B-cell, Antibody, Complement

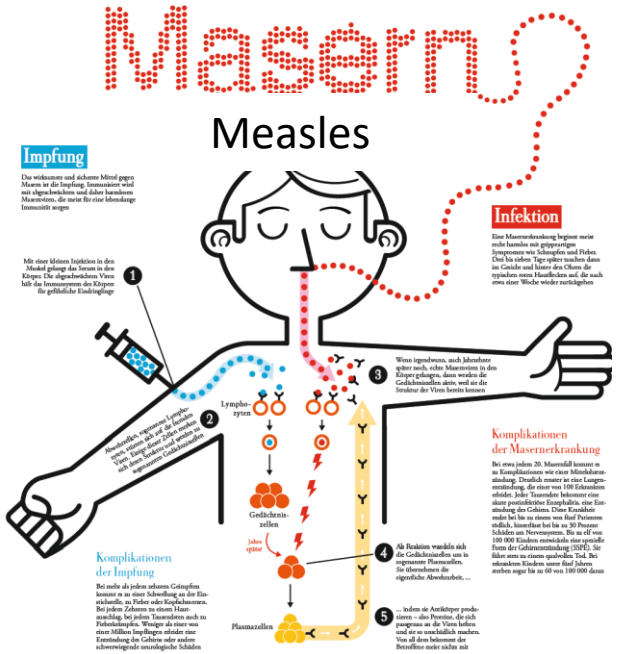
- **Antibody structure**
- **How B cell response is controlled**

- **Complement pathways and effects**

Protective immunity by antibody

Active immunization

- Infection
- Vaccination

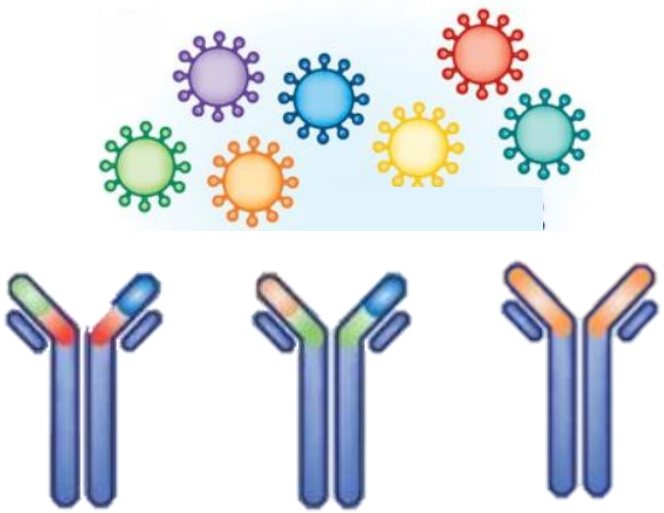


Passive immunization

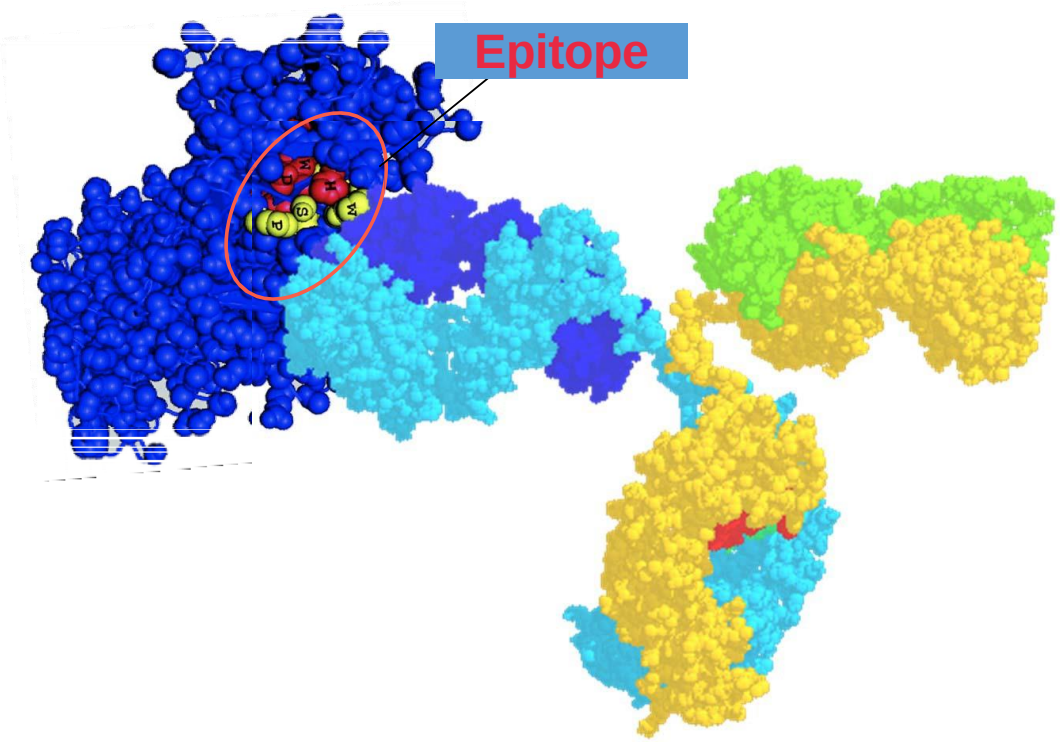
- Maternal antibodies
- Antibody injection (toxin, virus, lymphoma, PDL1)

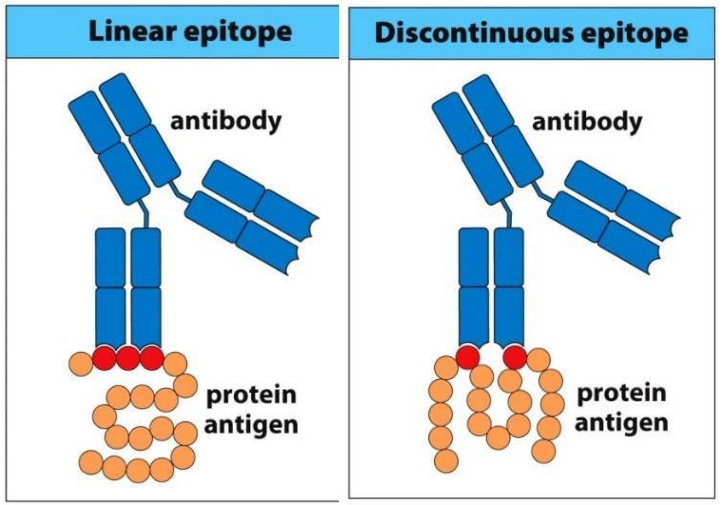
Broadly Neutralizing Antibodies (bNAbs)

HIV



Antigen-*antibody generator*





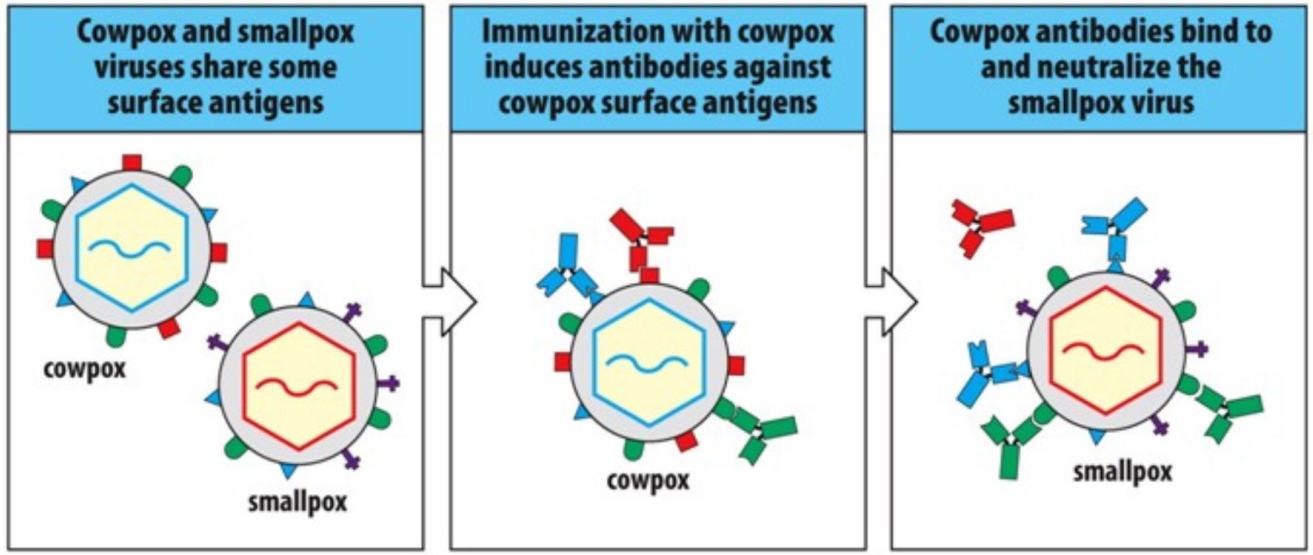
- Epitope is the antigen part that an antibody binds
- Epitope determines efficacy of antibody

Selection of protective epitope:

- Structurally mapping antibody repertoires
- Computational prediction and modelling

Cross-reactivity of antibody

Edward Jenner



Rheumatic fever

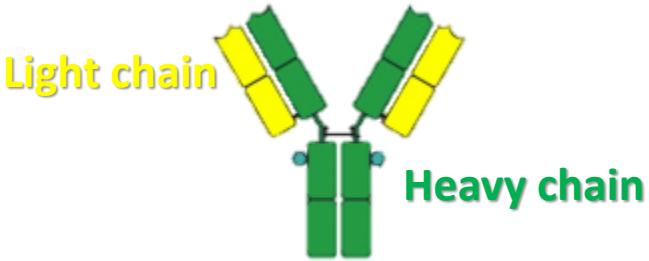
- M-Protein on group A Streptococcus
- Myocardial and muscle proteins

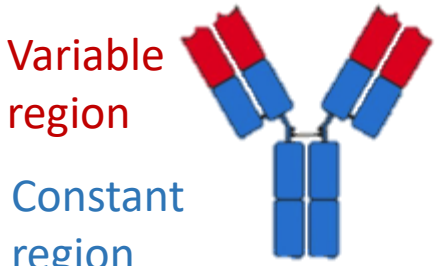
Antibody structure

A dimer of dimer

V_H, C_H

V_L, C_L





1908
1972

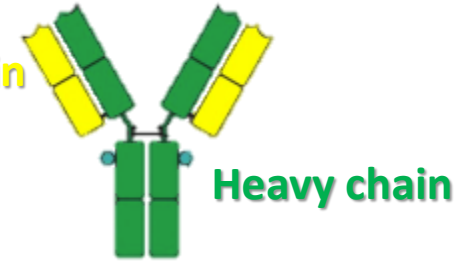
Human IgG Immunoglobulin
≃ 150 kDa

Nanobody

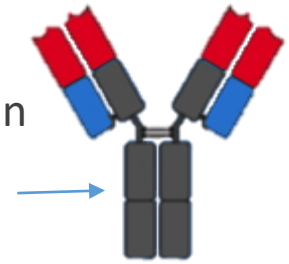
- Penetration
- Small epitope

On February 2019, FDA approved the first Nanobody-based medicine.

Antibody structure

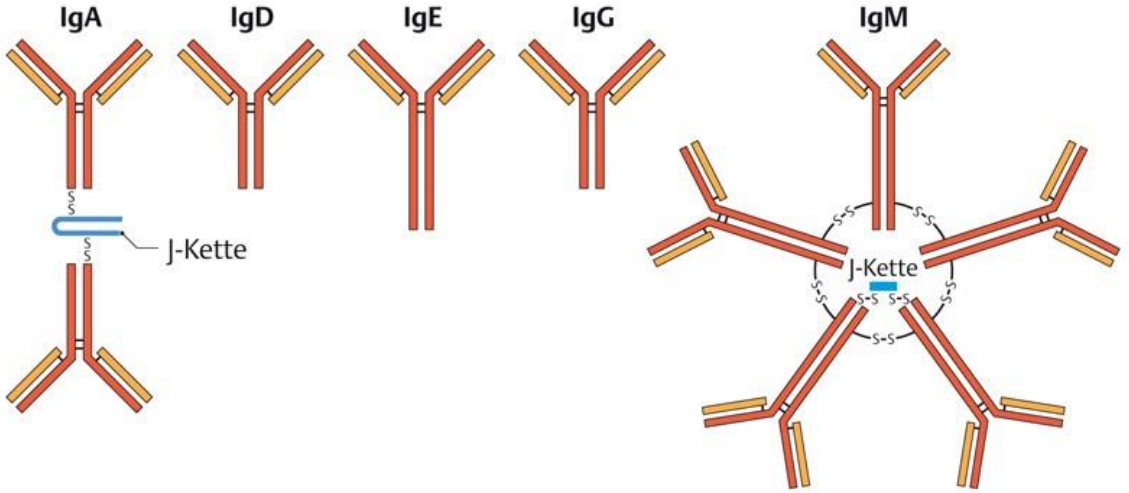


Light chains:
κ and λ (V_L and C_L)



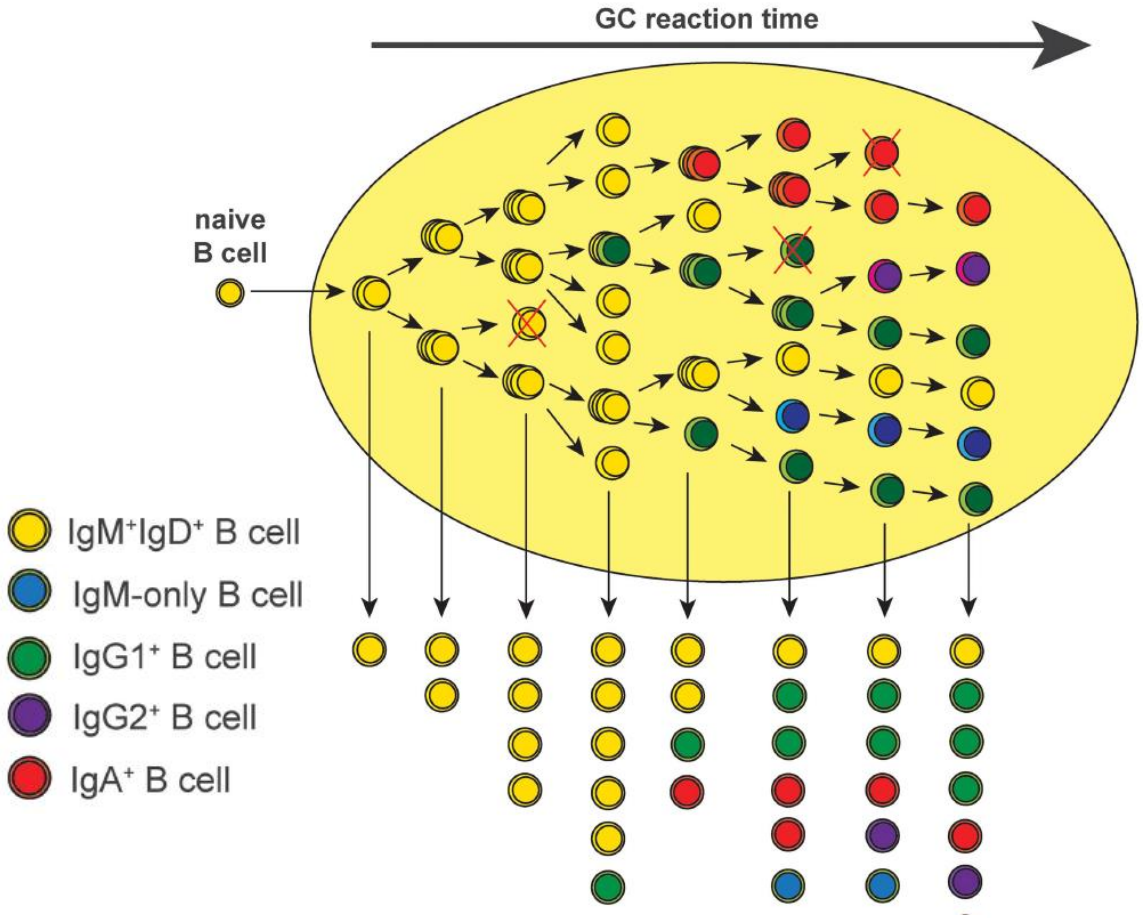
C_H chains: μ, δ, γ, α, ε

Immunoglobulin:
IgM, IgD, IgG, IgA, IgE

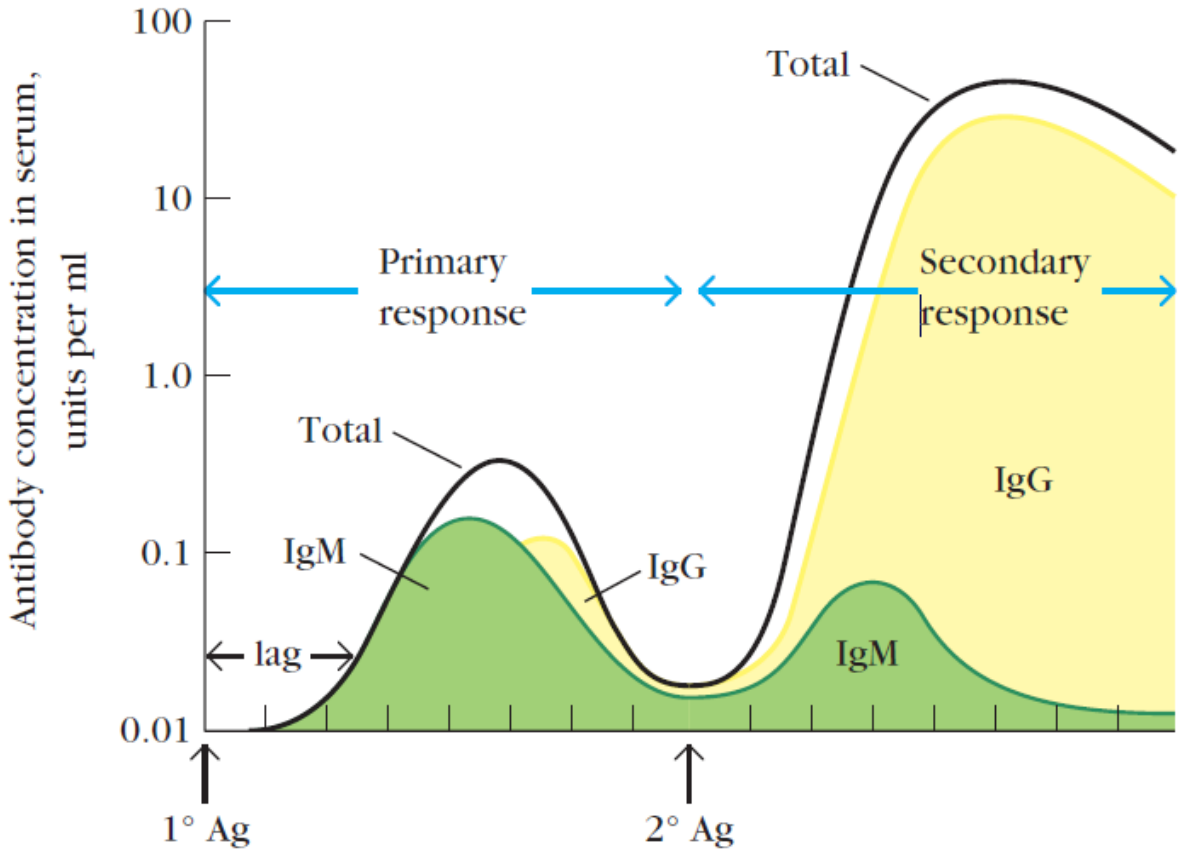


Antibody classes

Immunoglobulin: IgM, IgD, IgG, IgA, IgE

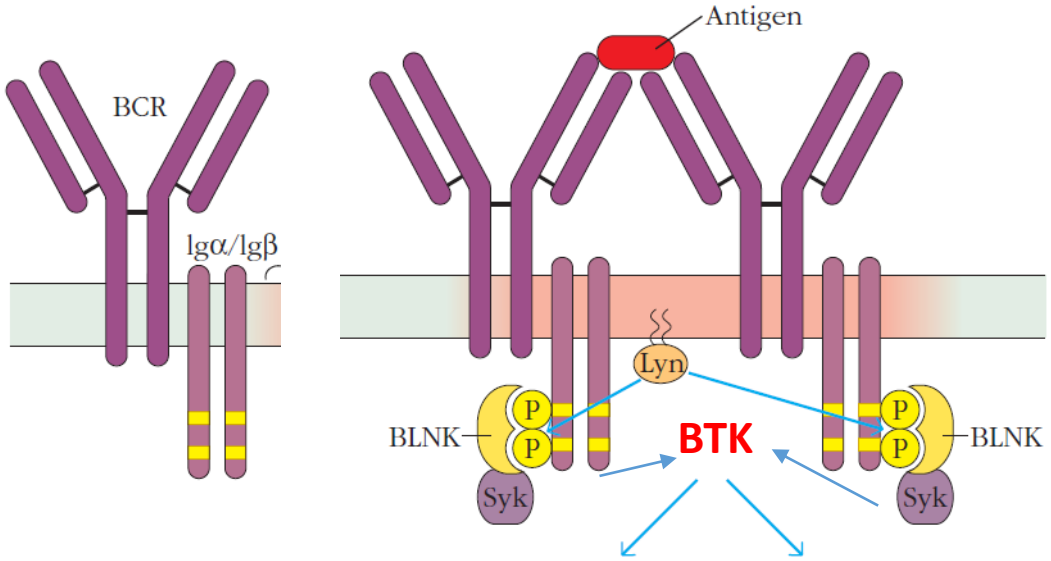


Memory B cell generation

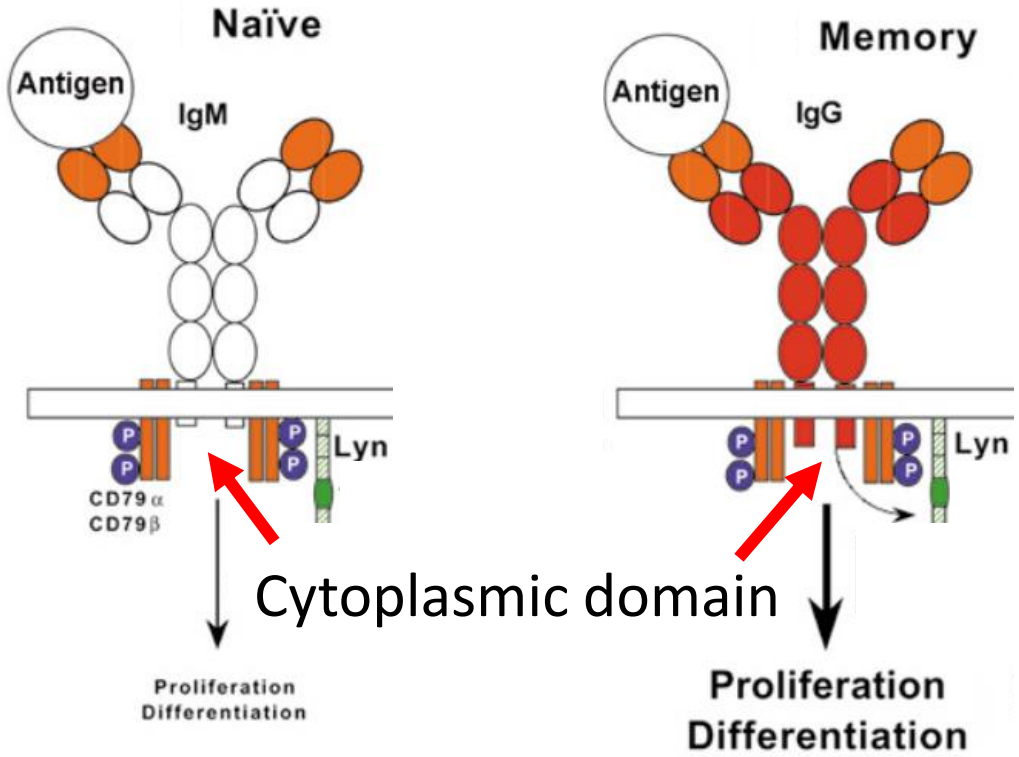


B cell receptor (BCR)

Membrane bound immunoglobulin +Igα/β



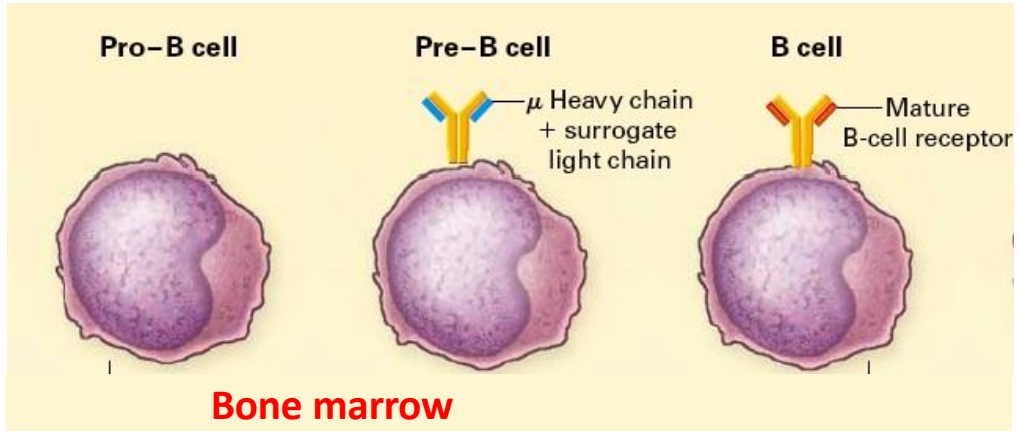
Signal transduction



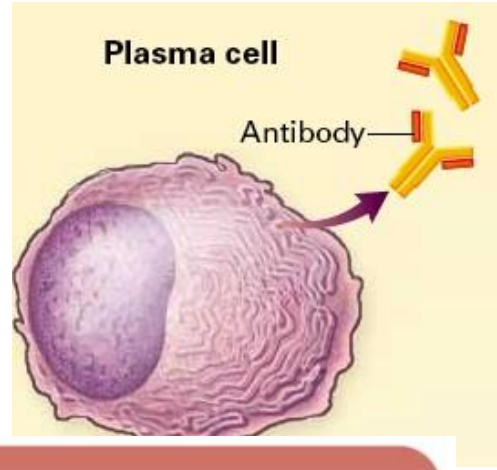
	Cytoplasmic domain sequence
mIgM (3aa)	KVK
mIgG (28aa)	KVKWIFSSVVELKQTLVPEYKNMIGQAP

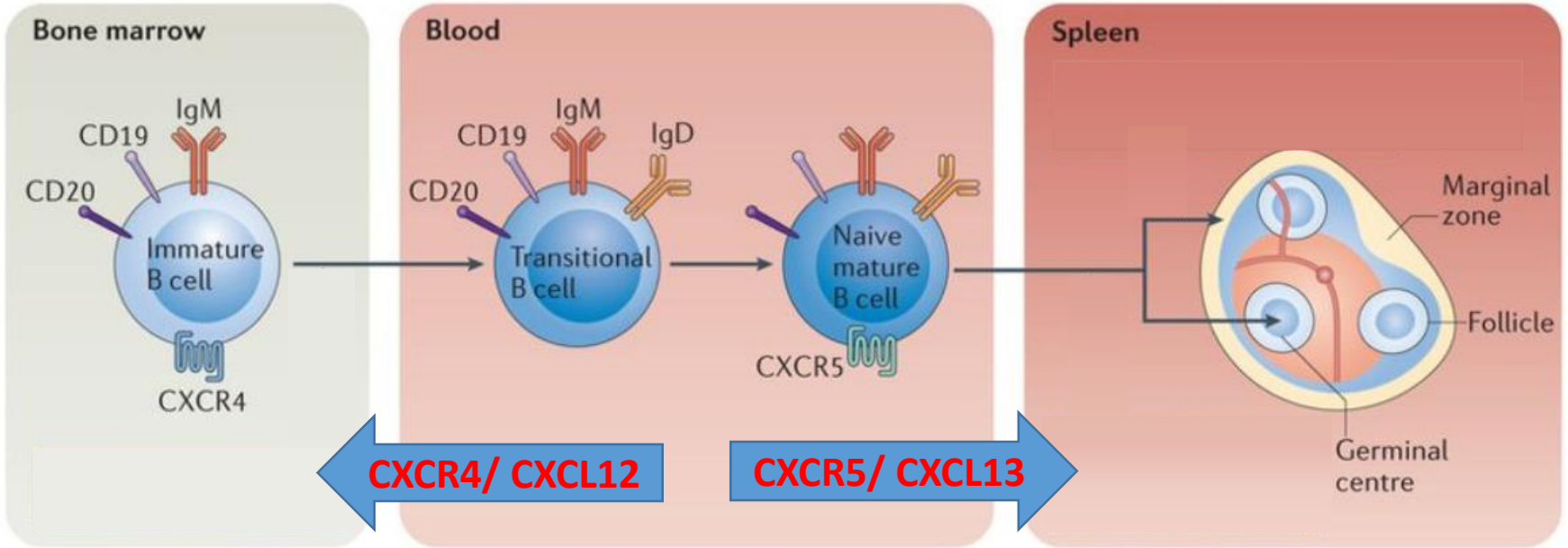
BTK (Bruton tyrosine kinase)
X-linked agammaglobulinemia

B cell development and migration



Secondary lymphoid organs (SLO)





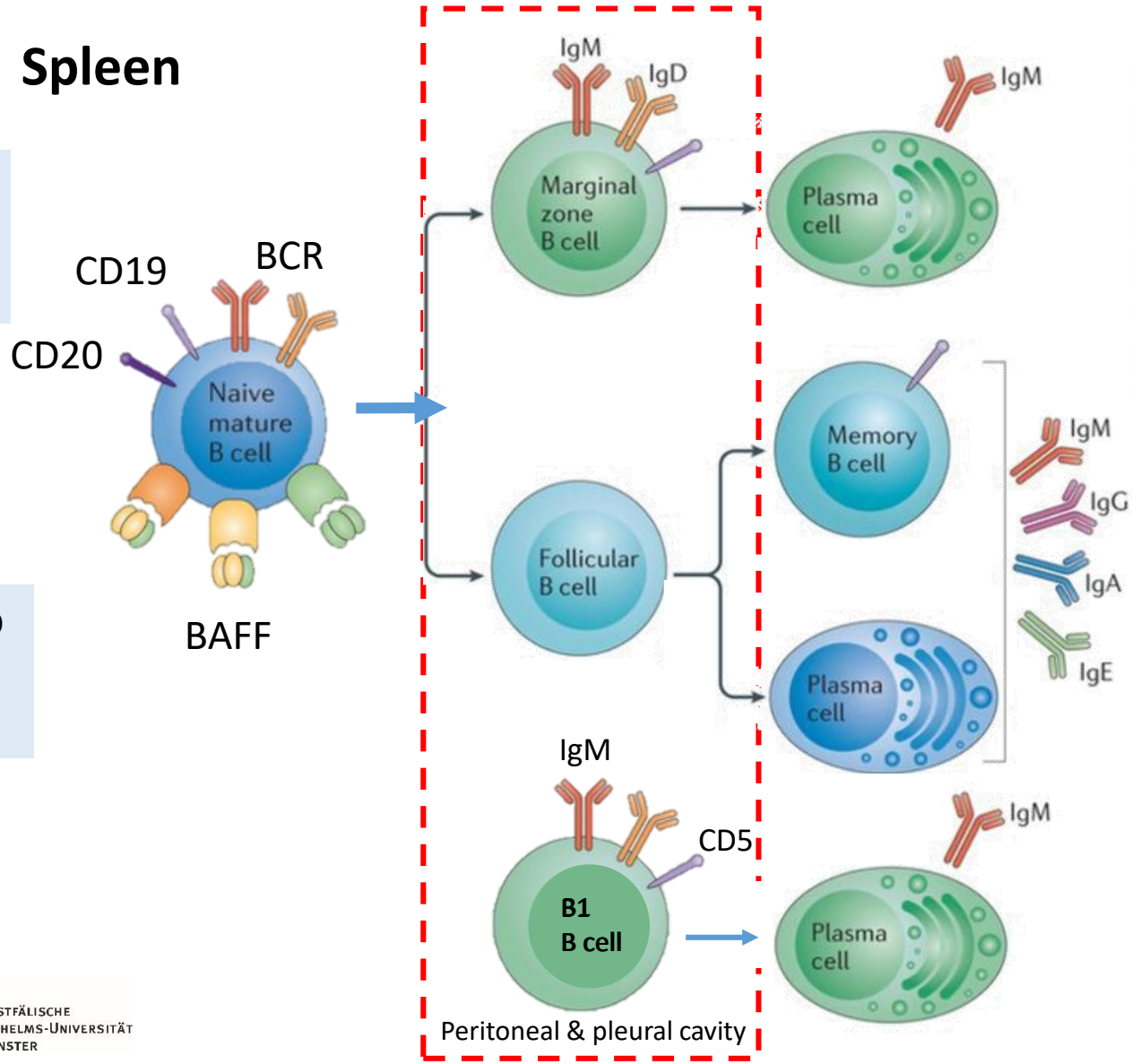
Chemokine: small protein attracting immune cells

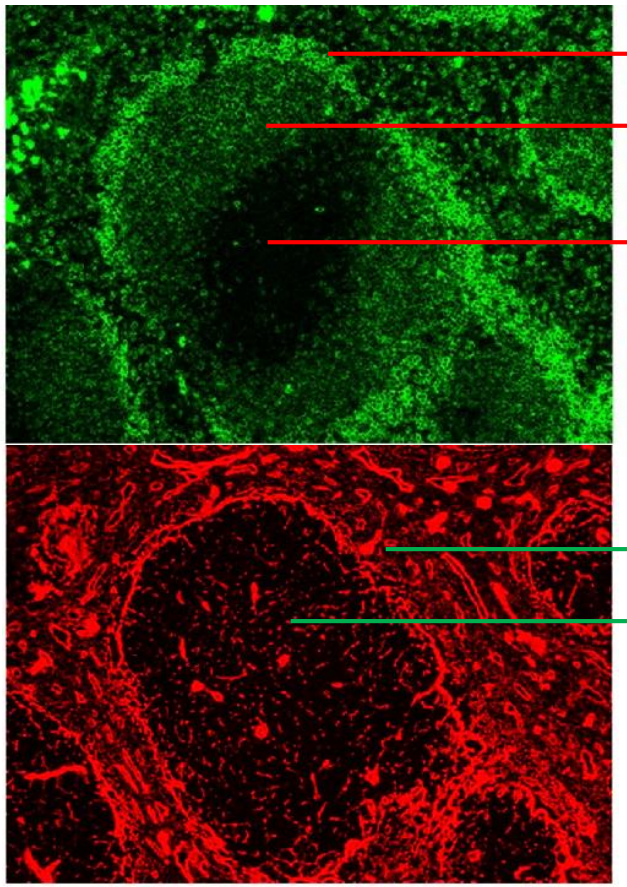
Naive mature B cells

Spleen

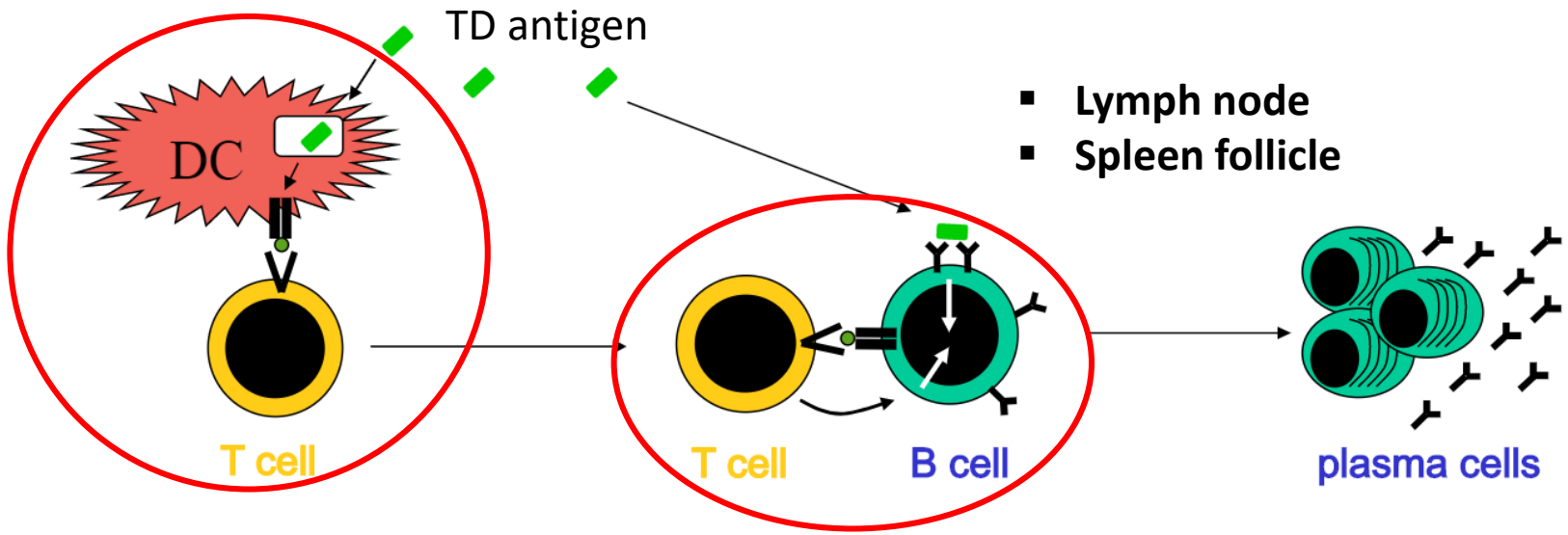
Rituximab
Anti-CD20
Lymphoma

Belimumab
Anti-BAFF
SLE

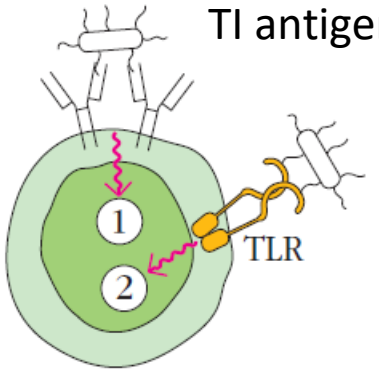




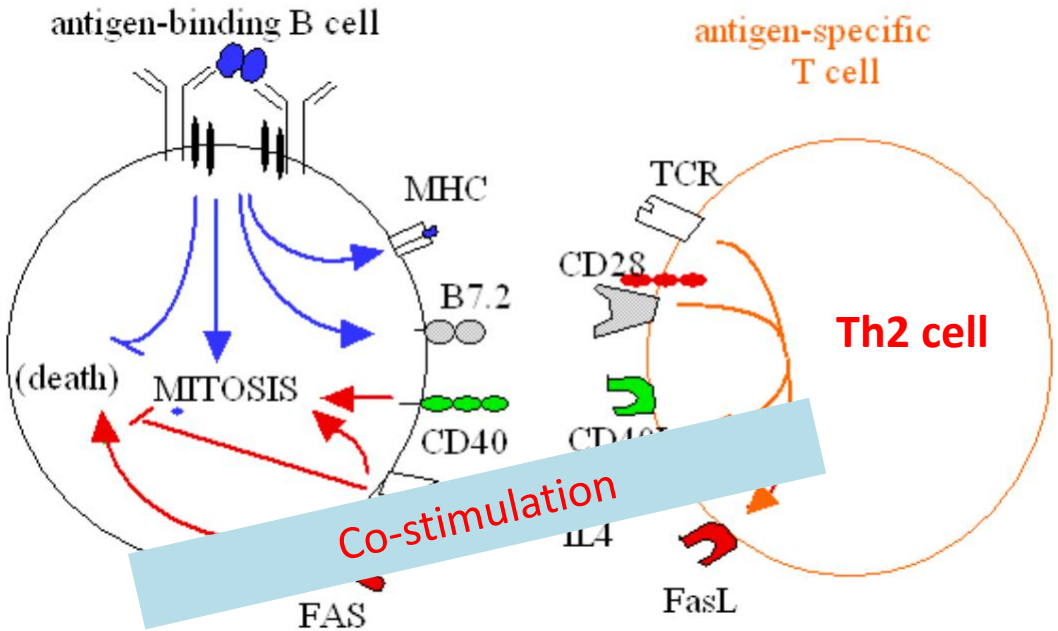
T helper cell and B cell activation



- Lymph node
- Spleen follicle



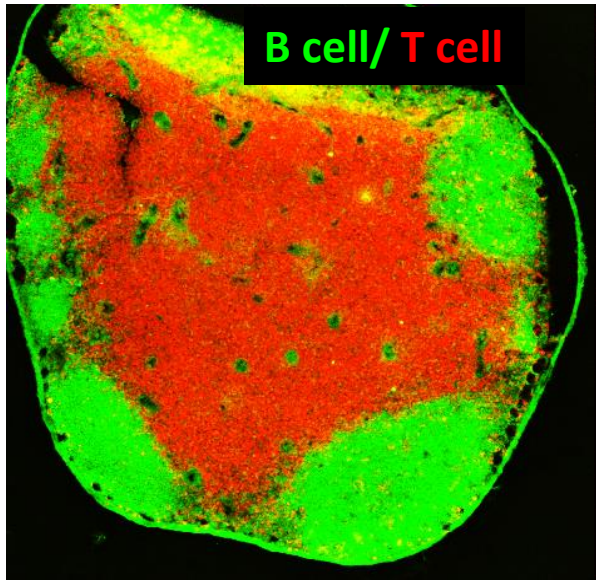
Spleen
Blood born antigen

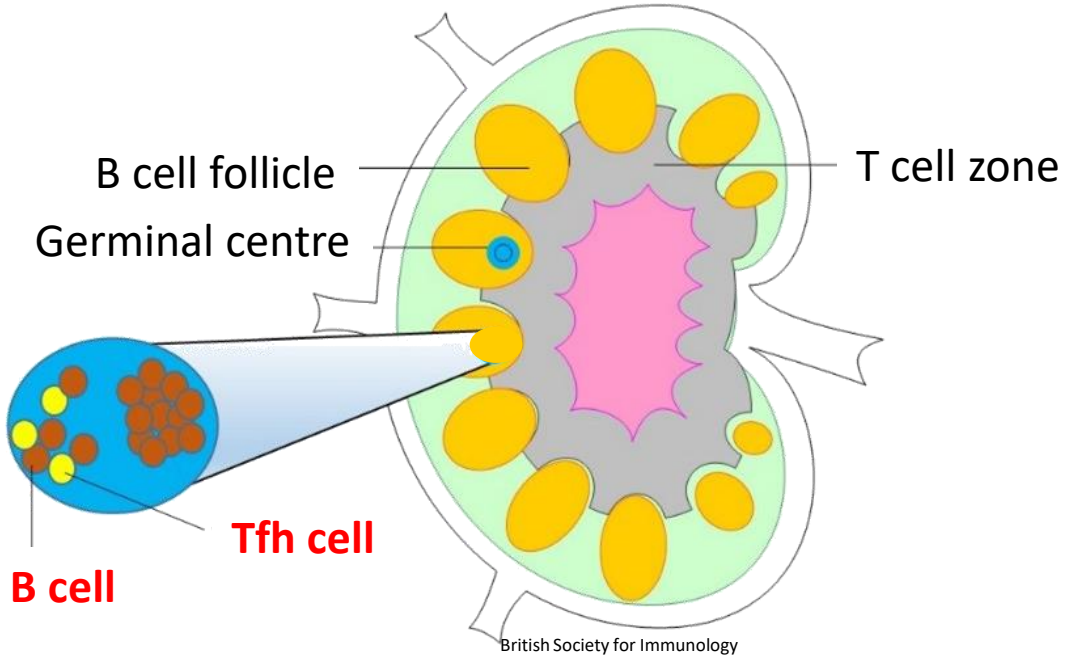


- B cell works as APCs
- T cell deficiency causes antibody impairment

T follicular helper (TFH) cells

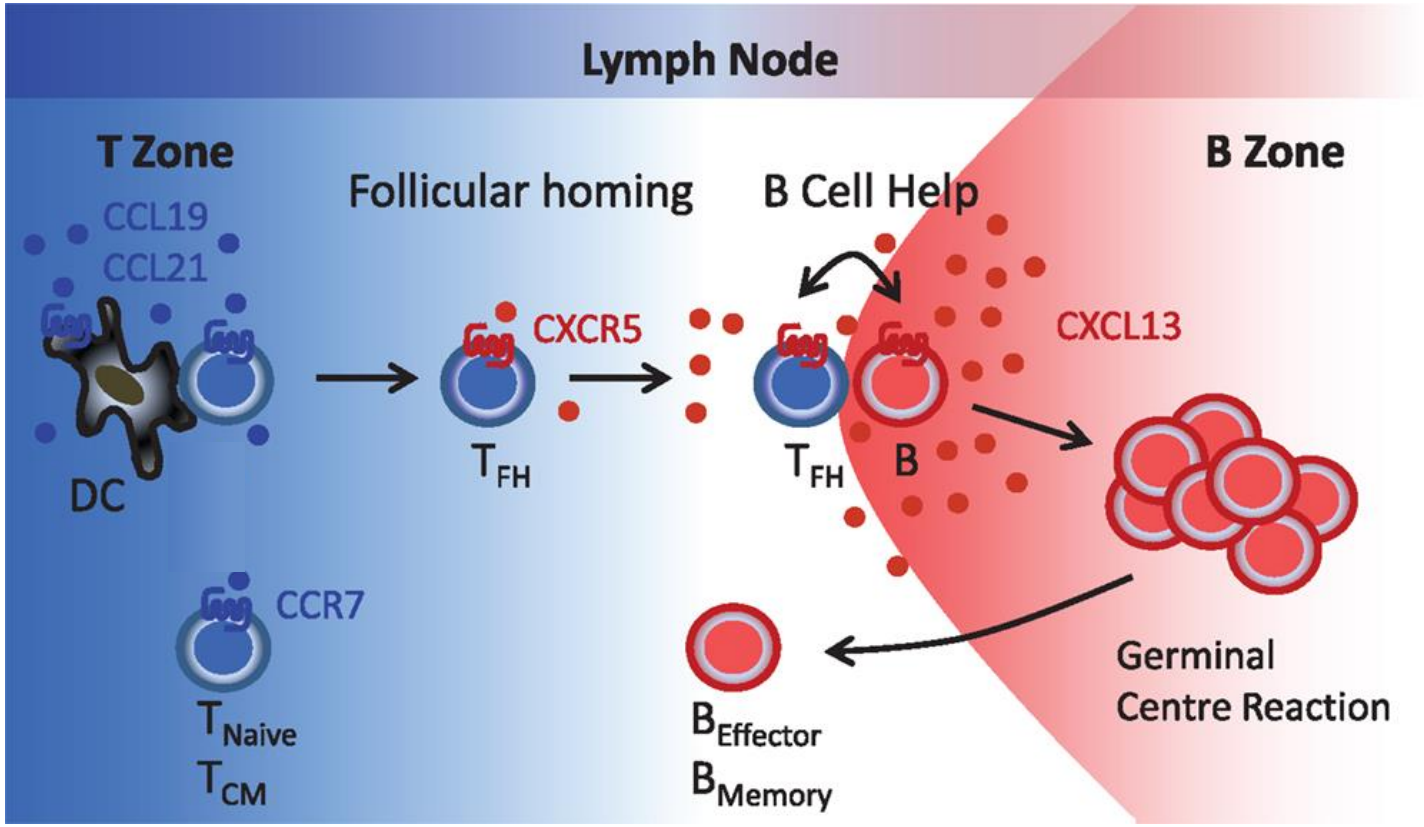
Lymph node





Where does B-T interaction take place?

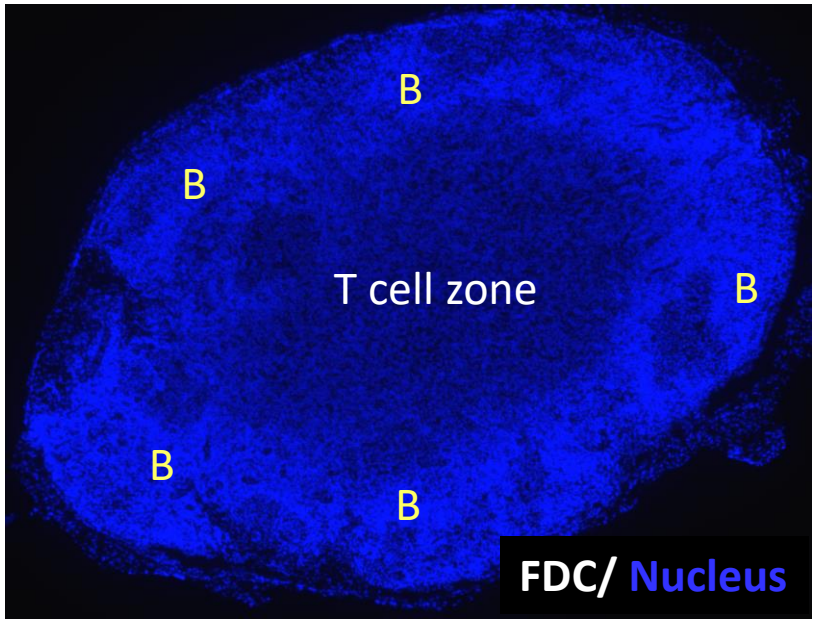
T follicular helper (TFH) cells

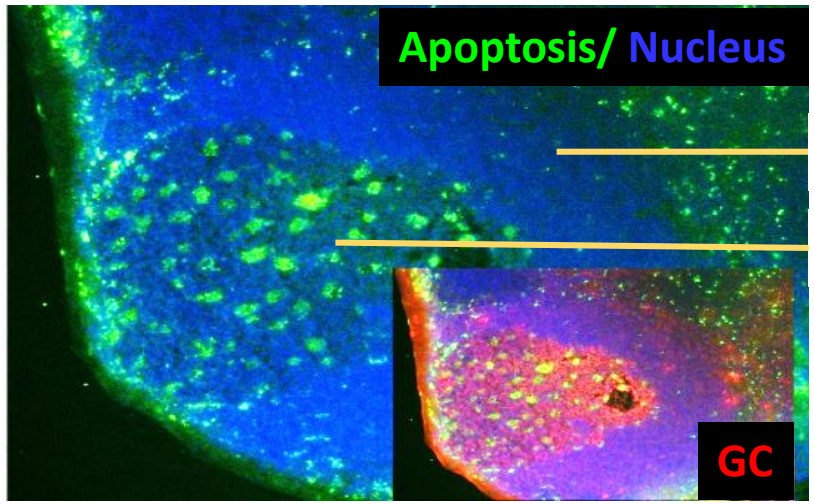


T follicular helper (TFH) cells:

- Expressing B cell chemokine receptor-CXCR5
- CD4 T cell subset that supports germinal center in B cell follicles

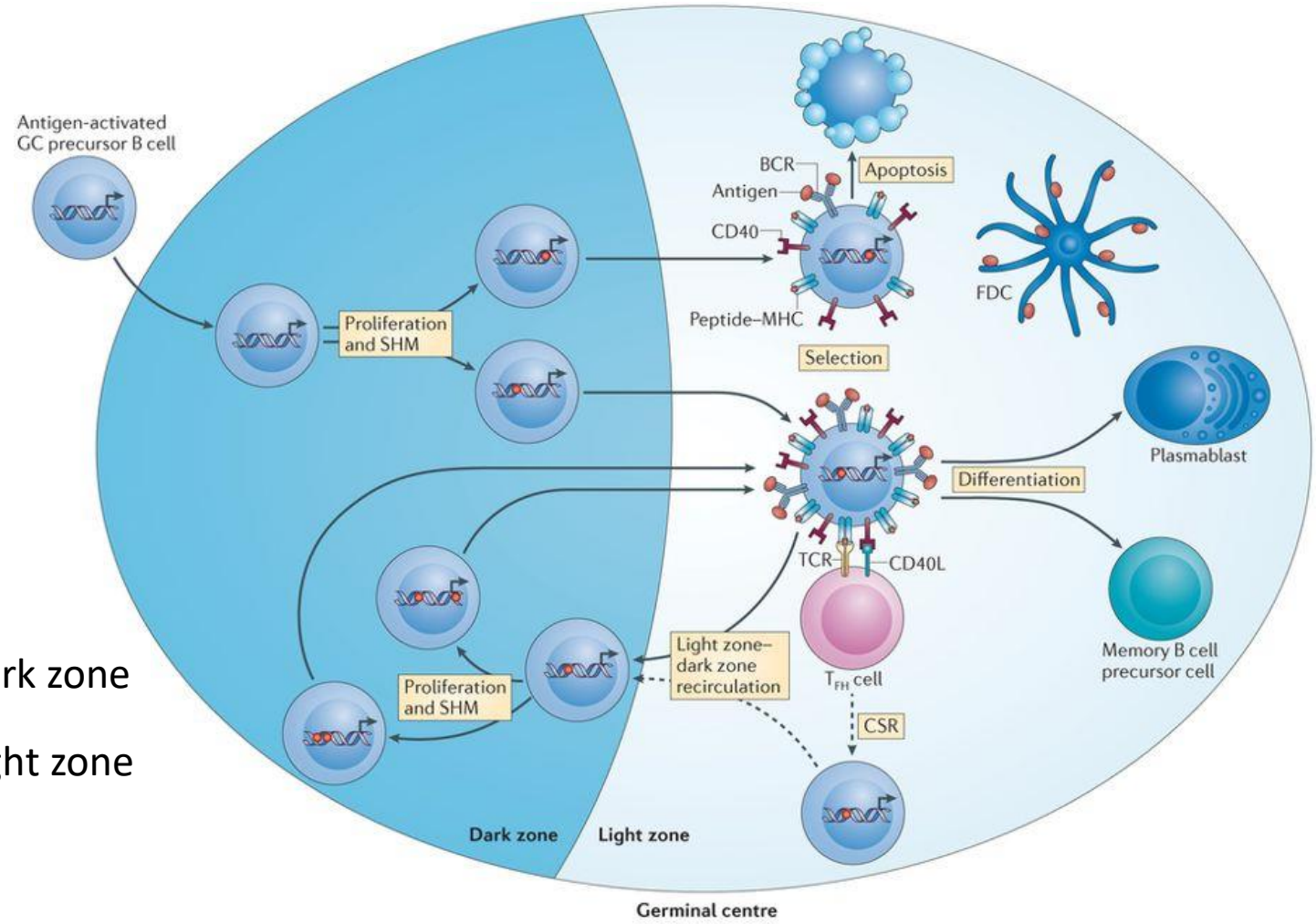
B cell activation in the germinal centre (GC)





Dark zone

Light zone



Germinal centre : proliferation, somatic mutation, class switch recombination, affinity selection

Antibody diversification

VDJ rearrangement 1987

- Recombination-activating gene (RAG)
- Severe combined immune deficiency (SCID)

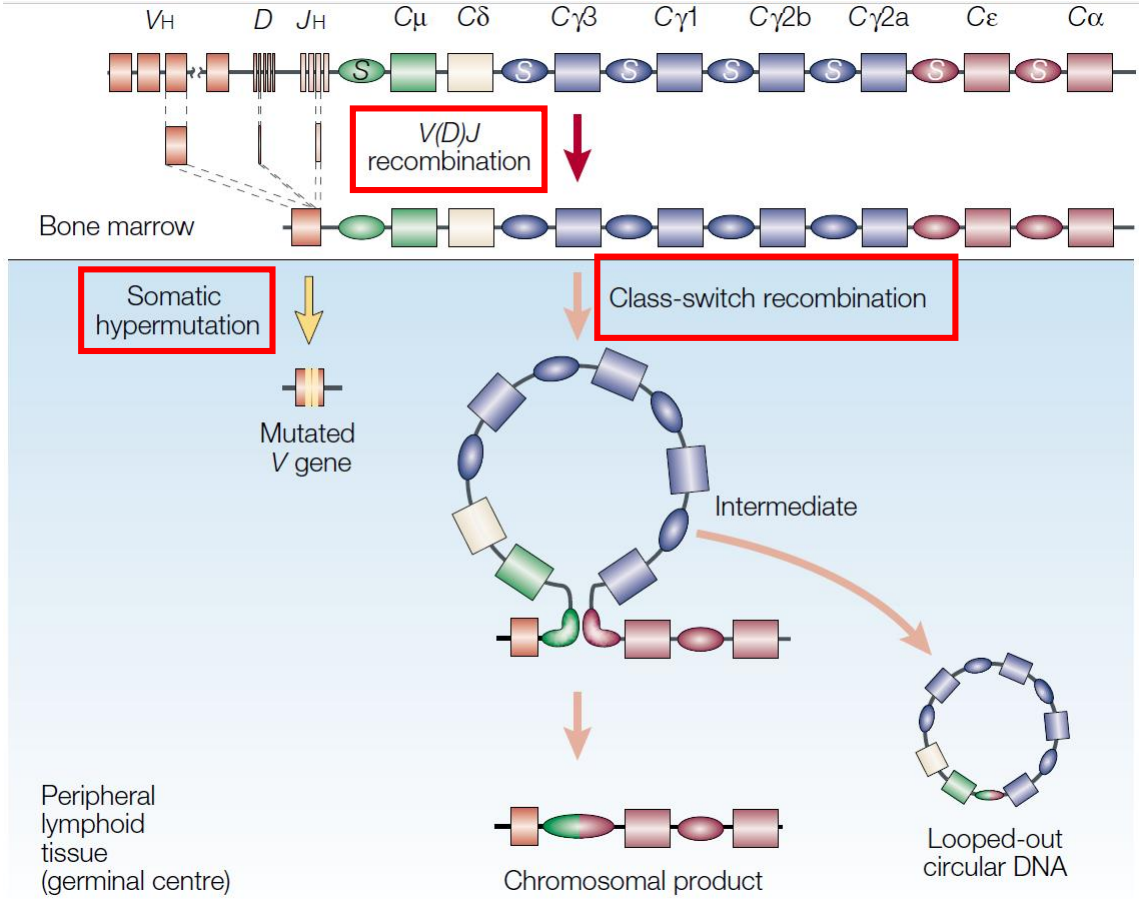
Somatic mutation

- Activation-nduced cytidine deaminase (AID)
- Common variable immunodeficiency (CVID)

Class switch recombination

- AID
- X linked hyper-IgM syndrome
- Selective IgA deficiency

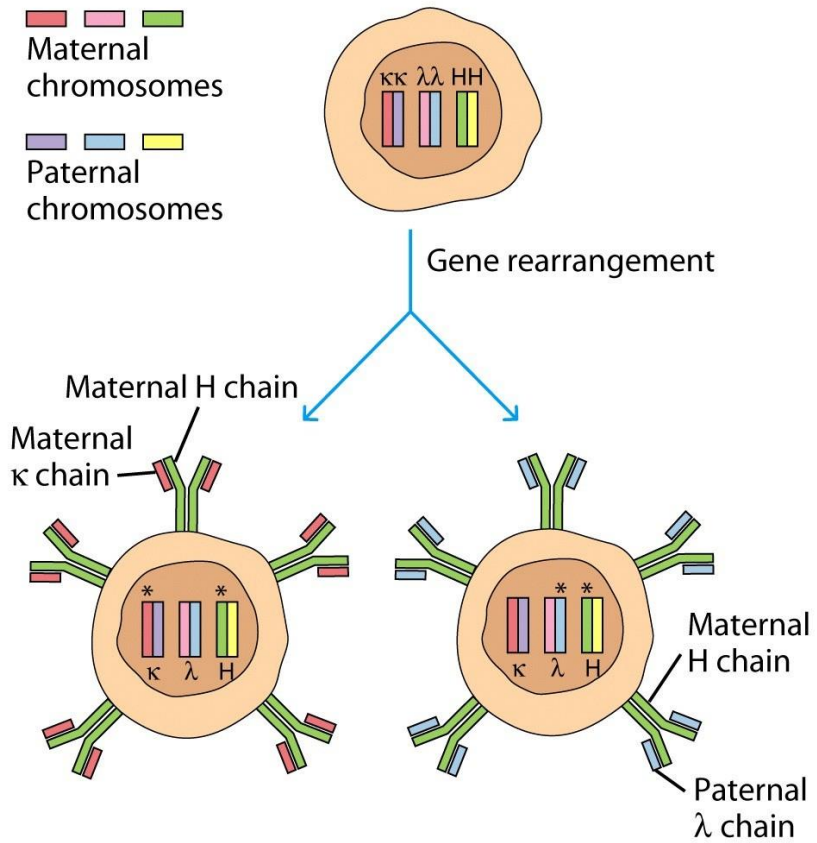
Generation of antibody diversity



Nature Reviews Molecular Cell Biology, (2001)

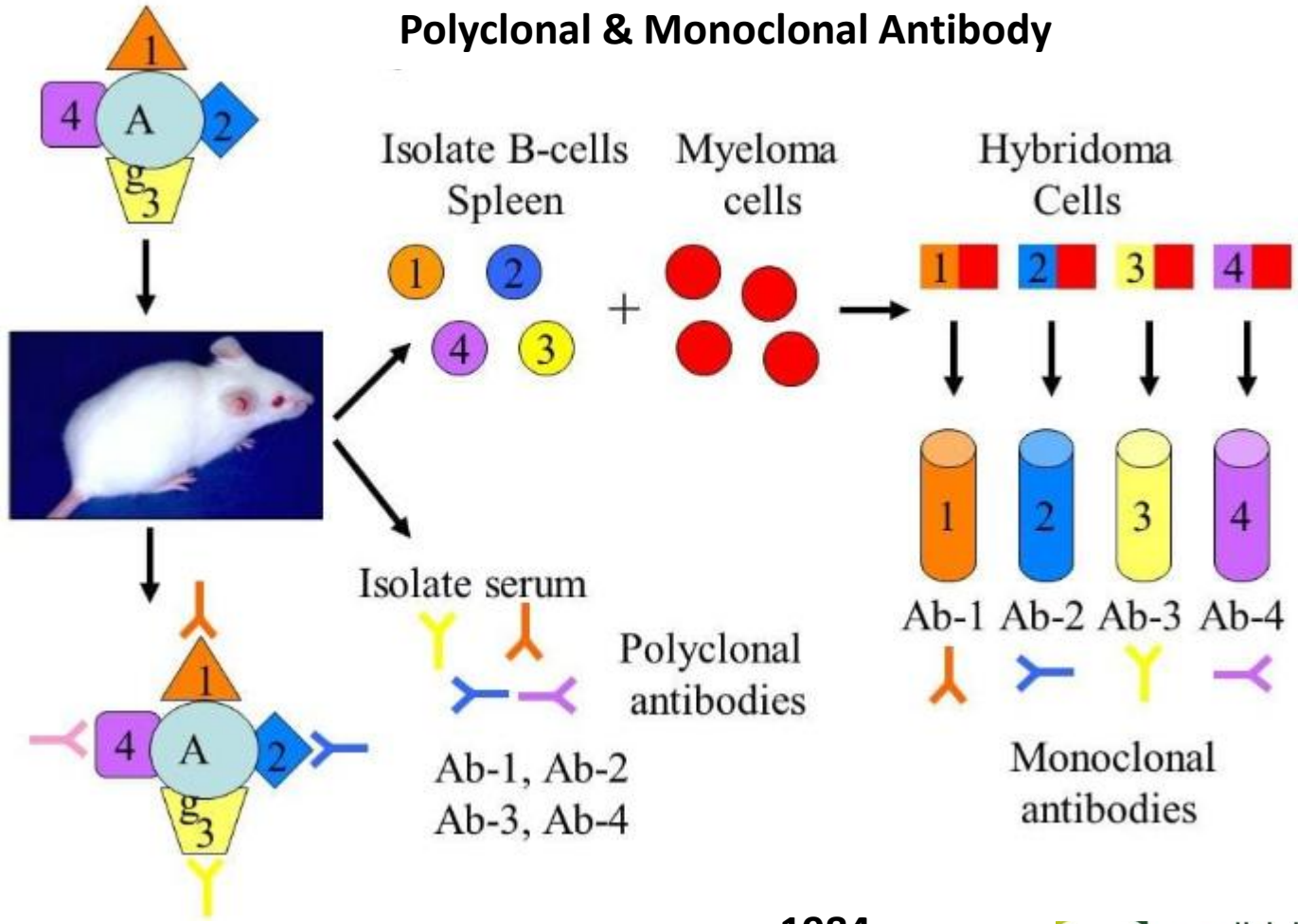
Allelic exclusion, clonal selection and monoclonal antibody

Allelic exclusion



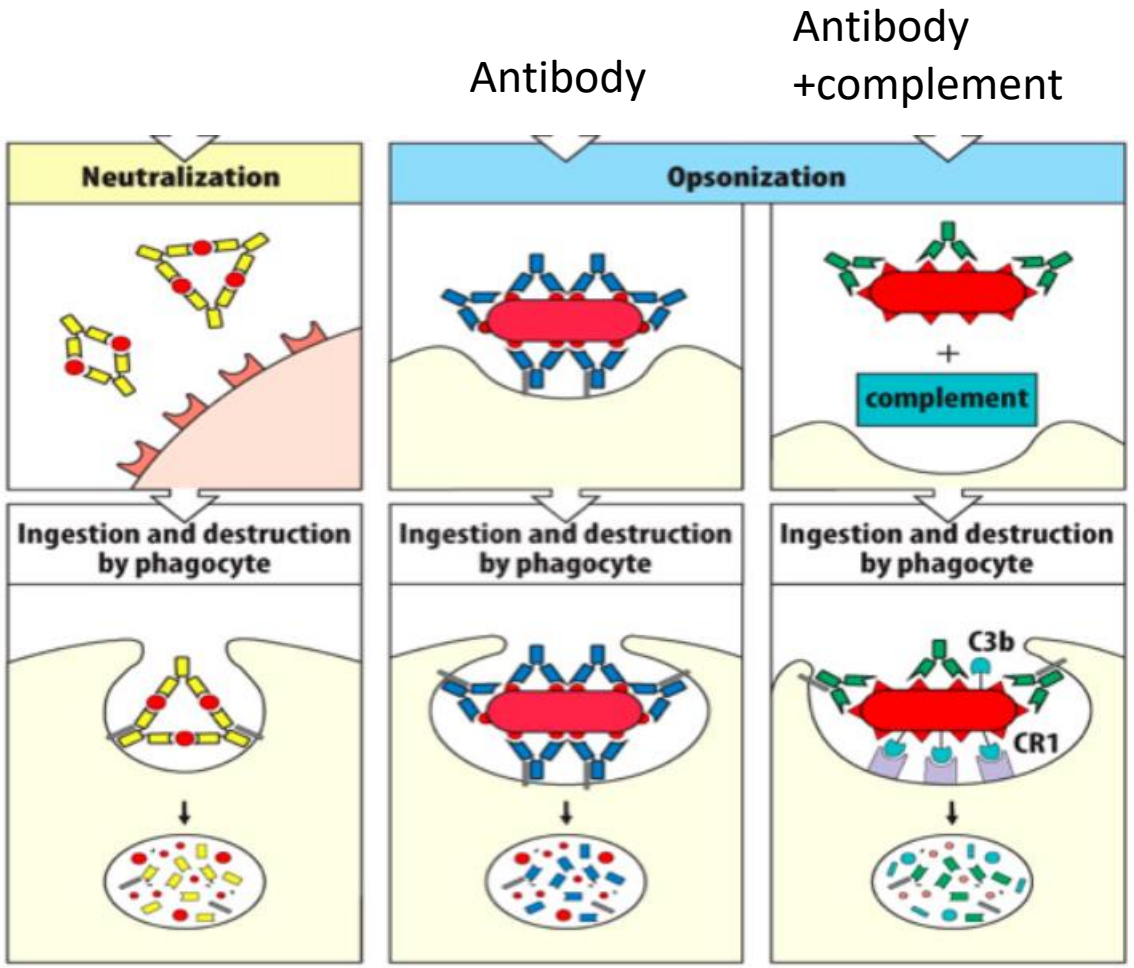
Only one of the allelic forms of a gene is permitted

Polyclonal & Monoclonal Antibody

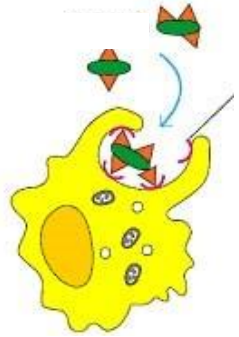


1984

Opsonization by antibody and complement



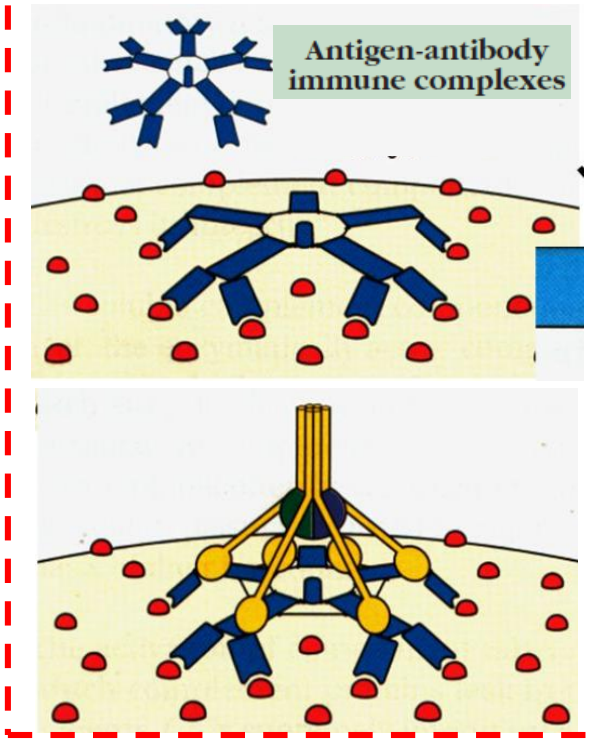
Complement



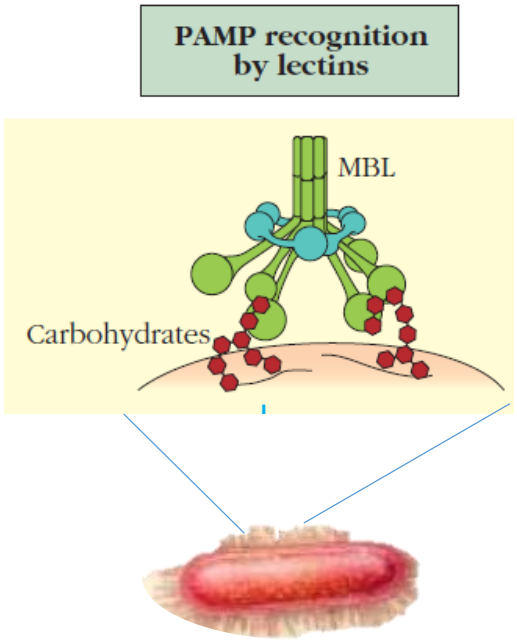
Phagocytes

Opsonization by antibody and complement

Classical pathway

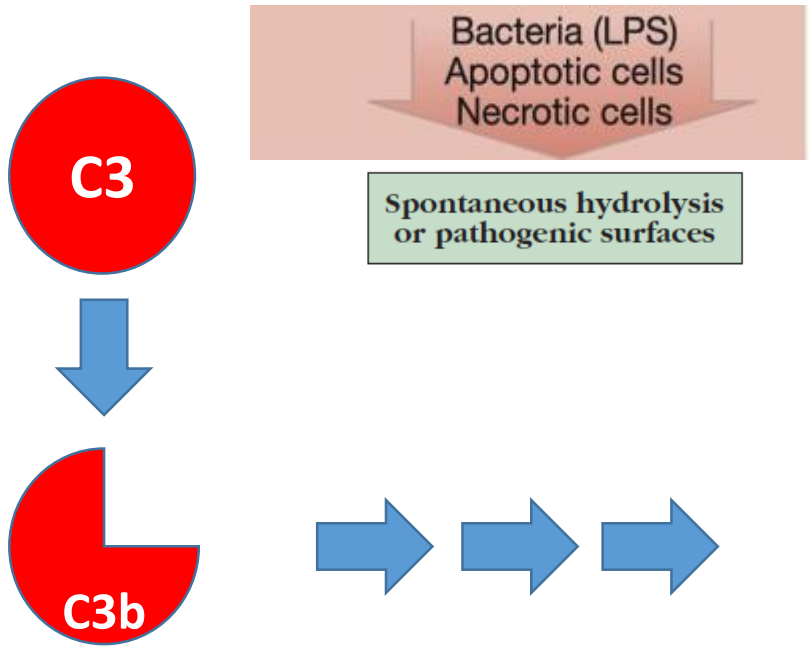


Lectin pathway

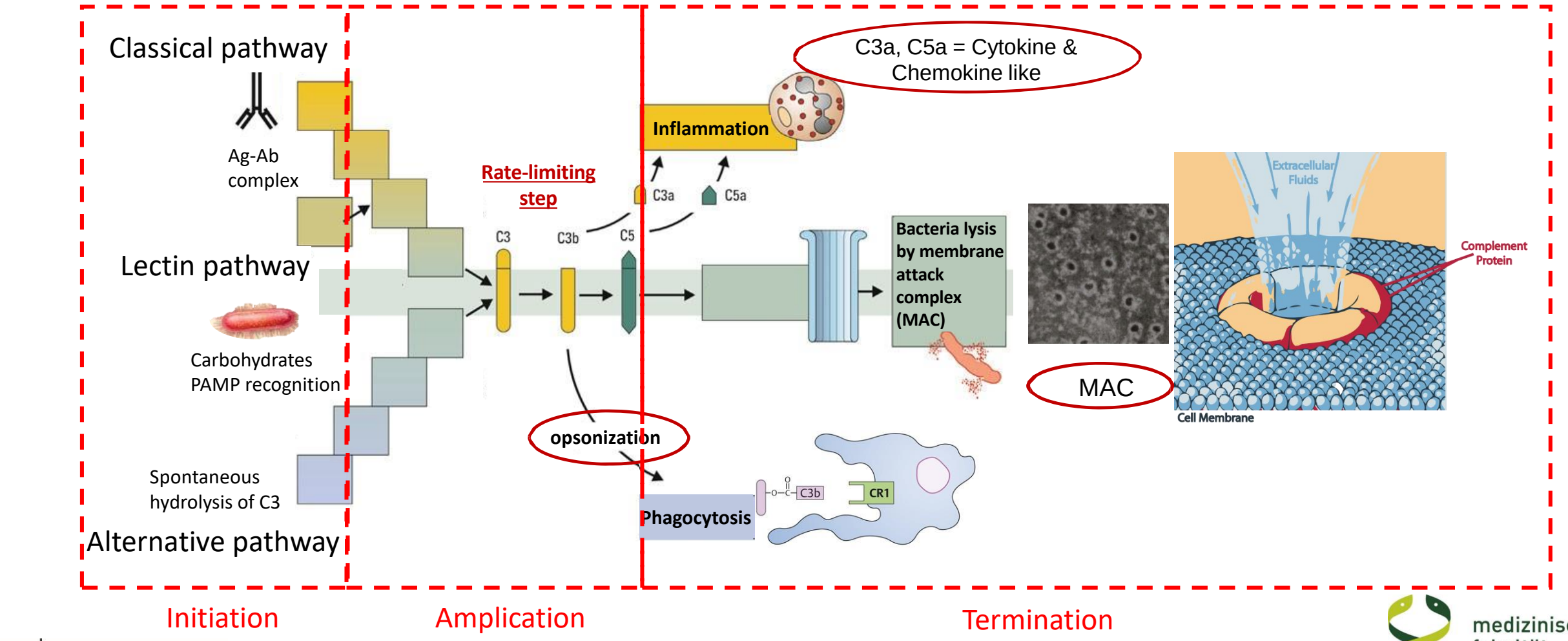


C3 convertase

Alternative pathway



Complement pathway, cascade and effect



Summary

Antibody

- Epitope (Cross-reactivity)
- Antibody structure
- Antibody classes
- B cell receptor signaling

Complement

- Opsonization
- Complement pathways
- Complement functions

B-cell (space and time)

- B cell development (BM and SLO)
- Naive mature B cell (MZ and FO)
- T-B interaction (TI and TD)
- Tfh cells and GC reaction (T and B cell zone)
- Antibody diversification
- Allelic exclusion and clonal selection

Thanks for Your Attention

Thanks for Your Attention