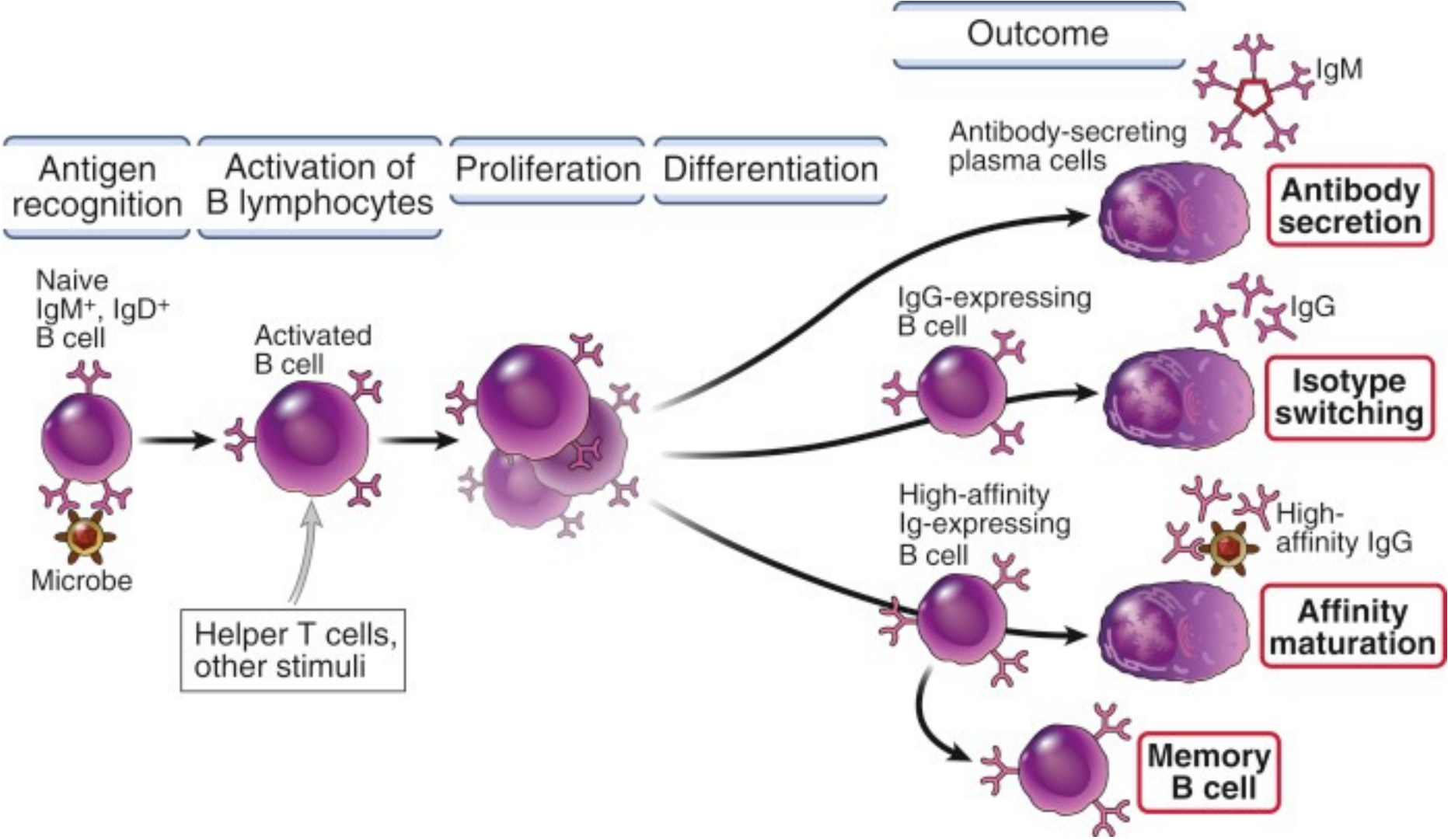


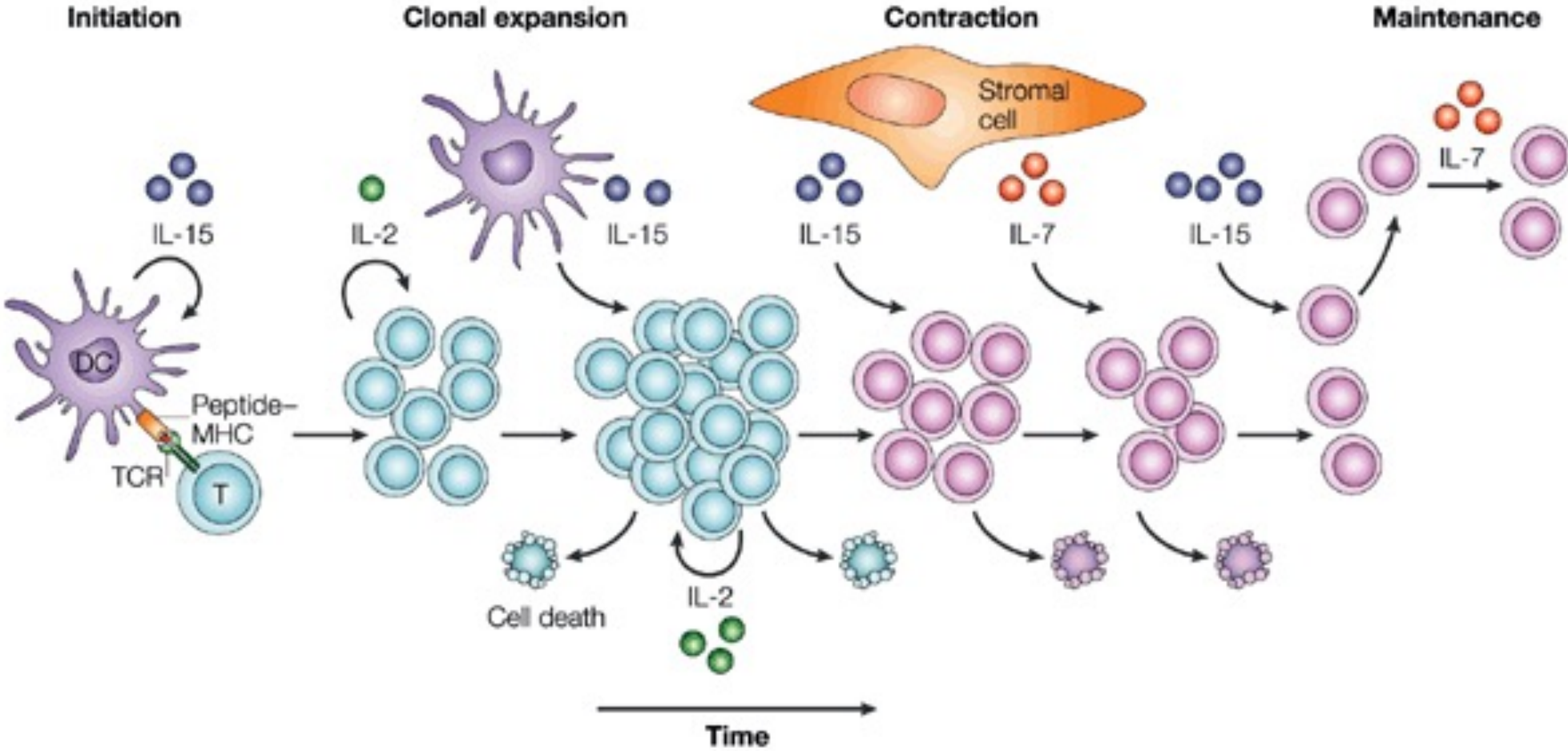
BMI5905

Lymphocyte activation and peripheral tolerance

Lymphocyte activation - clonal expansion, differentiation, effector mechanisms, control/regulation

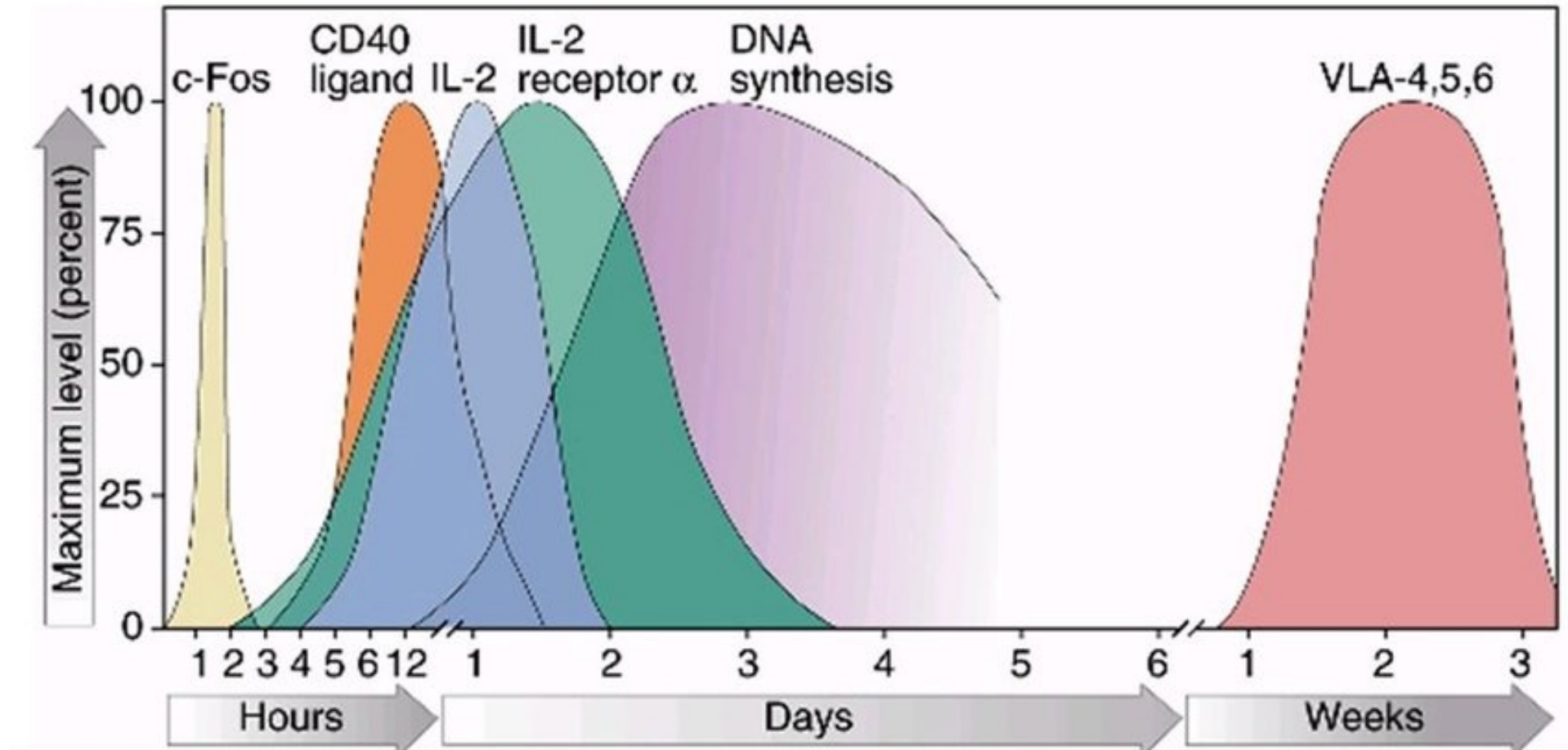


# Lymphocyte activation - clonal expansion, differentiation, effector mechanisms, control/regulation



Schluns, K., Lefrançois, L. Cytokine control of memory T-cell development and survival. *Nat Rev Immunol* 3, 269–279 (2003). <https://doi.org/10.1038/nri1052>

# Activation kinetics



## Adaptive responses activation requires 2 signals

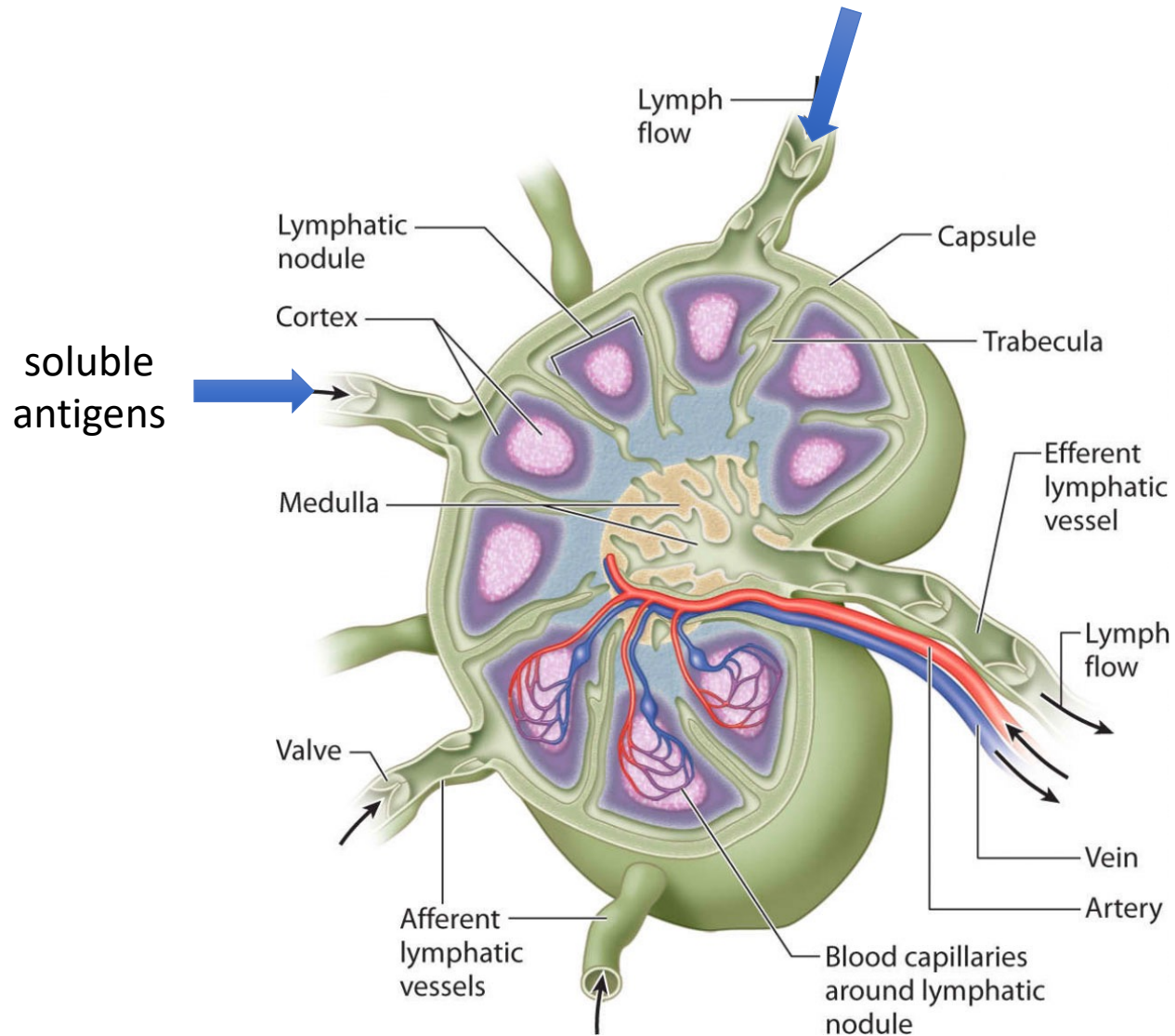
Antigen

Recognized by BCR or TCR

Co-stimulus/stimuli

Biochemical signals that indicate danger  
(receptors that activate PI3K and other  
signaling pathways that guarantee activation  
and cell survival)

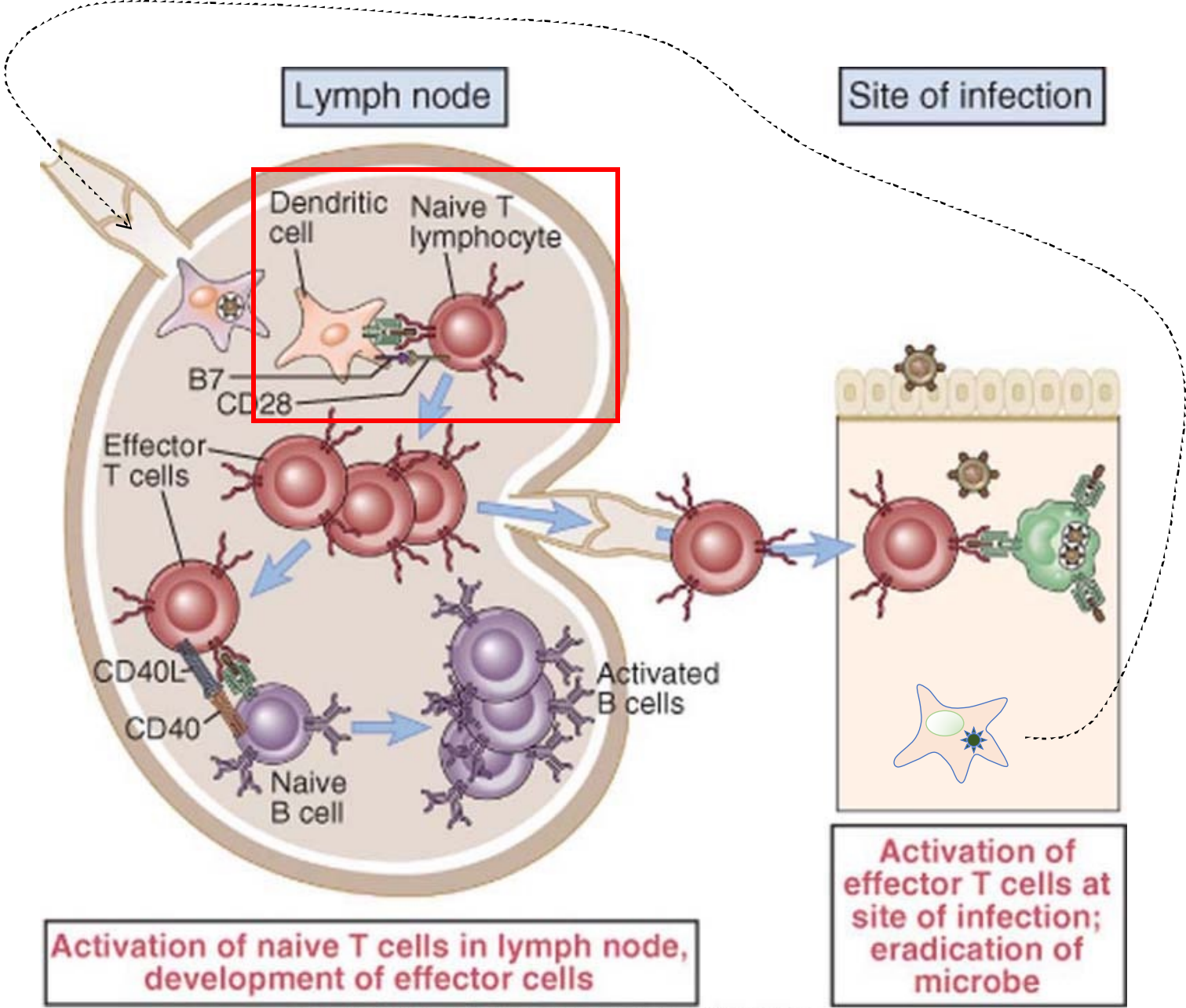
# Activation usually takes place in secondary lymphoid organs



[http://www.youtube.com/watch?v=Kh-XdNnTZUo&feature=player\\_embedded](http://www.youtube.com/watch?v=Kh-XdNnTZUo&feature=player_embedded)

T cell activation

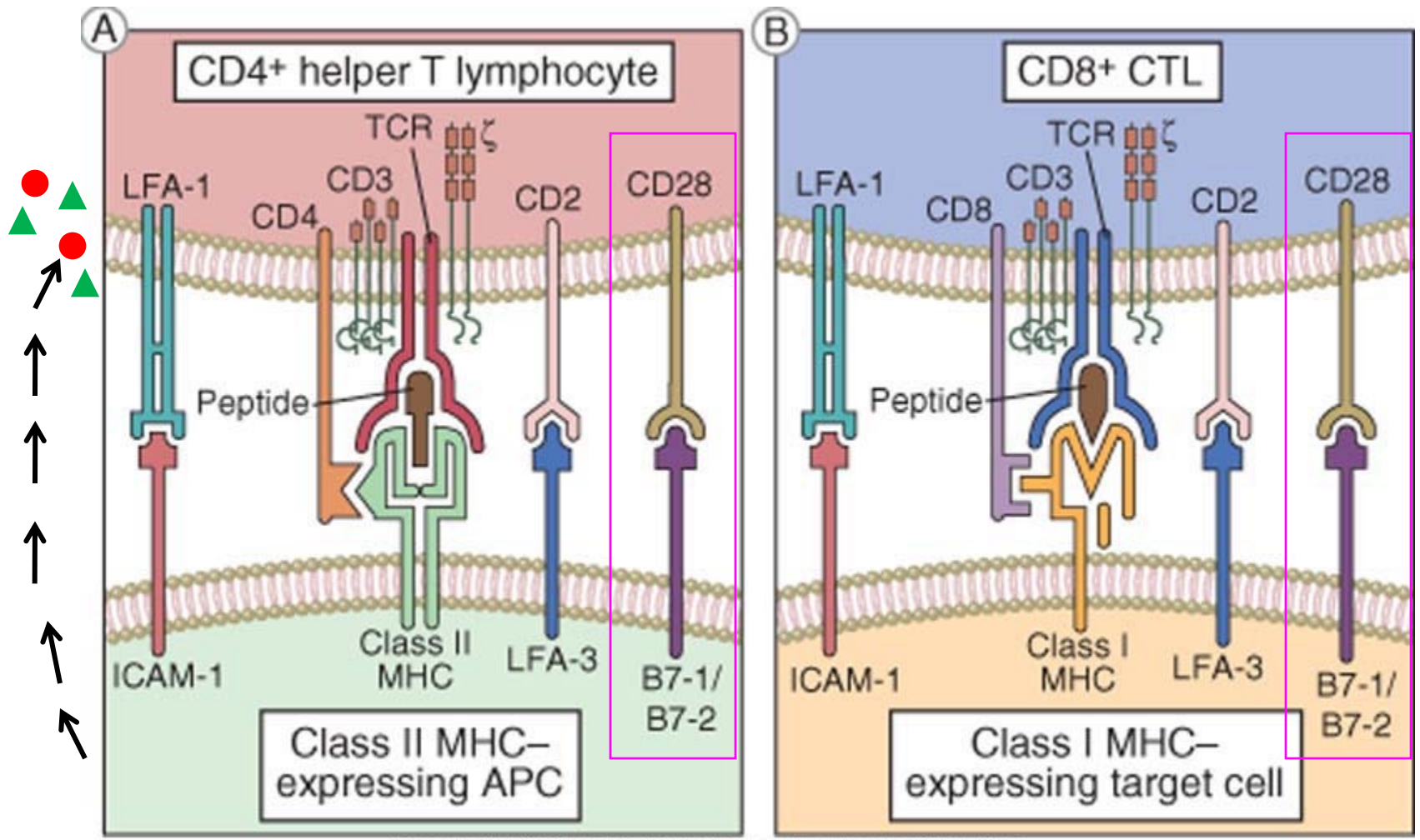
# Lymphocyte activation takes place in peripheral lymphoid organs





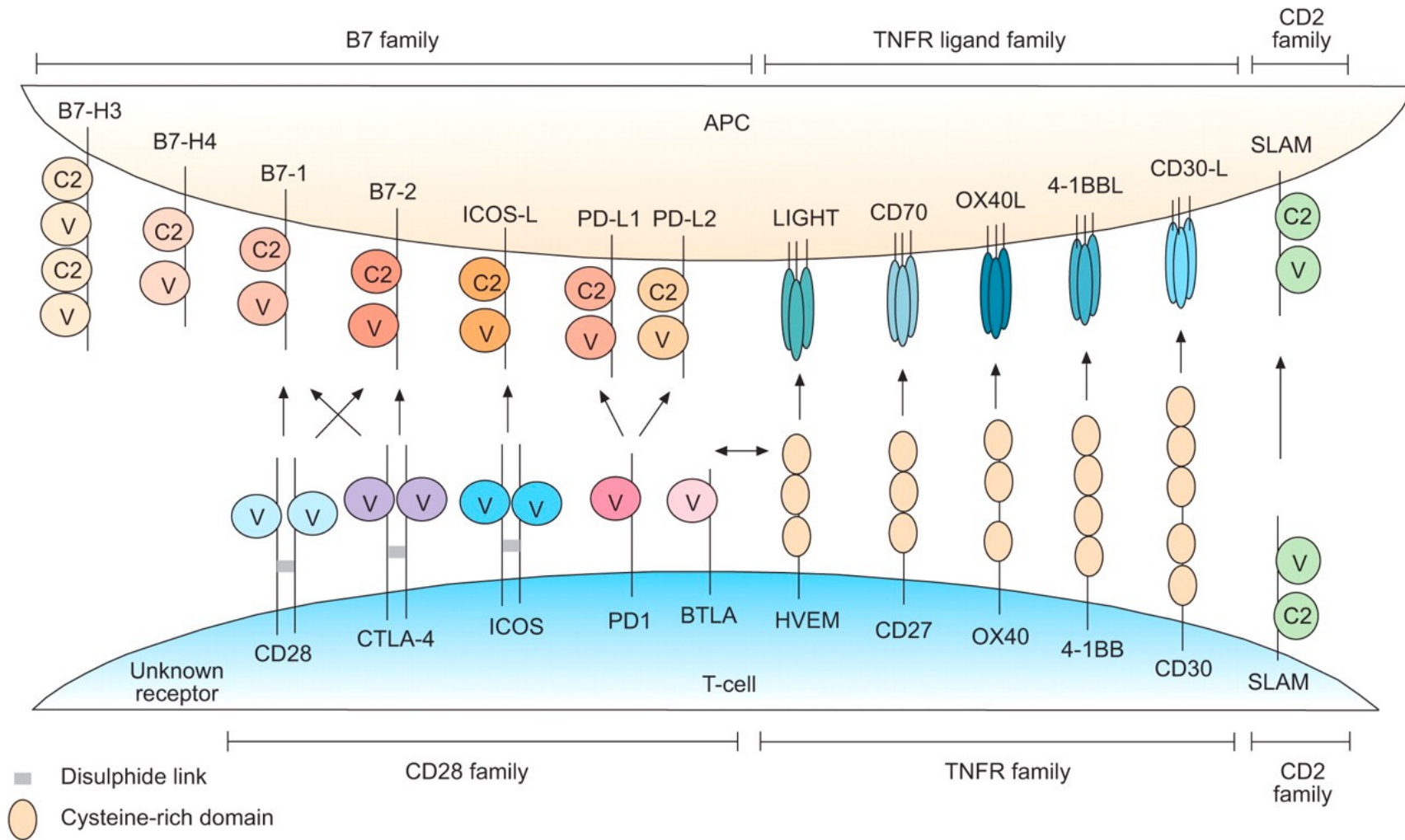
# Immunologic synapse

between antigen presenting cells and T cells  
between T cells and target cells

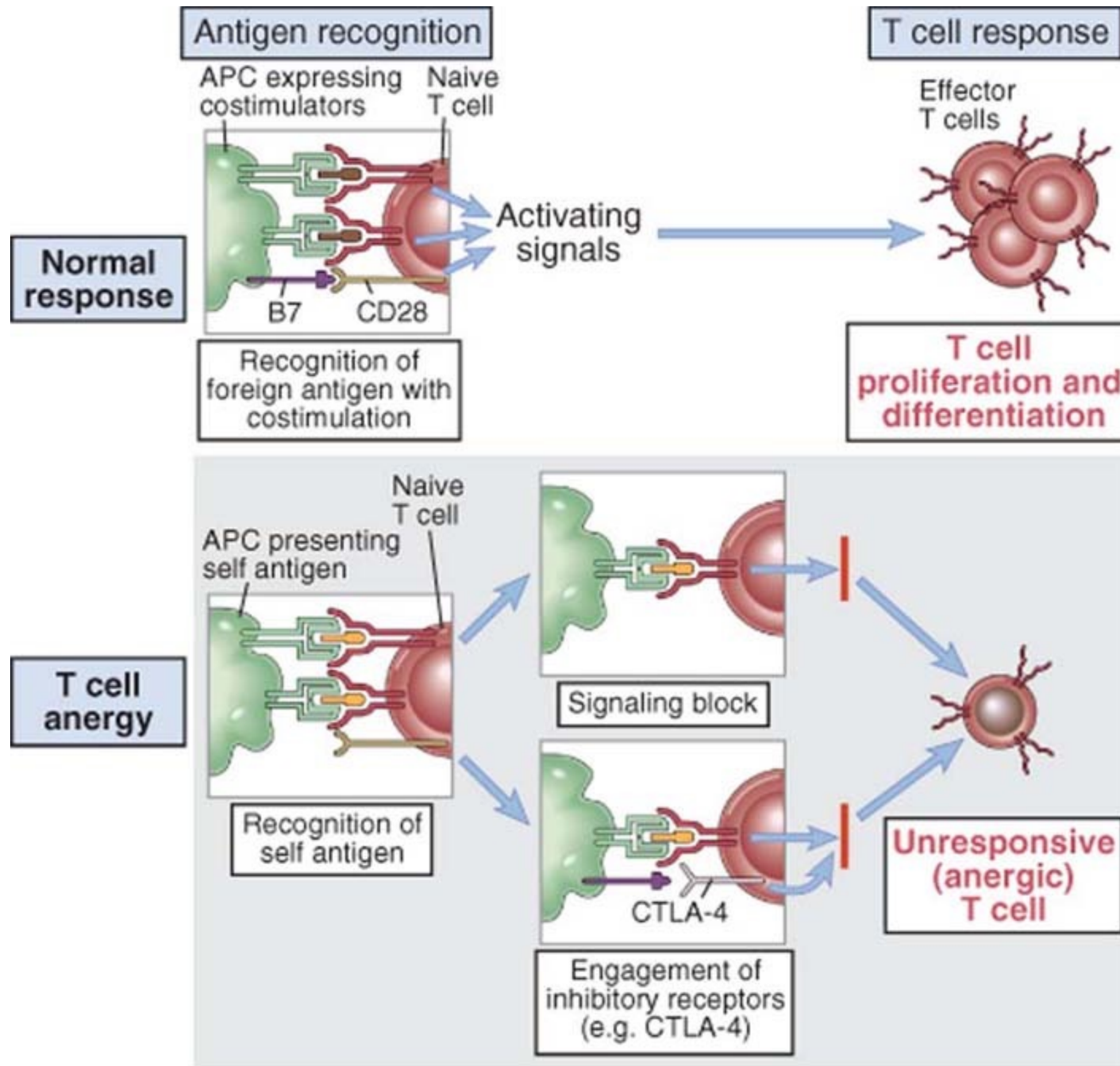


Abbas et al: Cellular and Molecular Immunology, Updated 6th Edition.  
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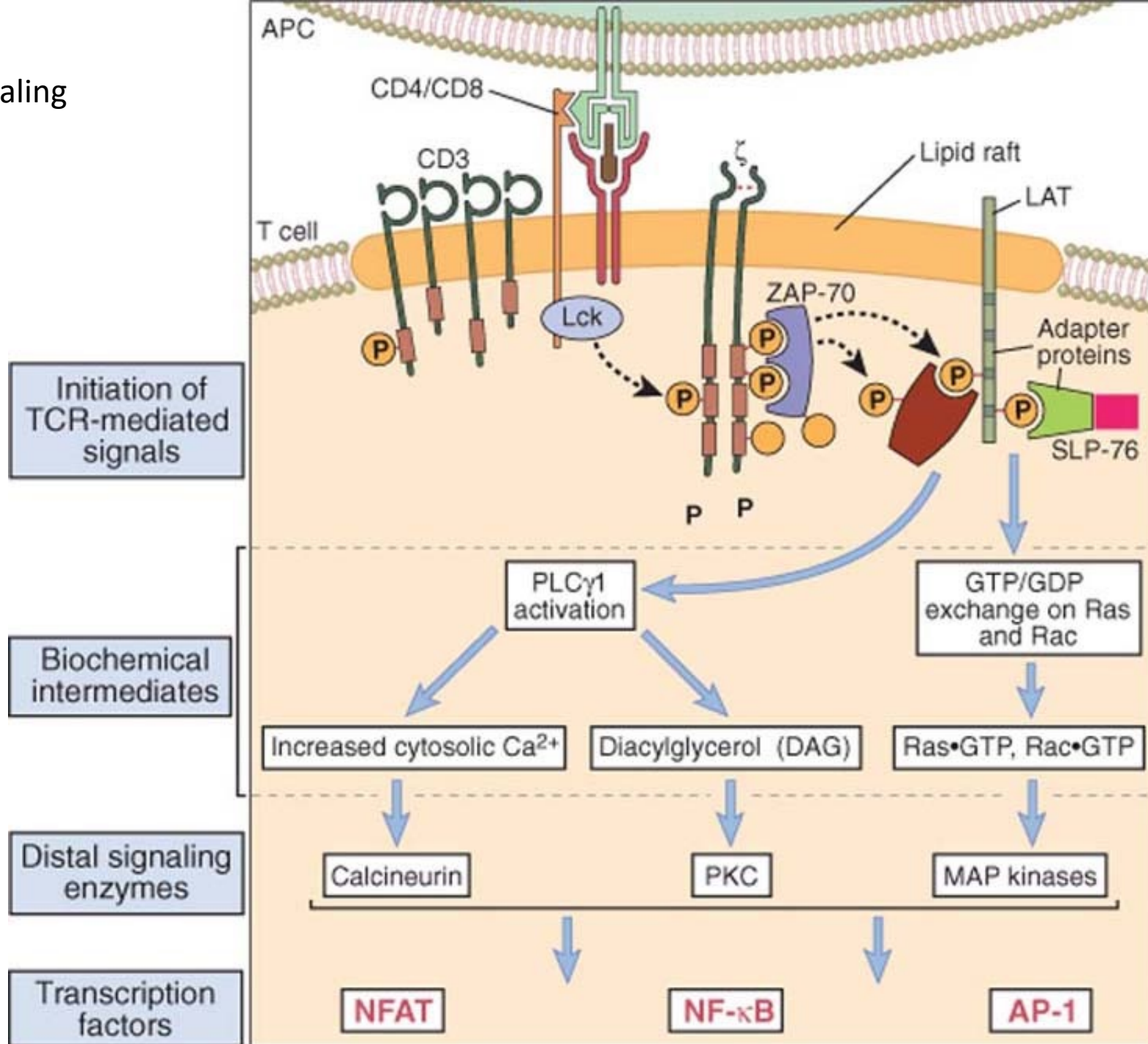
# Costimulatory molecules families



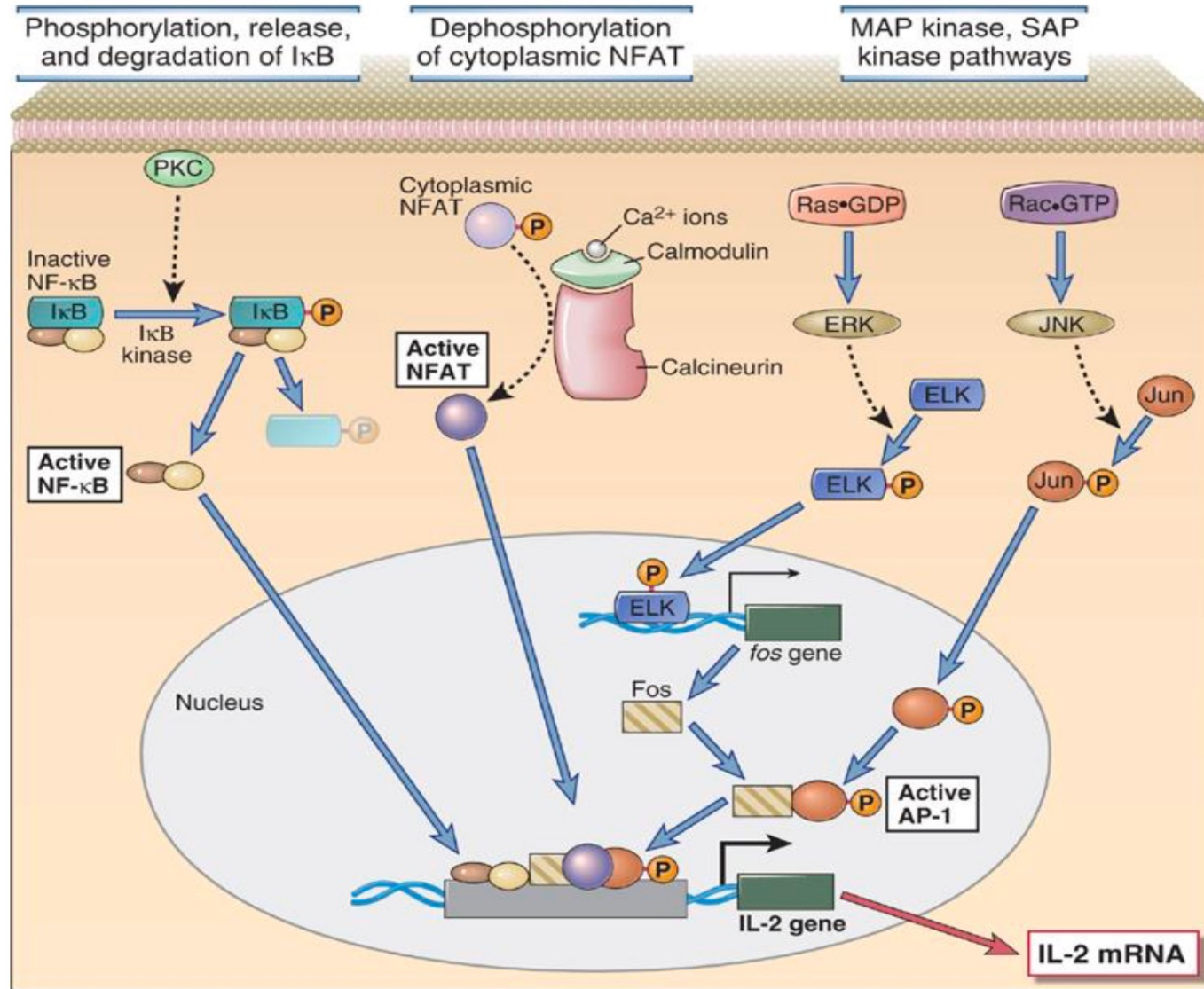
Activation x energy



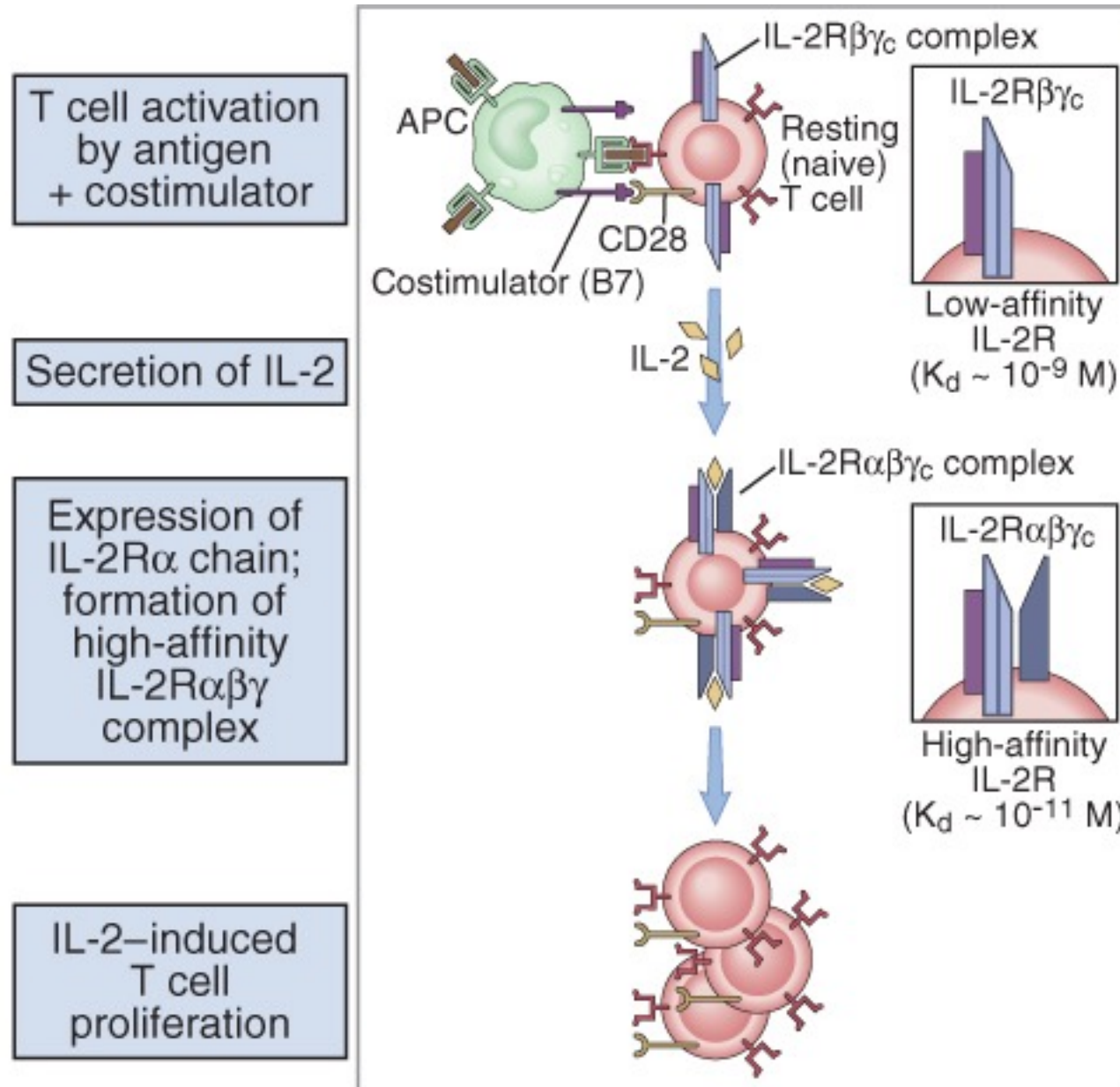
# Activation and signaling



TCR signaling promotes IL-2, a key growth factor for lymphocytes, expression

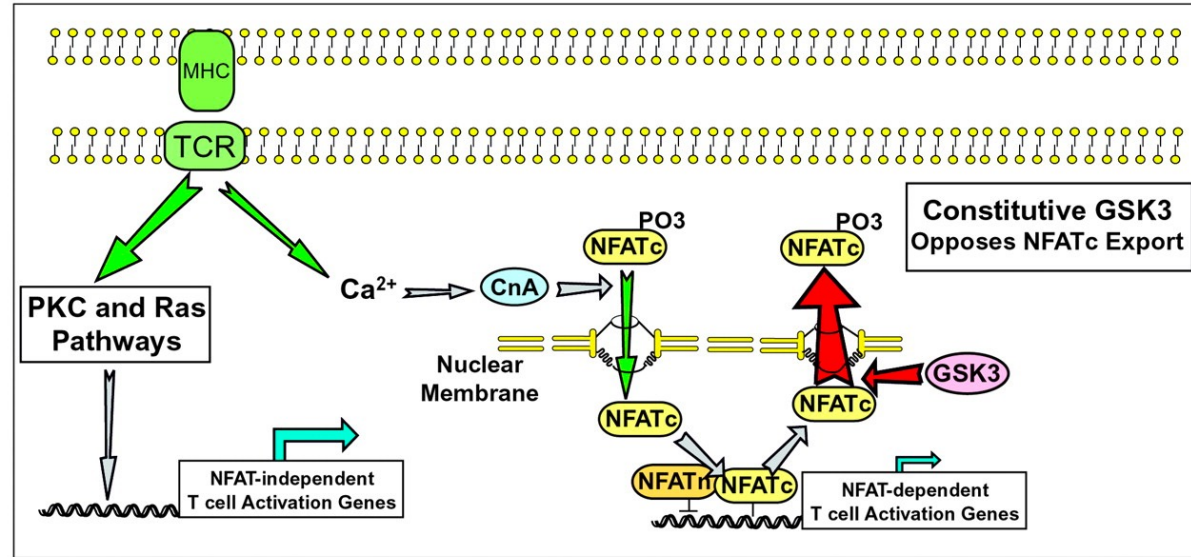


## IL-2 and its receptors

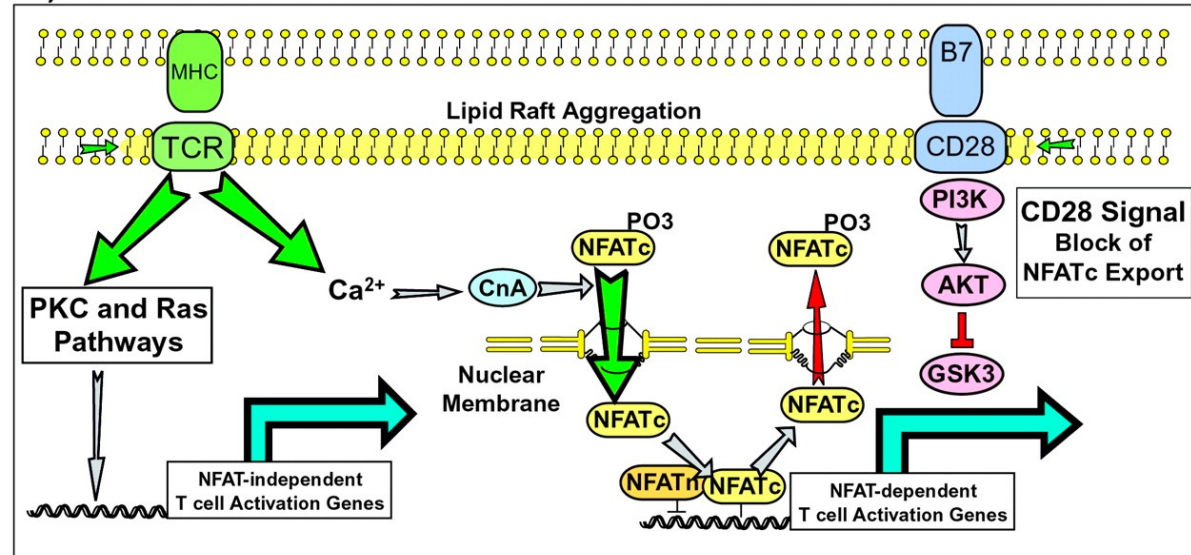


# Costimulus and TCR signaling

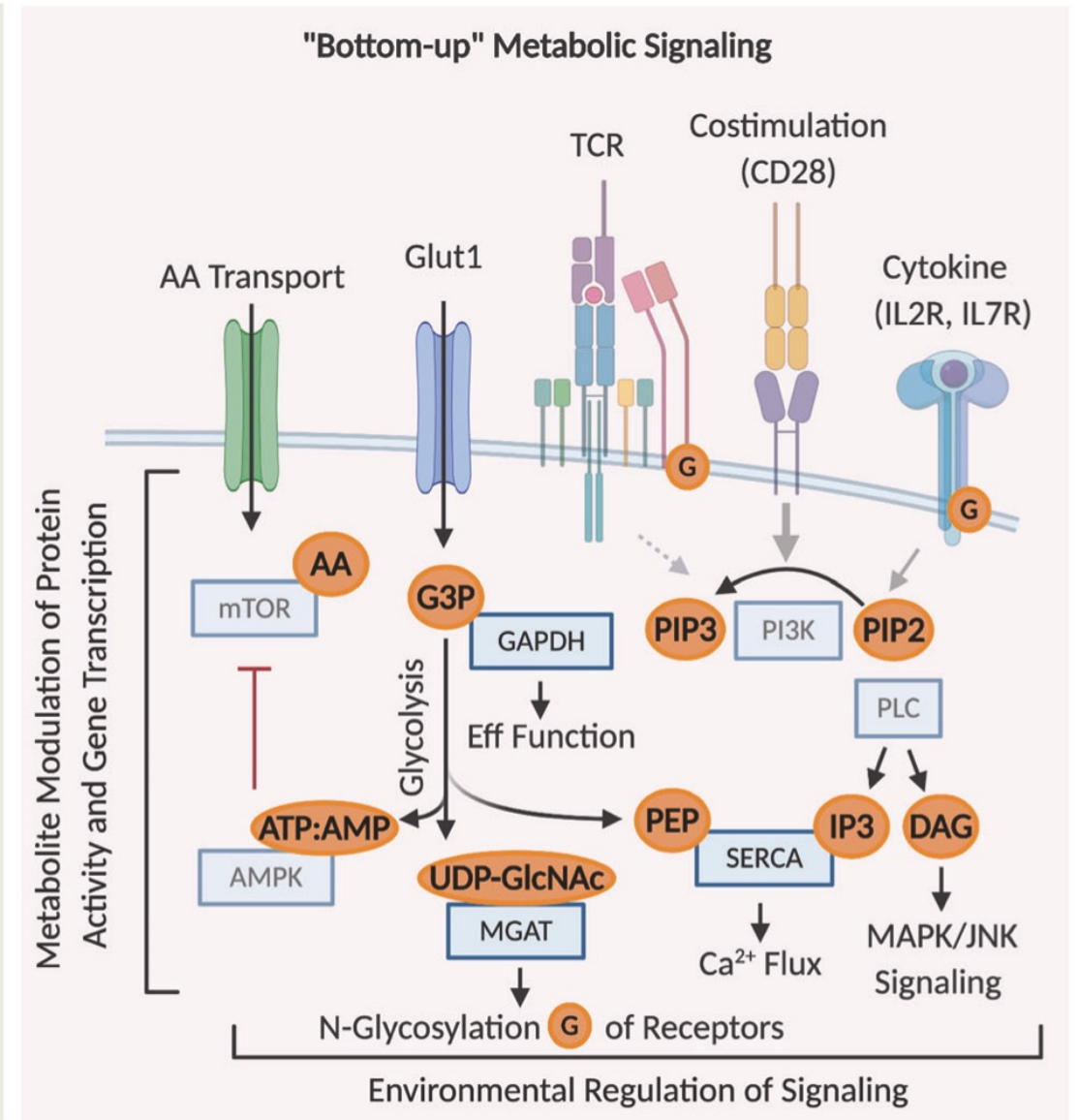
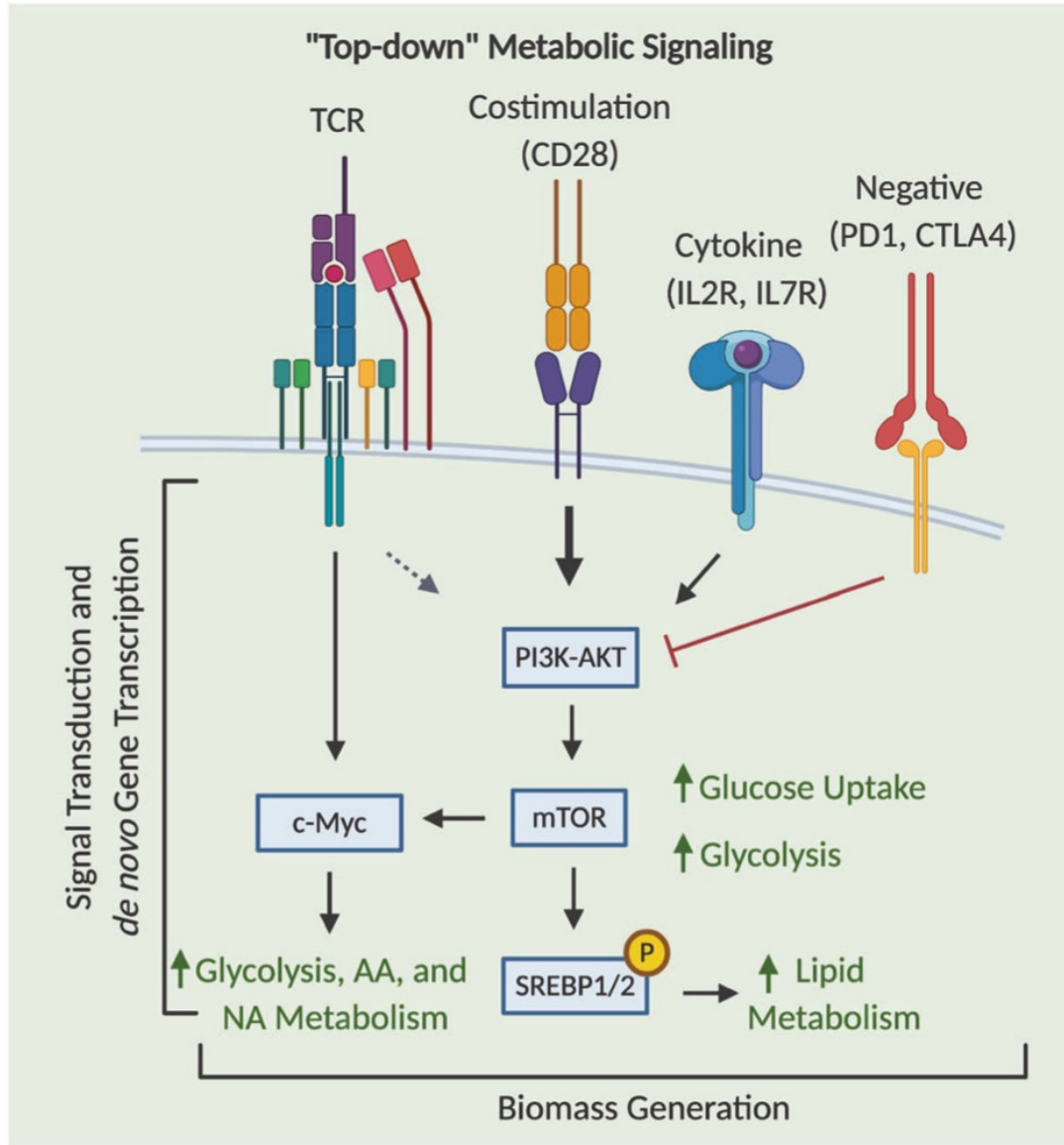
## A) TCR Signaling Alone



## B) TCR Plus CD28



# Metabolism and lymphocyte activation





B cell activation

- Quick review T dependent and independent B cell activation

T independent

Antigens have varied chemical structure or composition

Production of IgM>IgG

T dependent

Protein antigens (haptens)

Antigen presentation to T cells

More potent, isotype switching, affinity maturation

IgG, IgE, IgA

- Quick review T dependent and independent B cell activation – still need two signals....

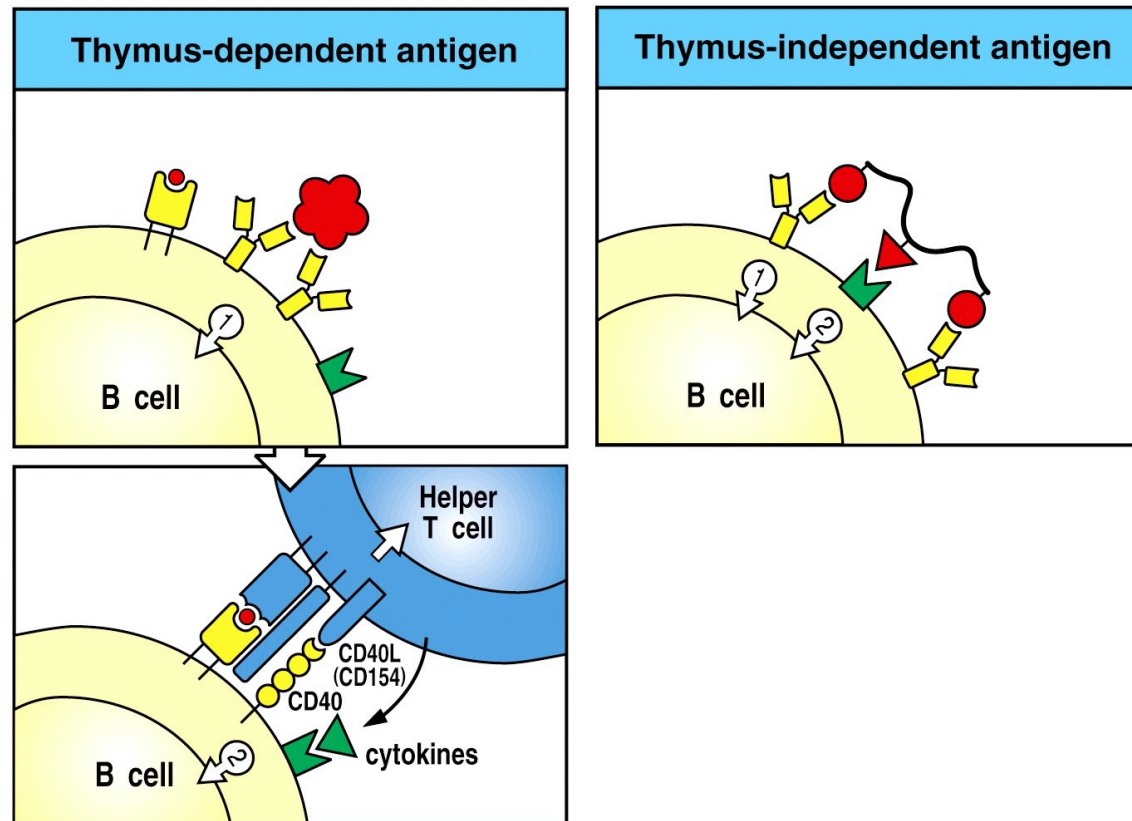
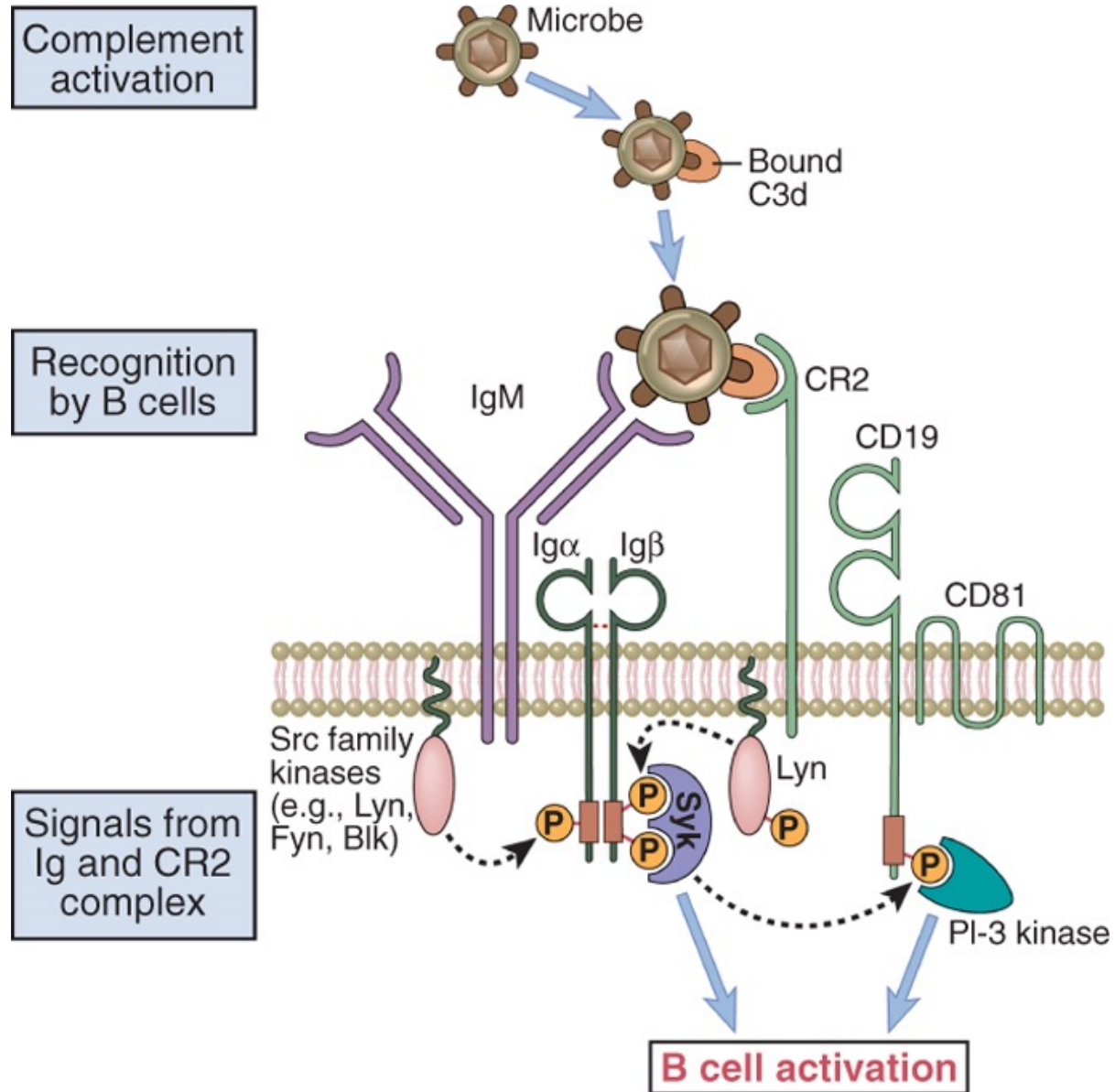


Figure 9-2 Immunobiology, 6/e. (© Garland Science 2005)

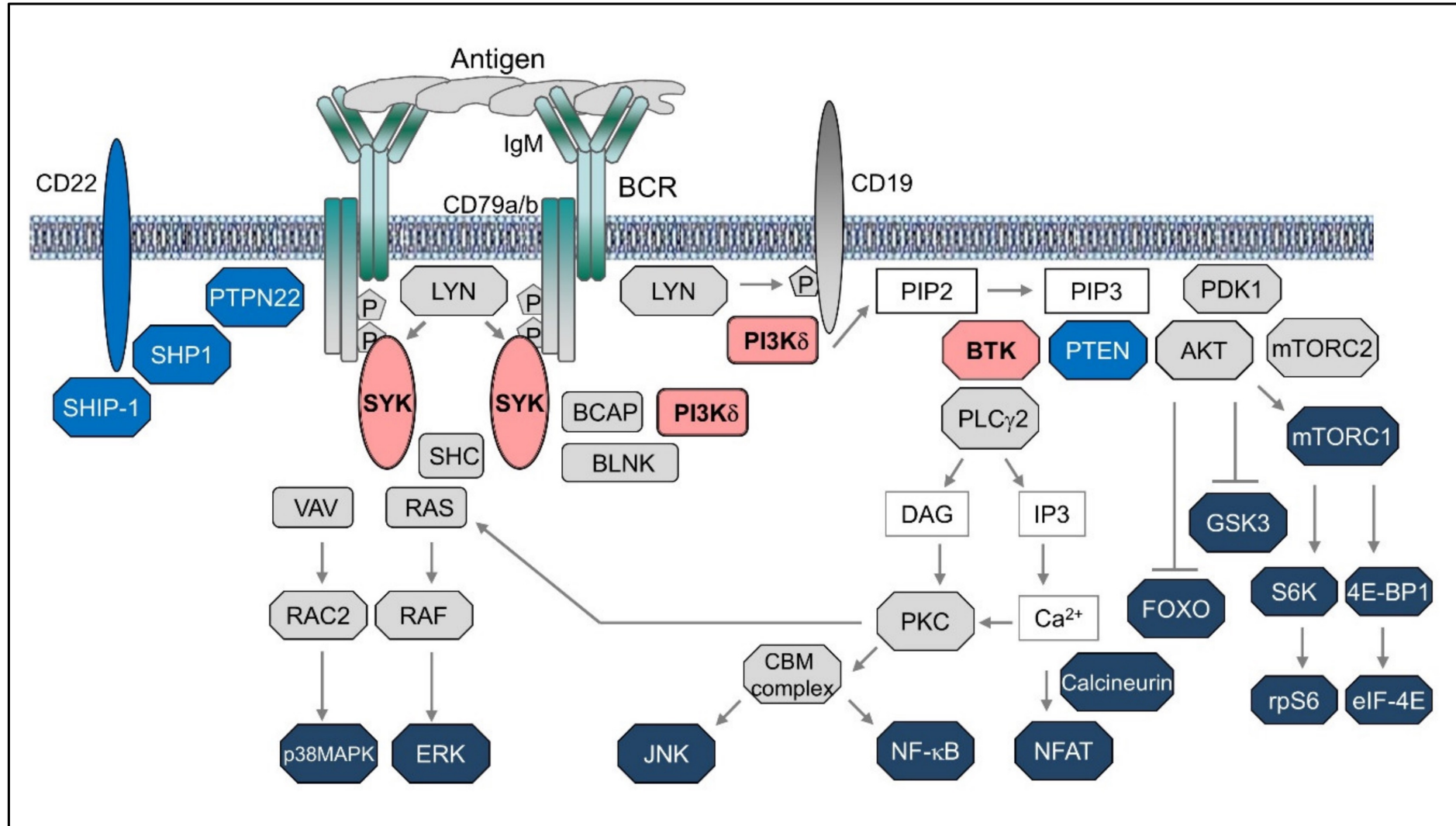
- proteins
- Lymph nodels
- estímulo de maturação
- estímulo de troca de Ig

- Multivalent antigens
- Different chemical compounds
- spleen

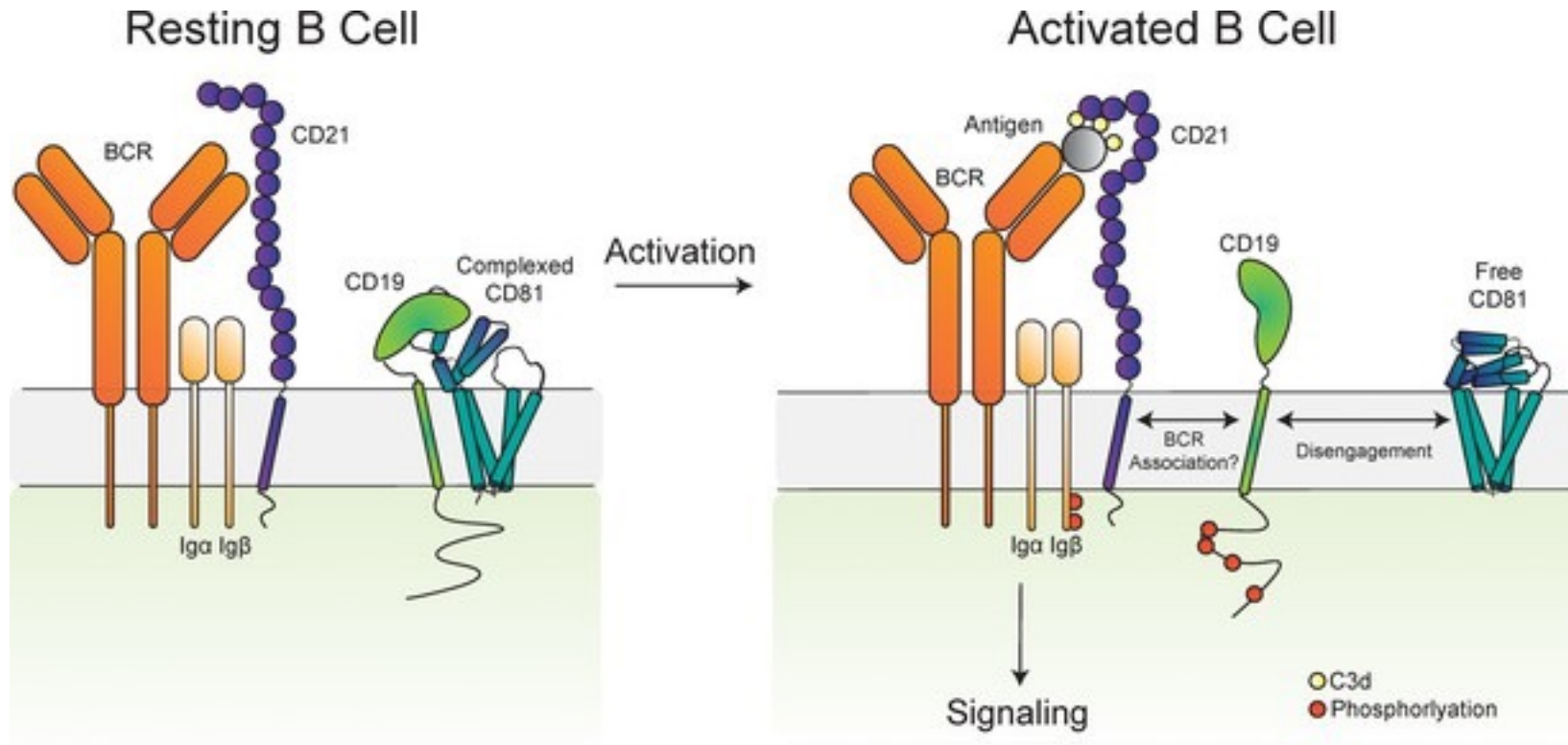
# T independent activation



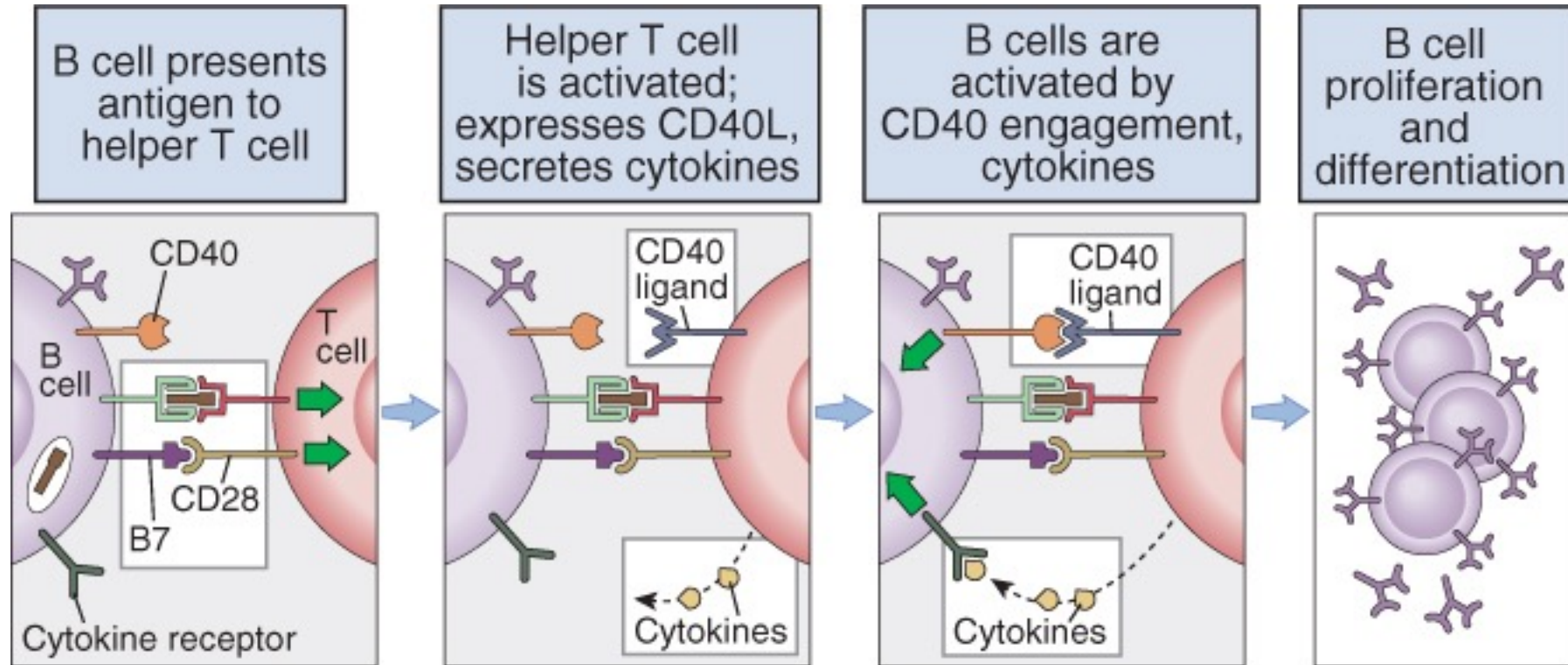
# BCR signaling



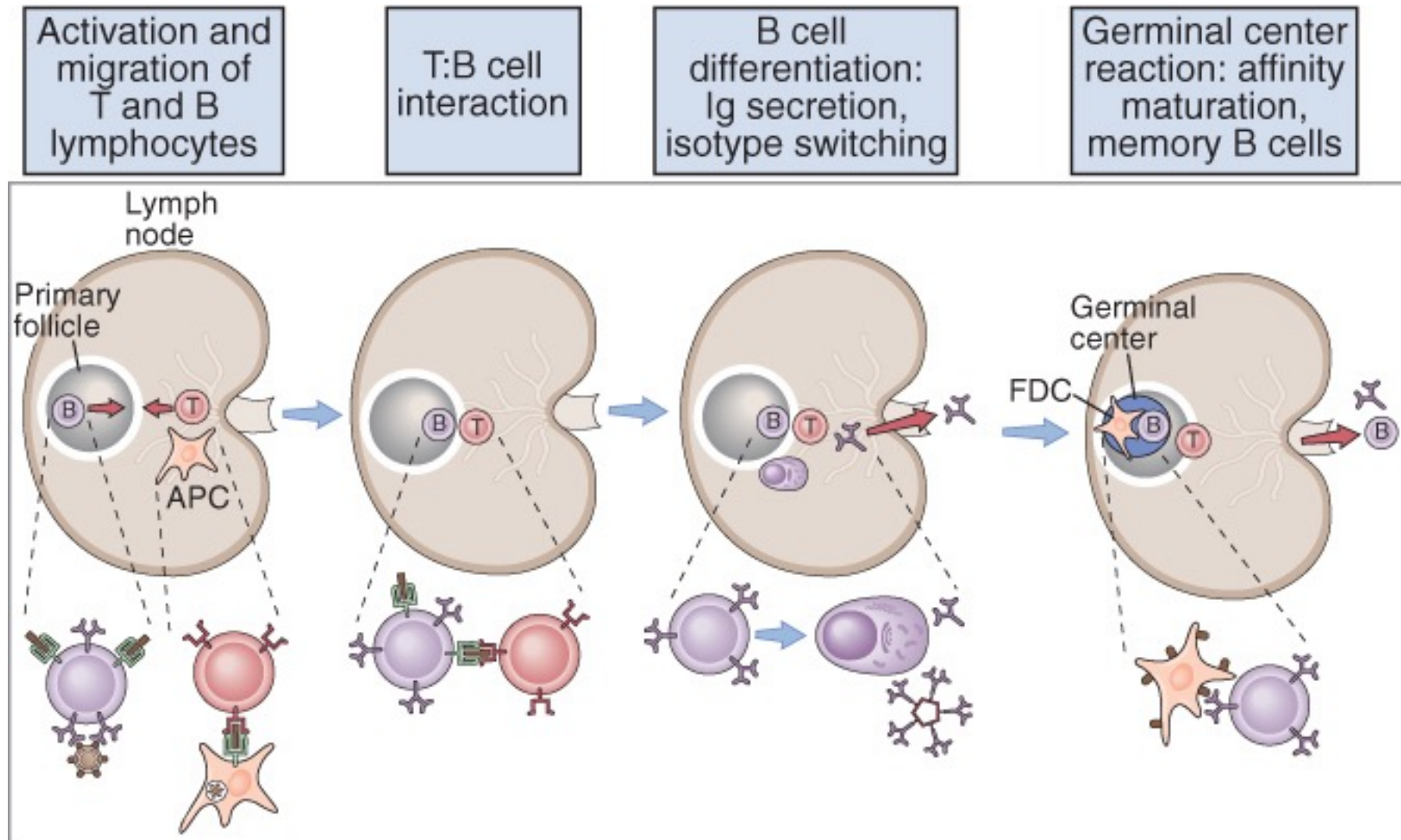
# B cell co-stimulation



# T dependent B cell activation

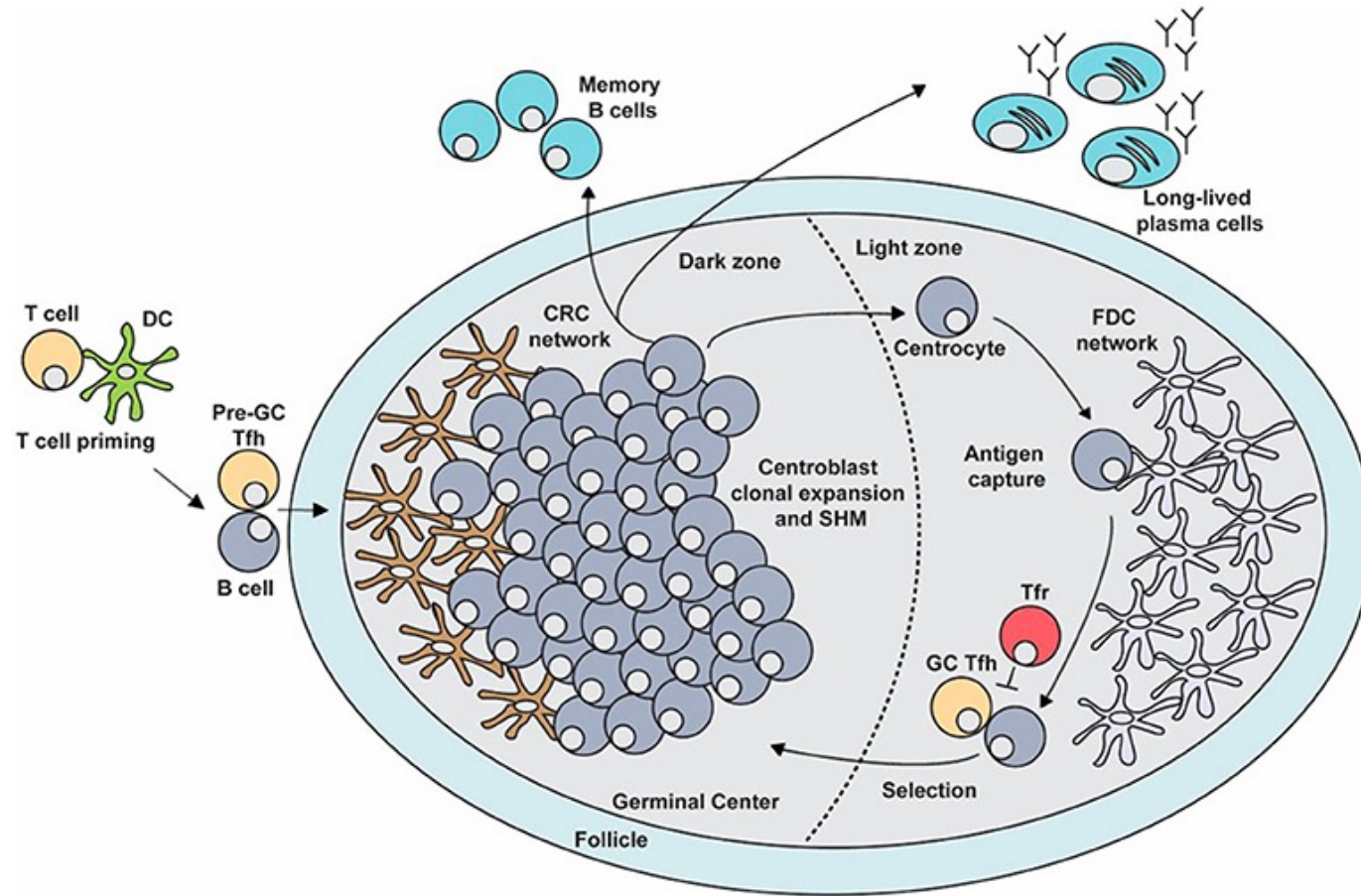


# T dependent B cell activation

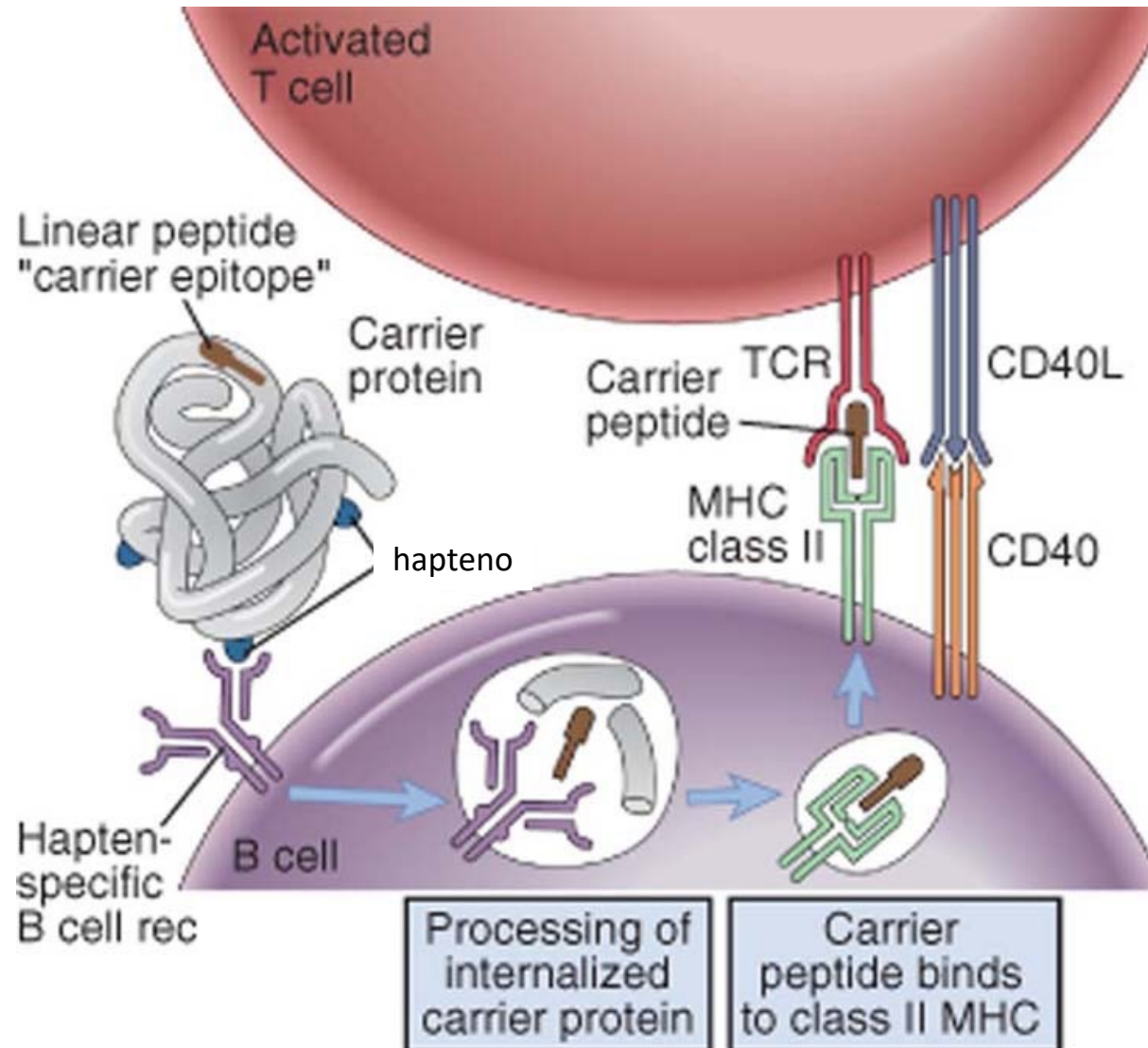




# Germinal center and B cell activation

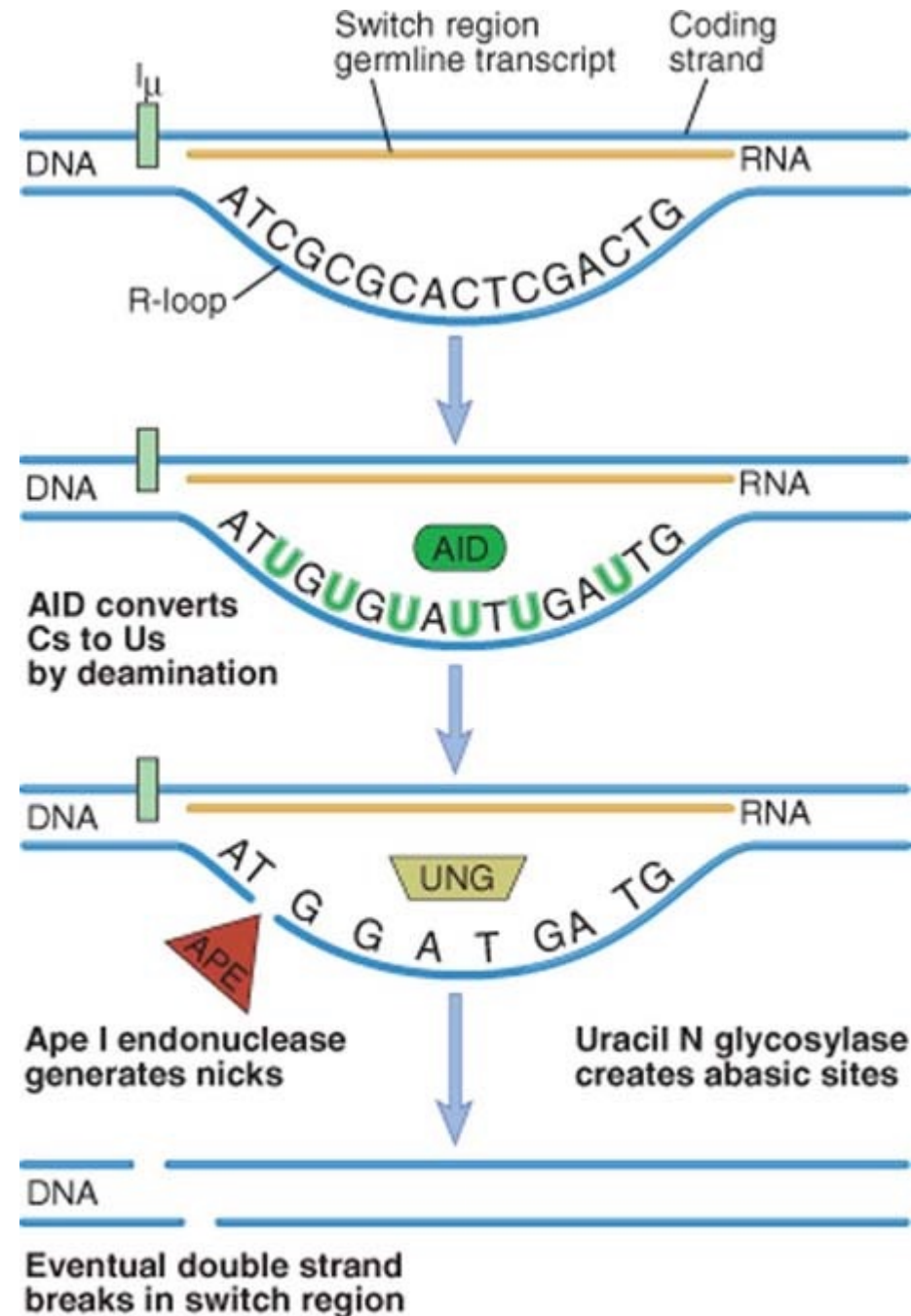
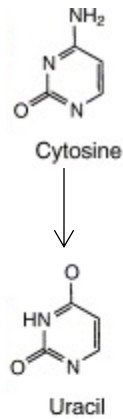


# Haptens



# Somatic hypermutation

Activation  
Induced  
Cytidine  
deaminase

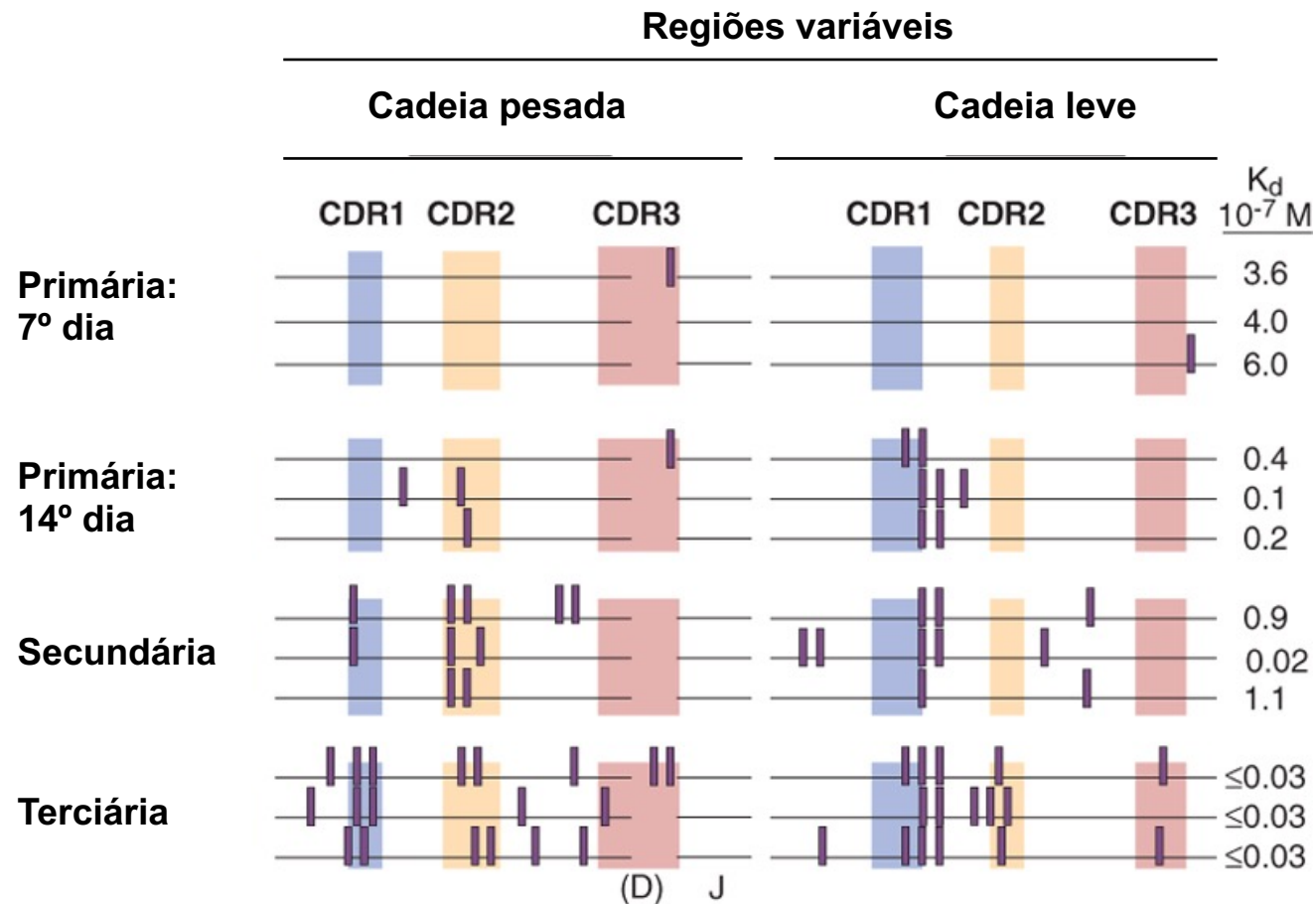


[https://www.youtube.com/watch?v=qGsyBwDVnTU&list=PLS\\_8RsEvYc3XEoHIXgrhg3uEY6WFc9DtL&index=3](https://www.youtube.com/watch?v=qGsyBwDVnTU&list=PLS_8RsEvYc3XEoHIXgrhg3uEY6WFc9DtL&index=3)

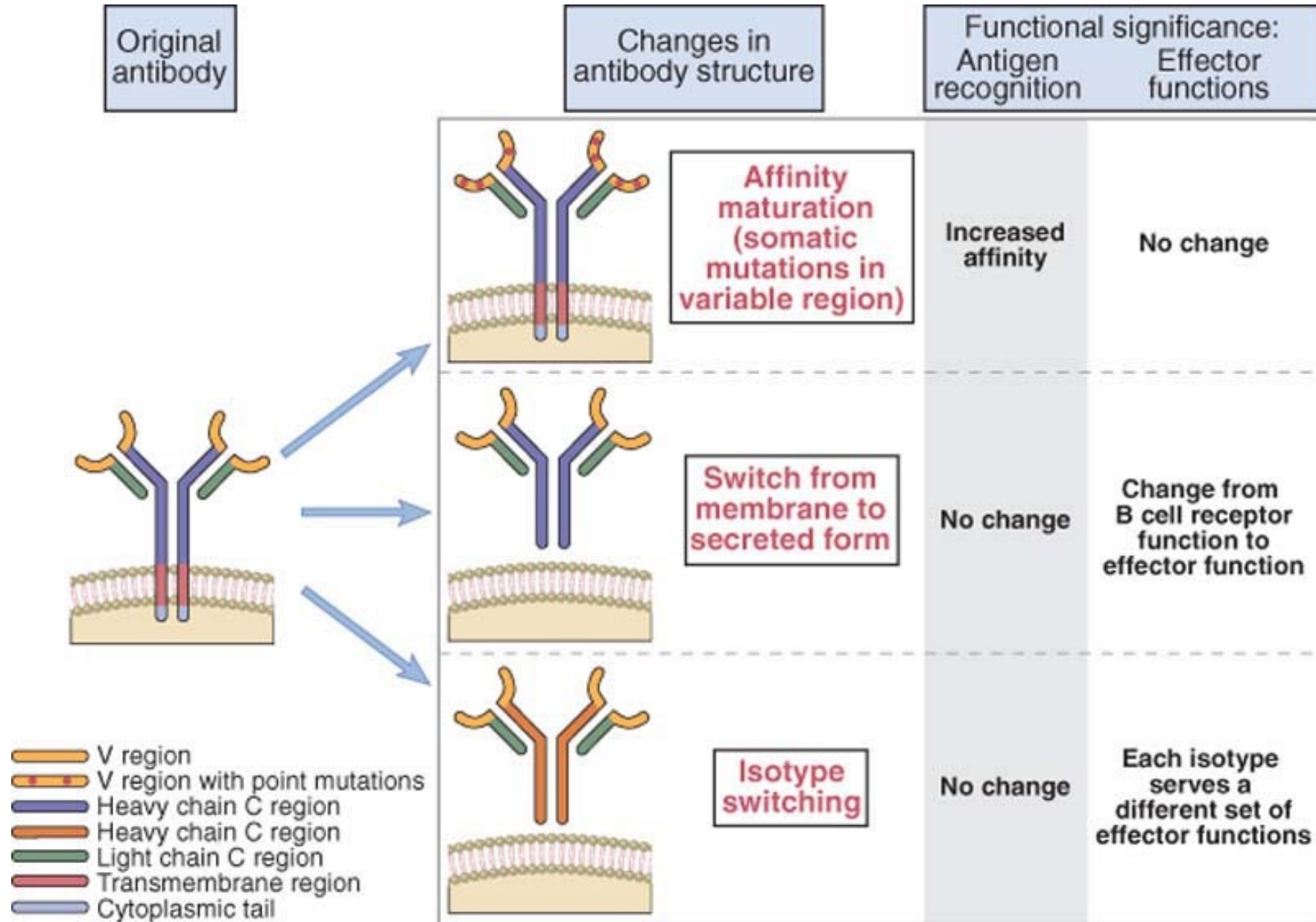
# Somatic hypermutation and antibody-antigen affinity

## Hipermutação somática

*substituições aleatórias de 1 nucleotídeo que alteram a especificidade antigênica*

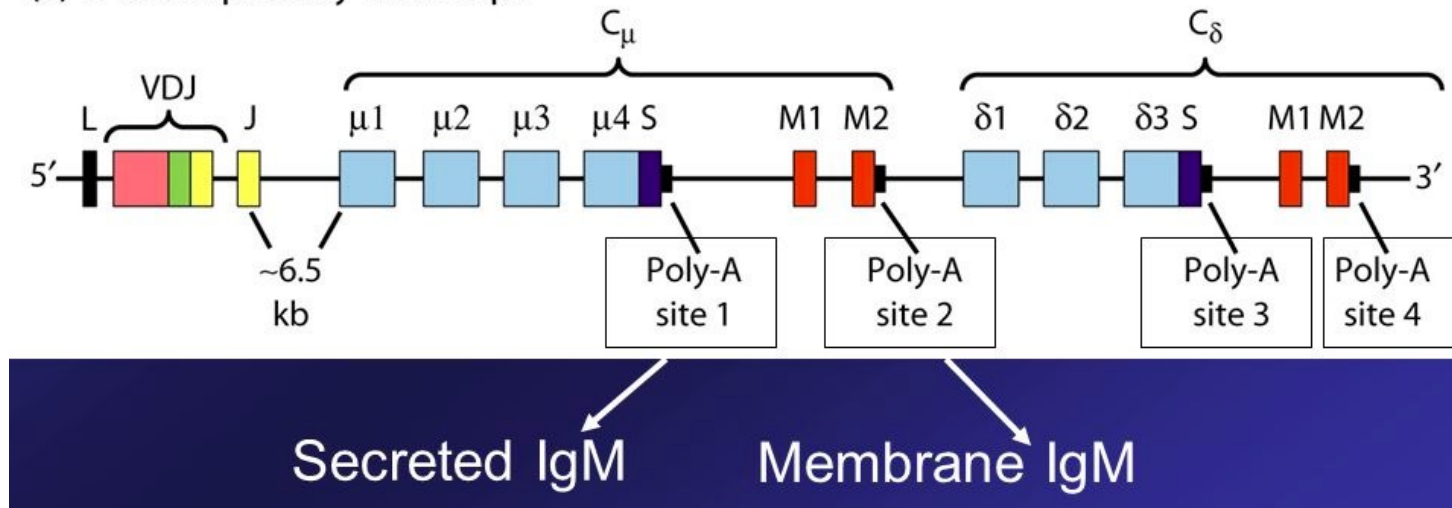


# Isotype switching and antibody secretion

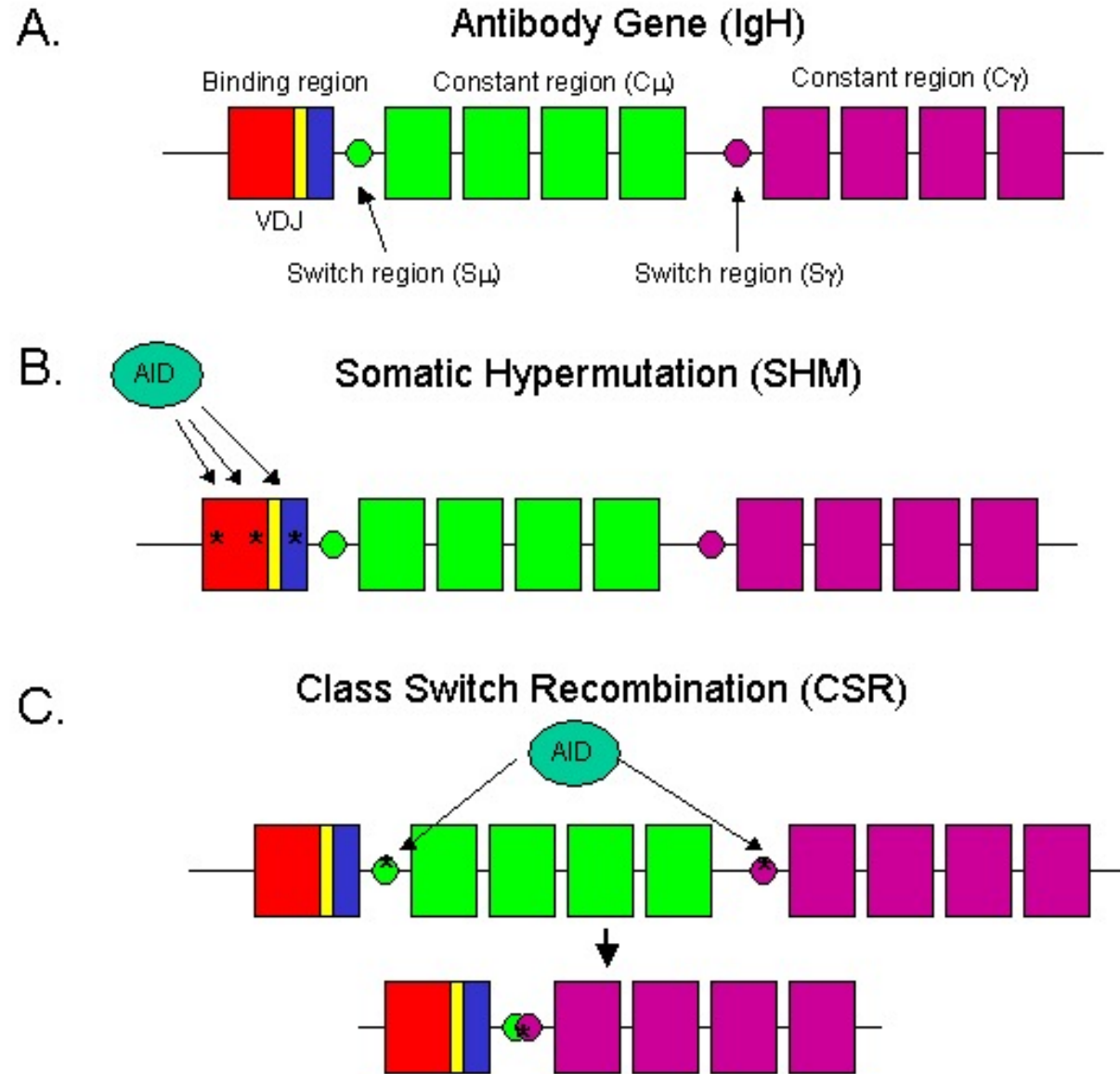


# BCR x Antibody

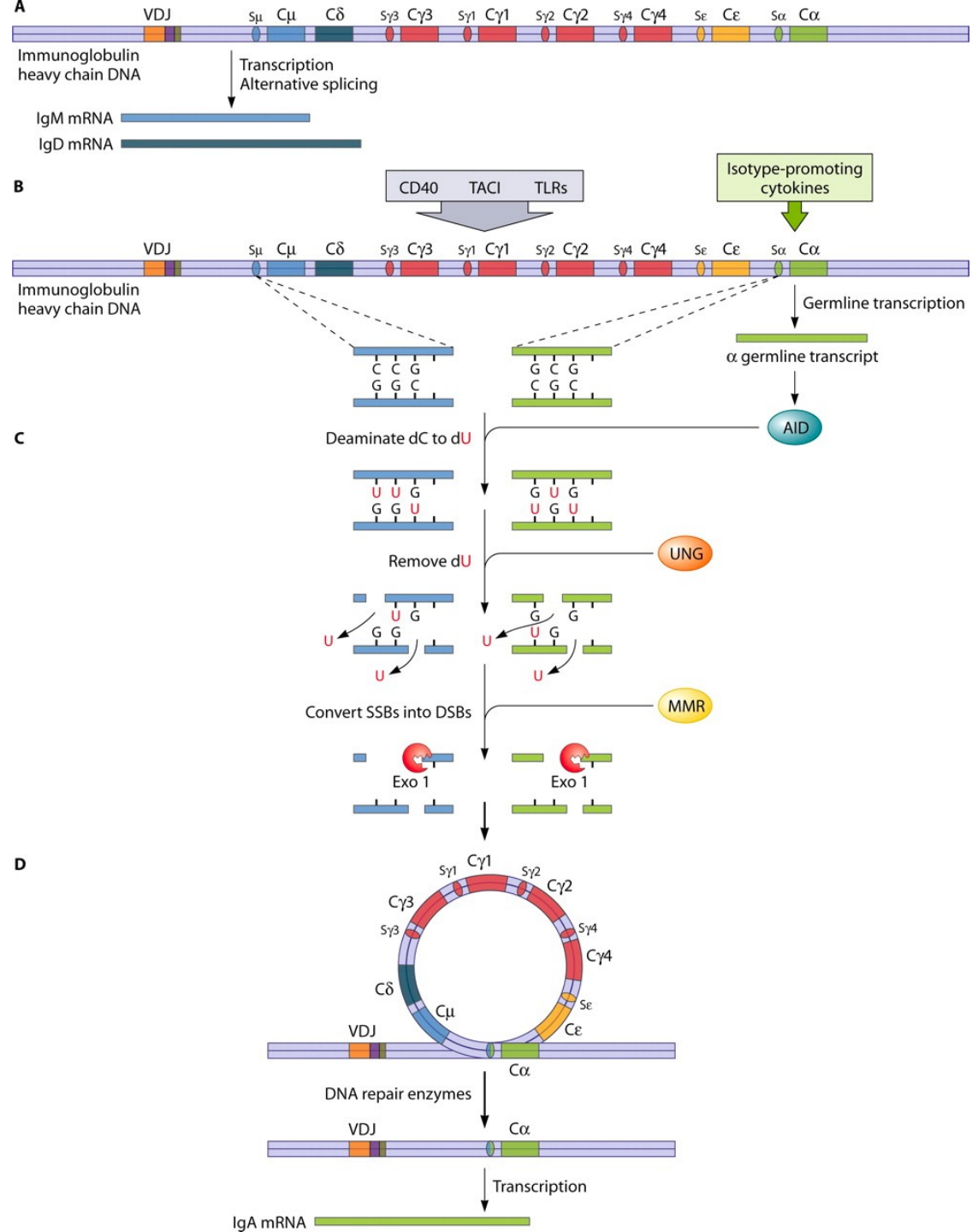
(a) H-chain primary transcript



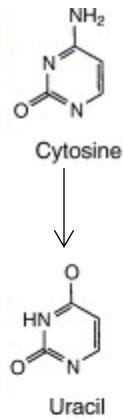
# Isotype switching



# Isotype switching

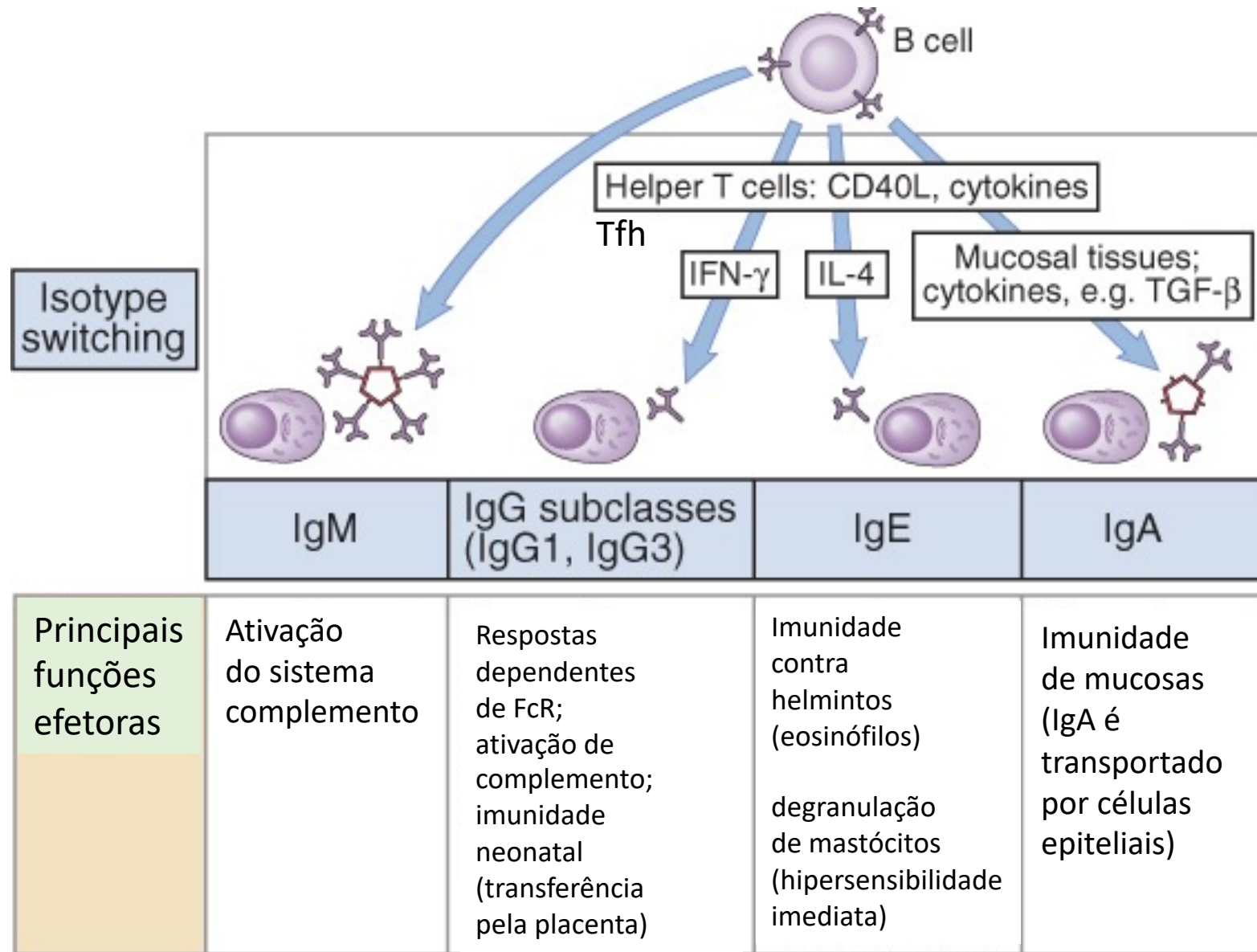


Activation  
Induced  
Cytidine  
deaminase

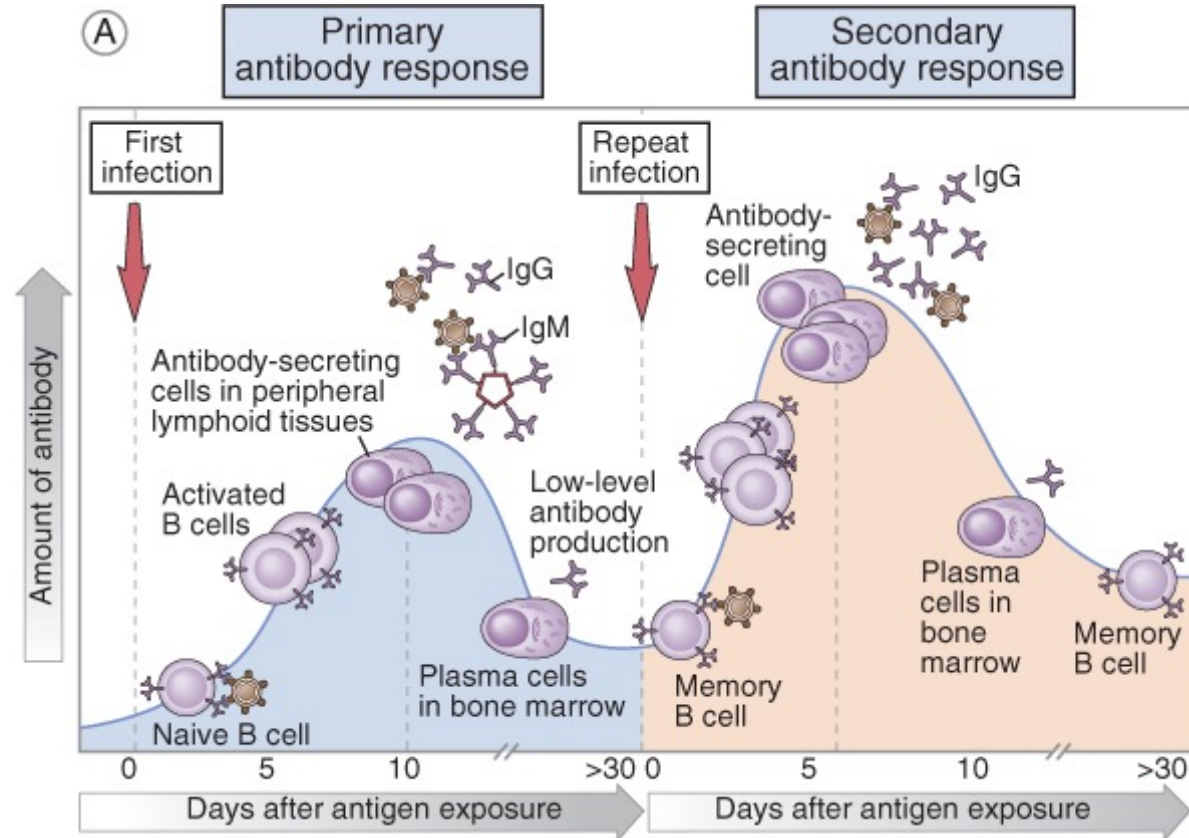




# Isotype switching



# Dynamics



(B)

	Primary response	Secondary response
Lag after immunization	Usually 5-10 days	Usually 1-3 days
Peak response	Smaller	Larger
Antibody isotype	Usually IgM>IgG	Relative increase in IgG and, under certain situations, in IgA or IgE (heavy chain class switching)
Antibody affinity	Lower average affinity, more variable	Higher average affinity (affinity maturation)

