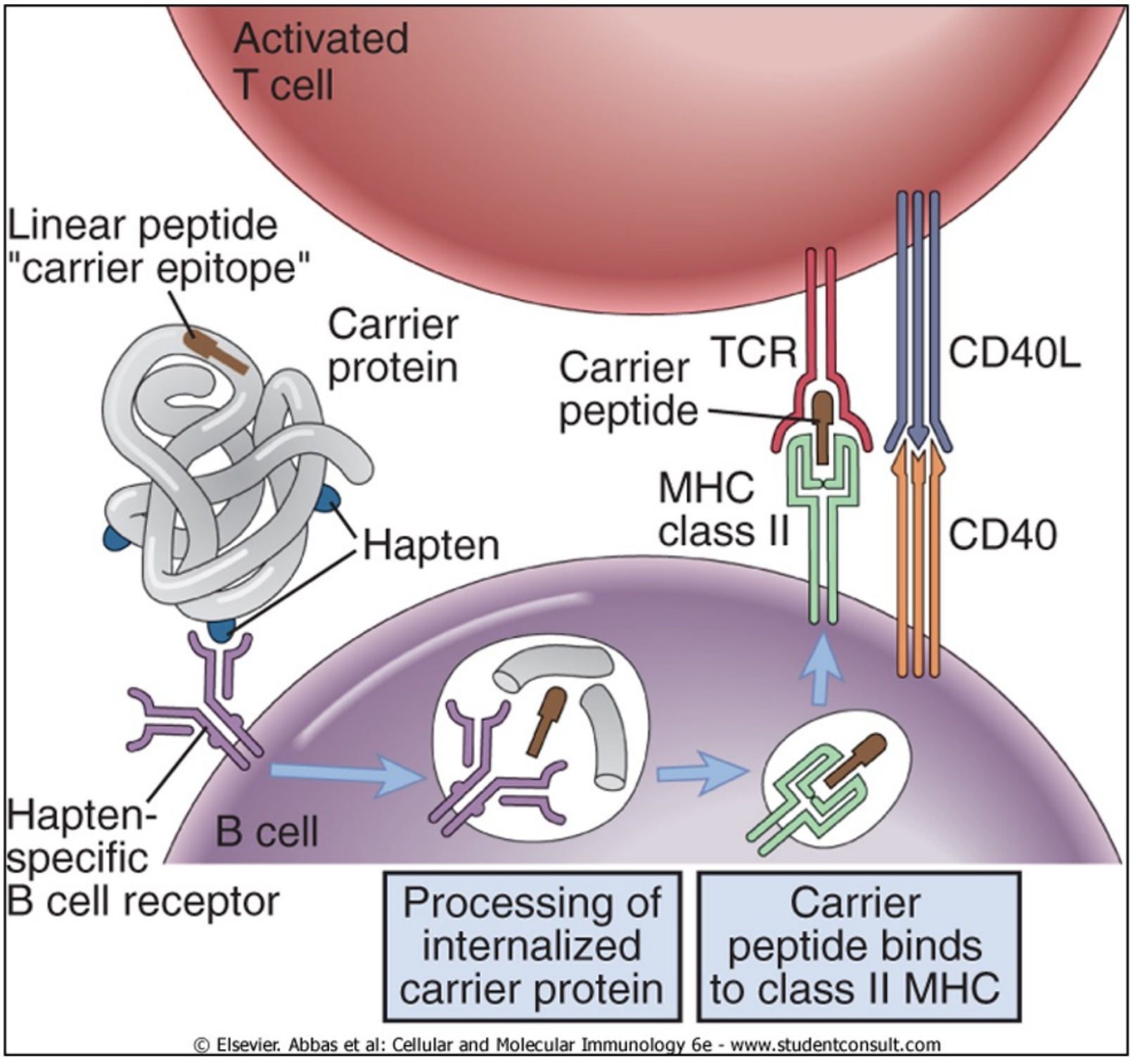
Activated helper T cell expresses CD40L, secretes cytokines

B cells are activated by CD40 engagement, cytokines

B cell proliferation and differentiation



Hapten-carrier effect



The germinal center reaction in a lymph node