Introduction to Antibody Structure

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What is an antibody? (Structurally)
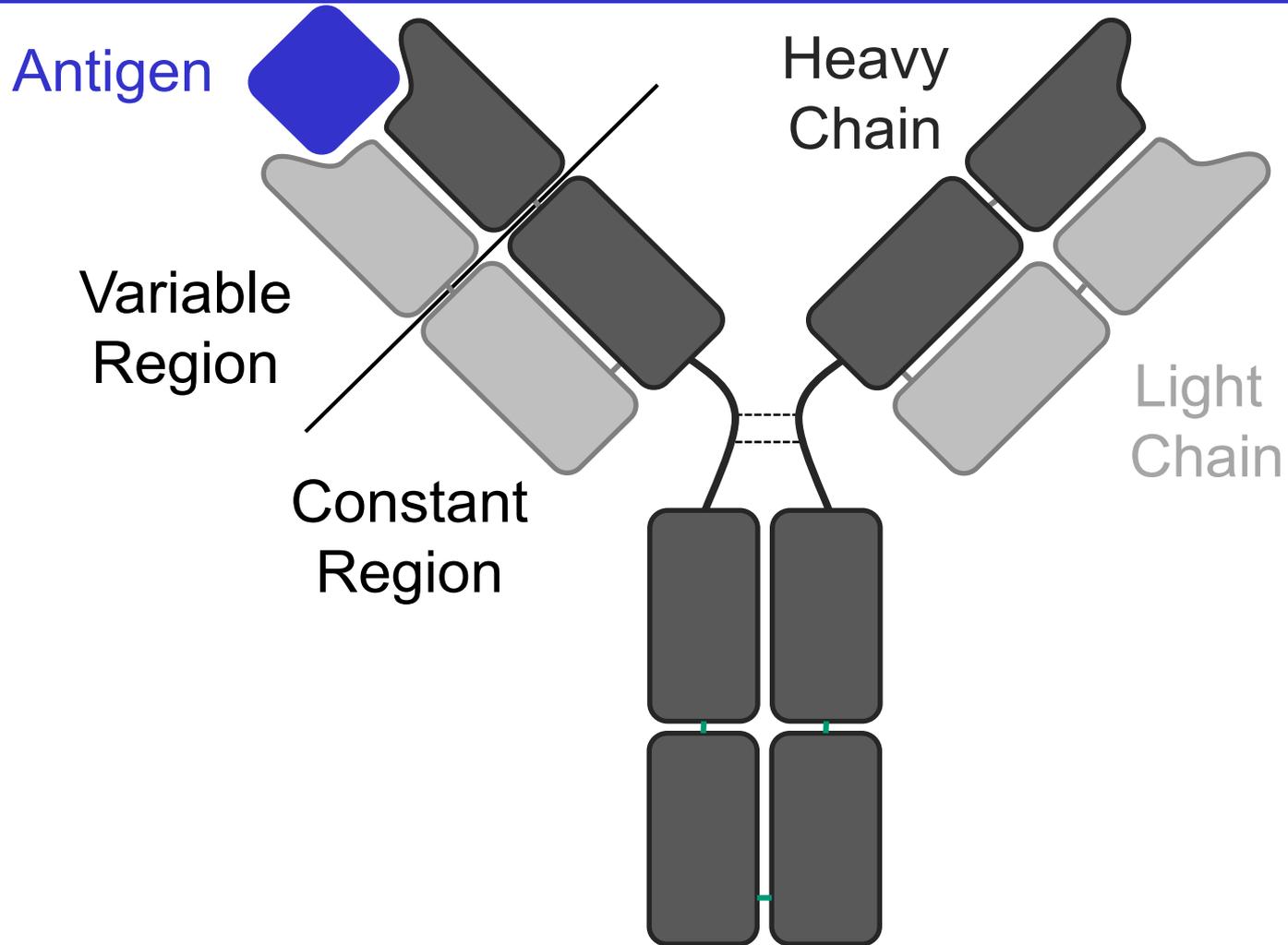
Antibody terminology: Ig
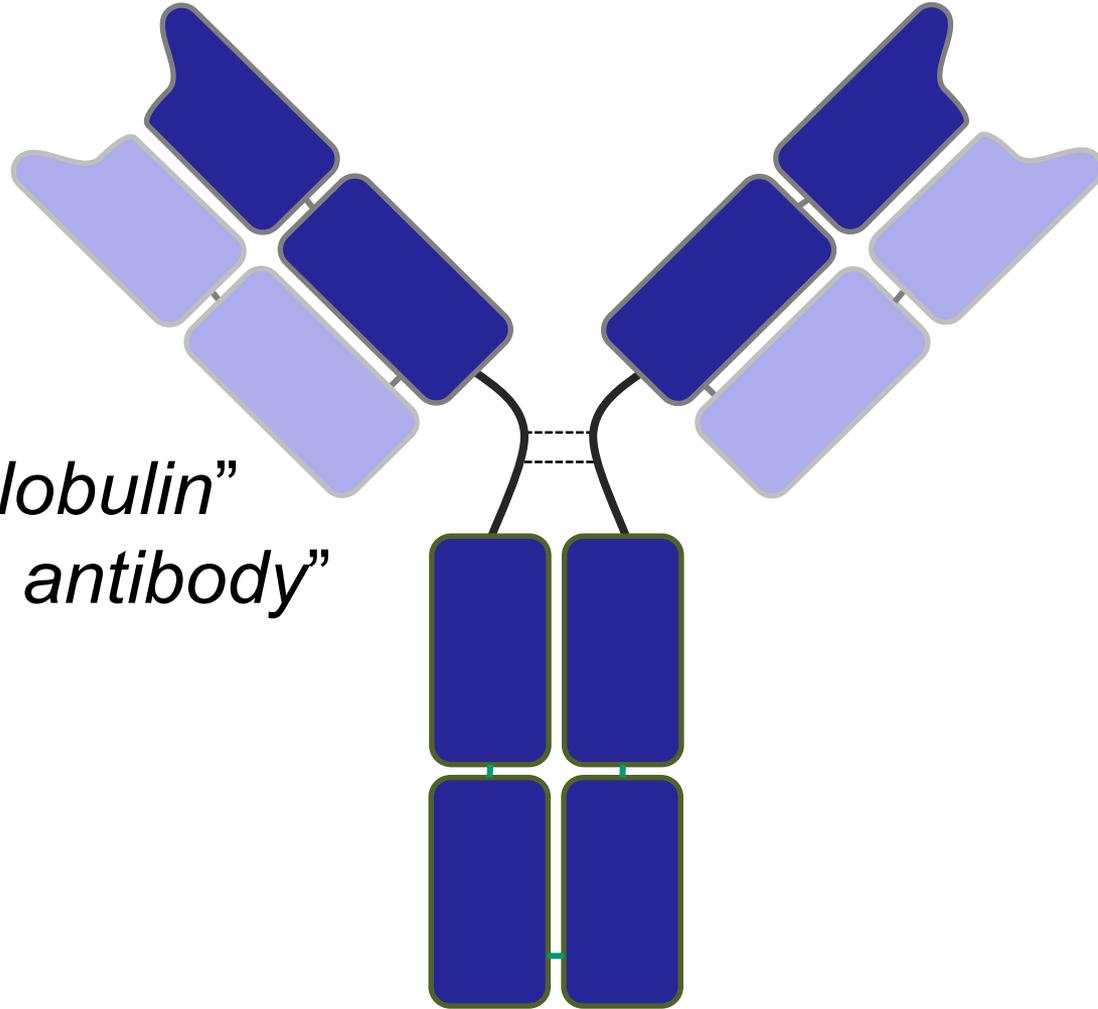
"Immunoglobulin"
or *"full length antibody"*

Antibody terminology: Fab

"Fragment antigen-binding"
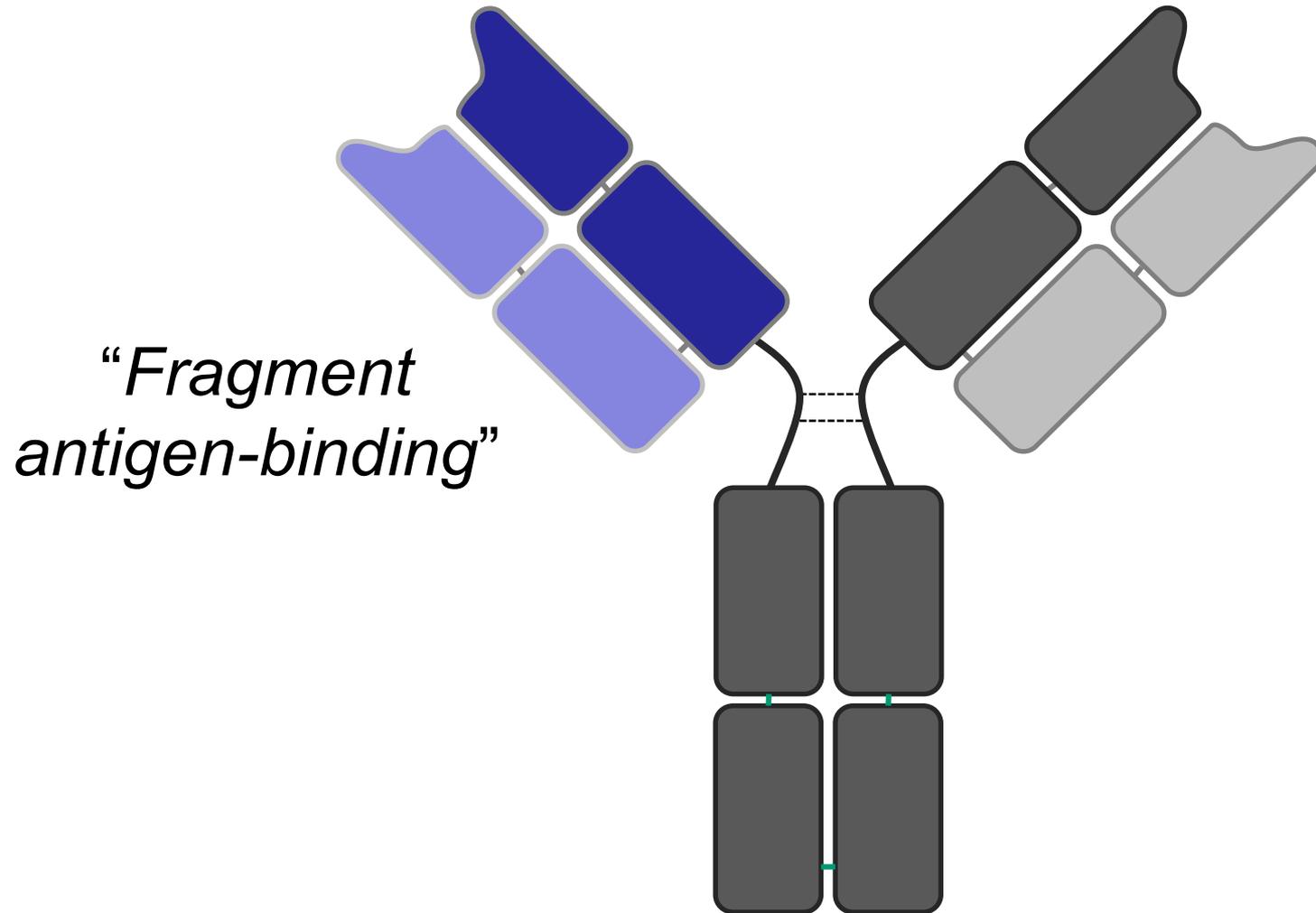
Antibody terminology: Fv

"Fragment variable"
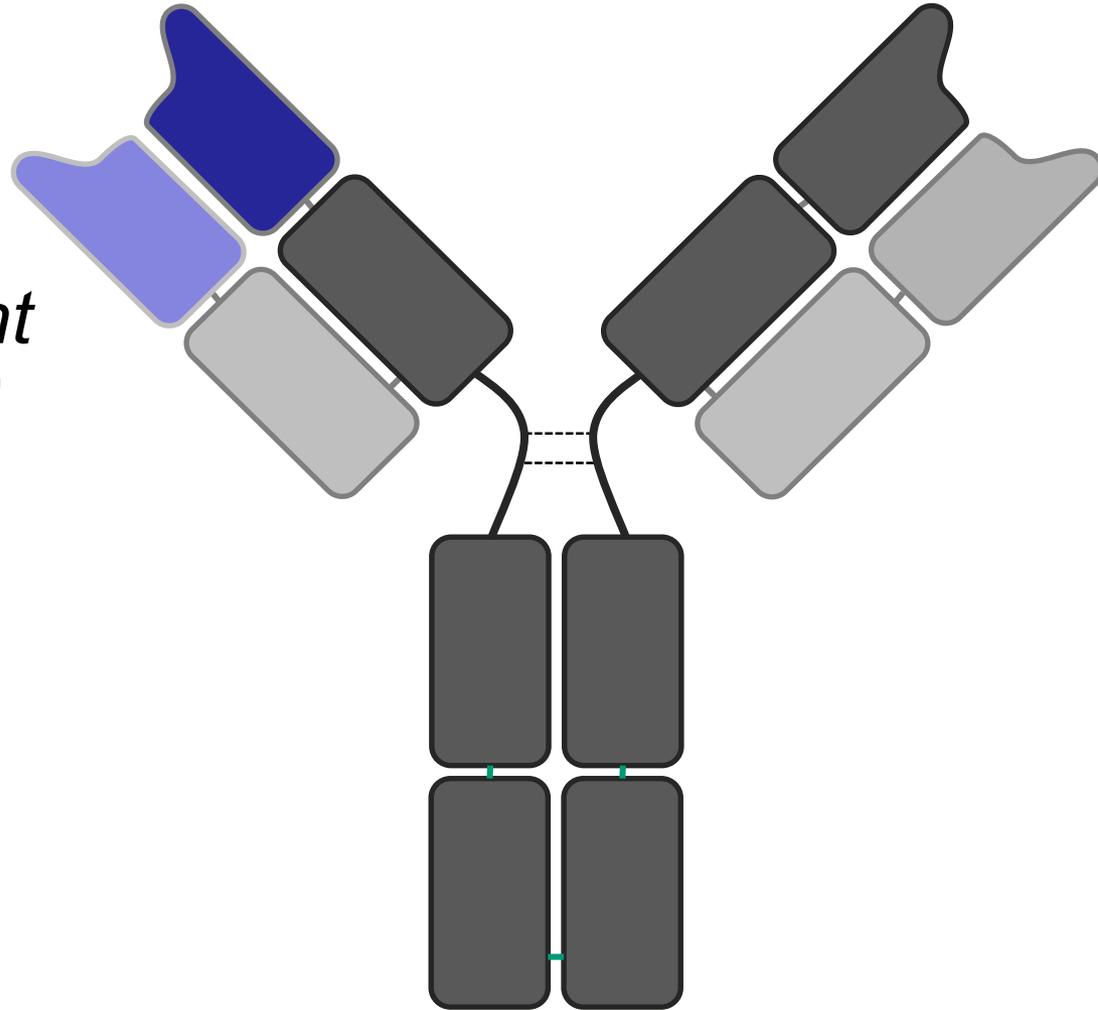
What is an antibody? (Structurally)
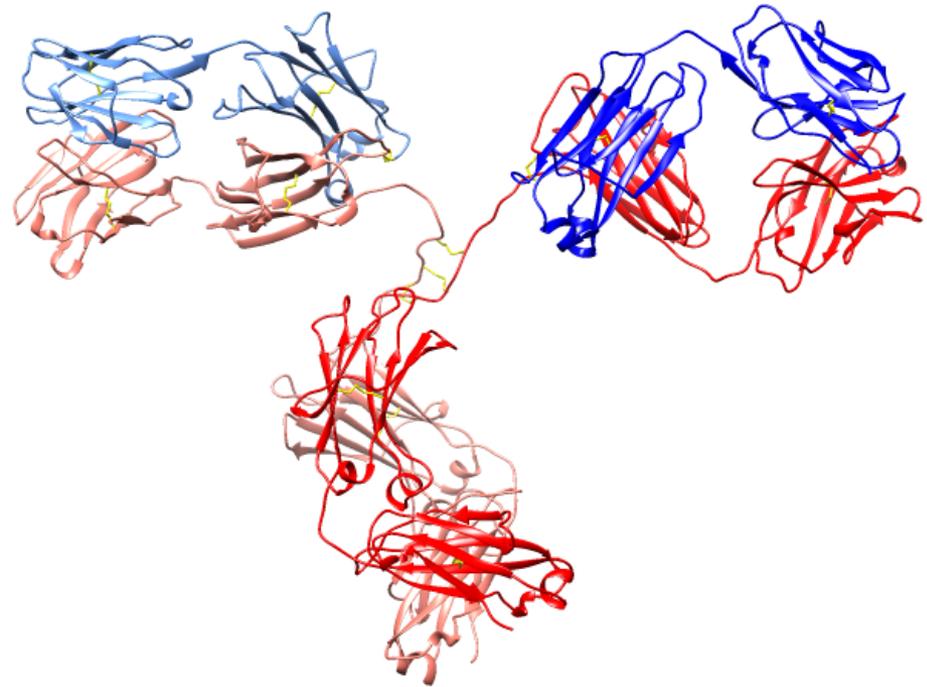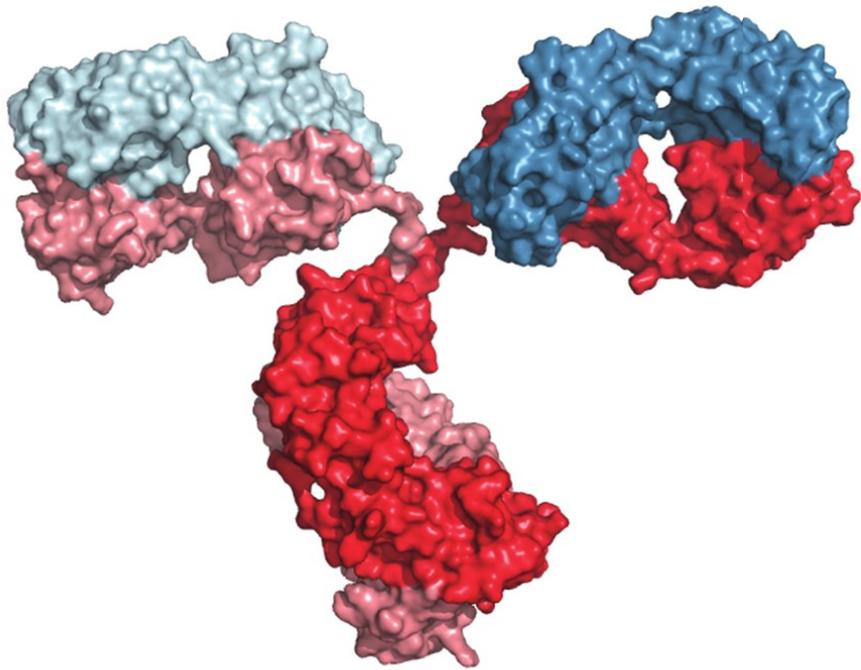
The immunoglobulin domain fold
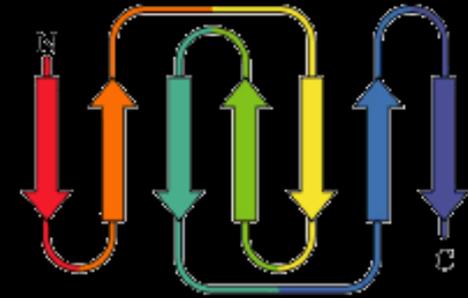
stacked 4-stranded and 3-stranded antiparallel β-sheets

Anthony S. Serianni

Complementarity determining regions
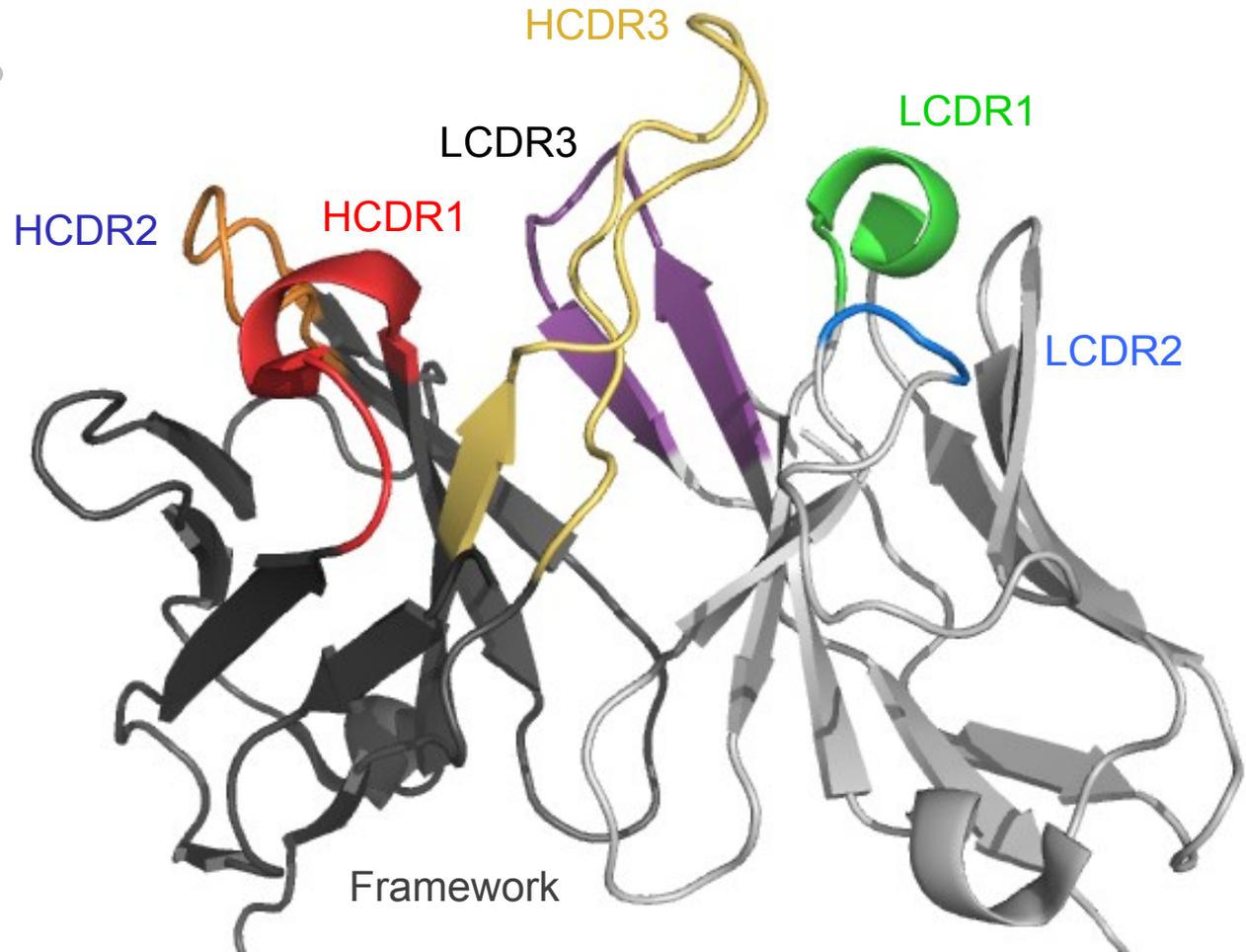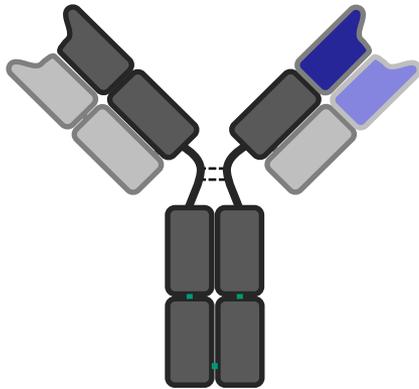
CH65
PDBID: 3SM5

CDR are hypervariable
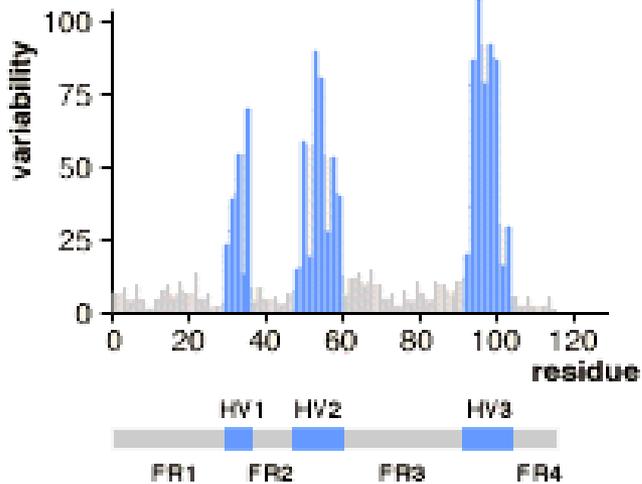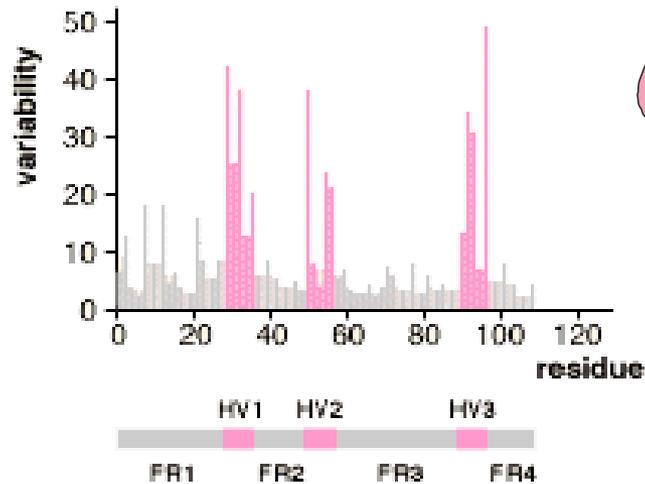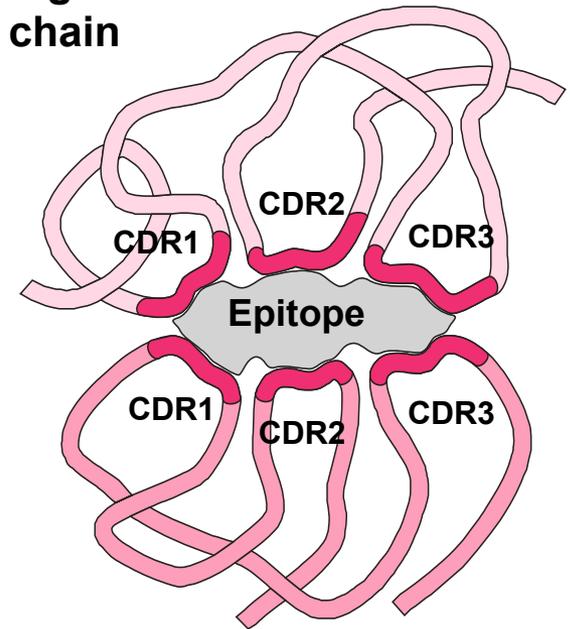
Recognition of antigens

Protein-protein interactions are determined by shape and physicochemical properties of solvent exposed loops, such as CDR loops.

PDB ID: 3SM5
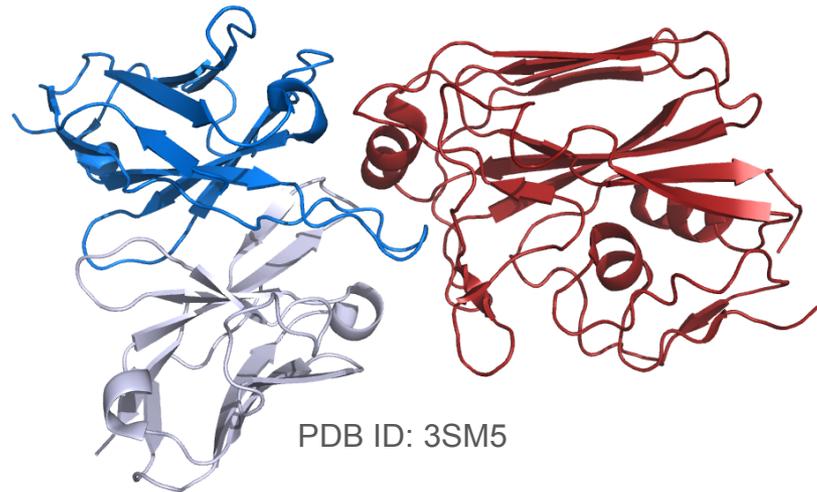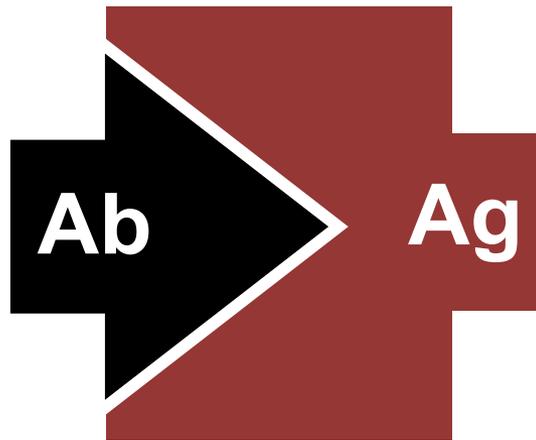
Sequence ➡ Structure ➡ Function

Antibodies are produced by B cells
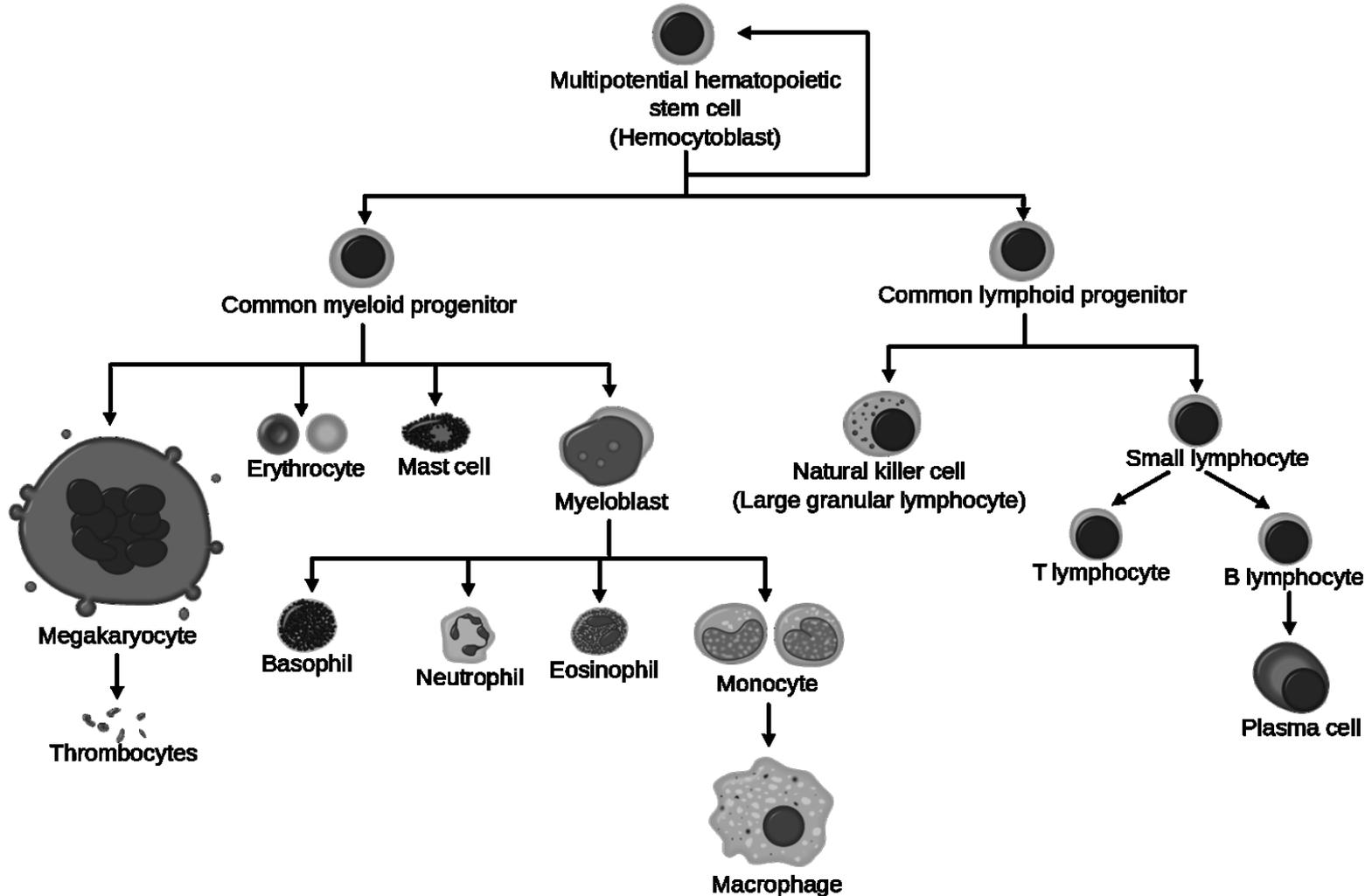
Antibody generation is an integral part of B cell development

| Stem cell | Early pro-B cell | Late pro-B cell | Large pre-B cell | Small pre-B cell | Immature B cell | Mature B cell |

Bone Marrow   Periphery
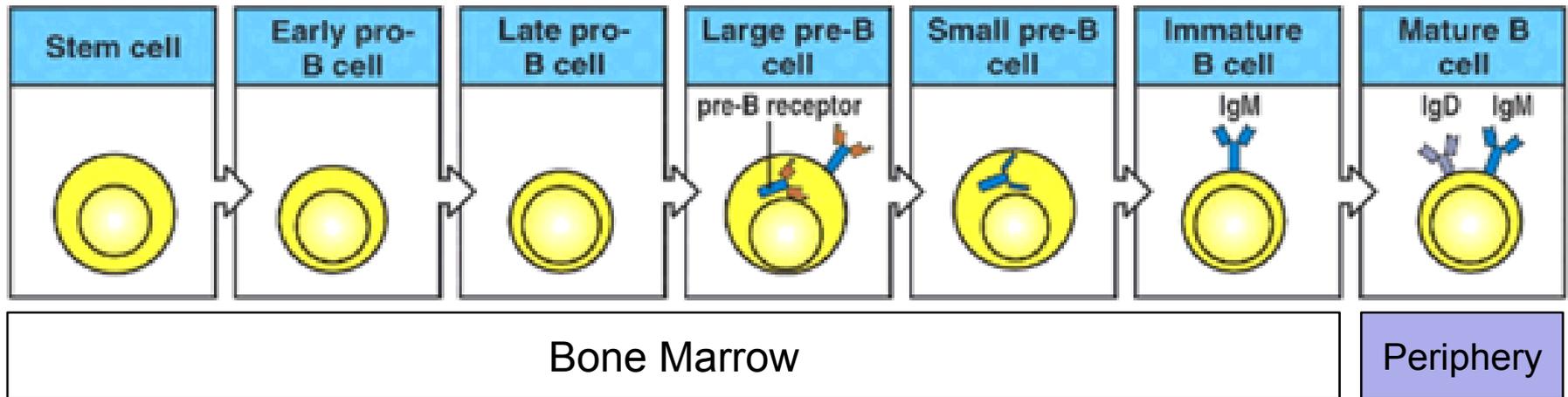
Antibody diversification is achieved primarily through four mechanisms

Locus	V Genes	D Genes	J Genes
IGH	38-46	23	6
IGK	34-38	0	5
IGL	29-33	0	4-5

V(D)J Recombination

'P' nucleotides generated by RAG

'N' nucleotides added by TdT

Hybridization and DNA repair

Junctional Diversity

Heavy Chain   Light Chain

Heavy/Light Chain Pairing
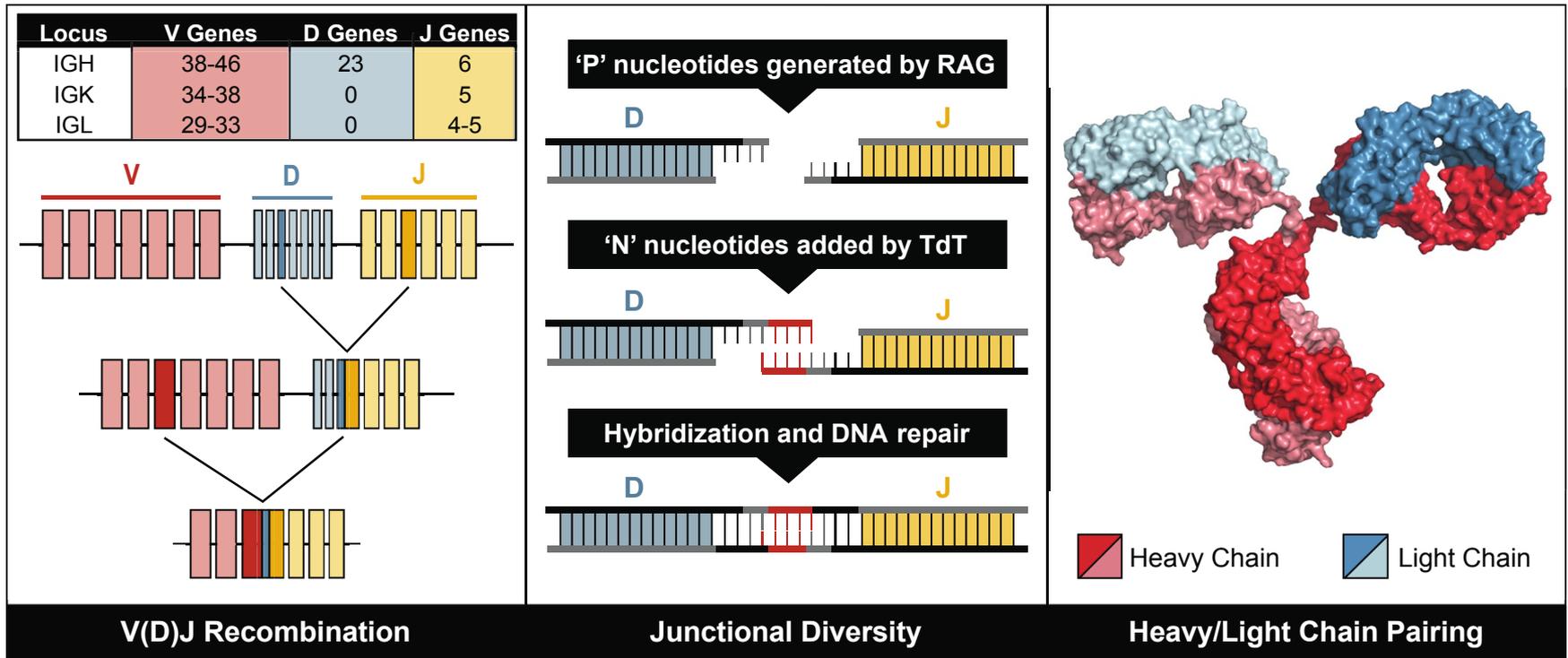
… and affinity maturation.

V(D)J recombination

Locus	V Genes	D Genes	J Genes
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Junctional diversity

'P' nucleotides generated by RAG

D   J

'N' nucleotides added by TdT

D   J

Hybridization and DNA repair

D   J
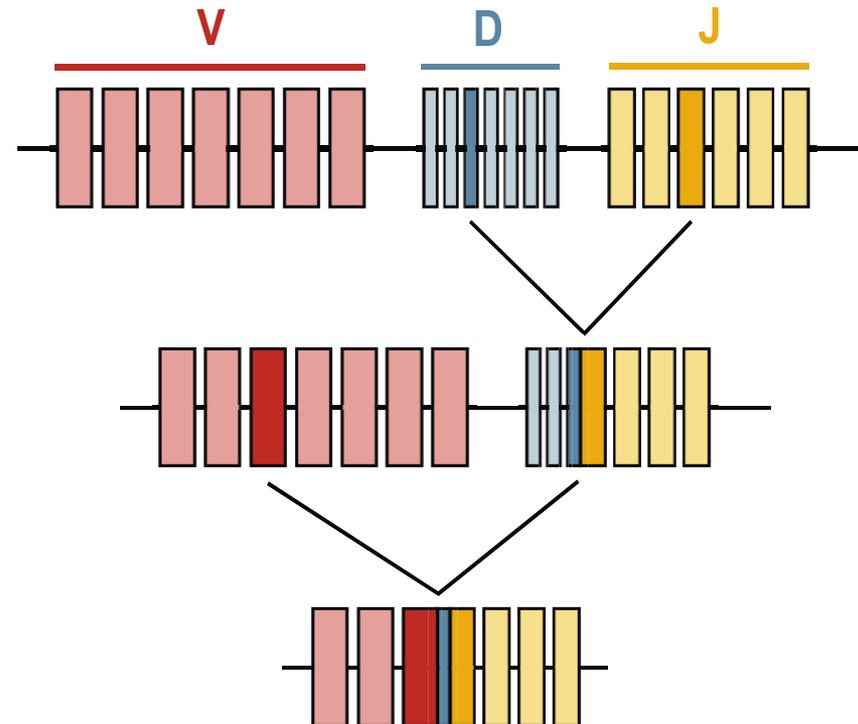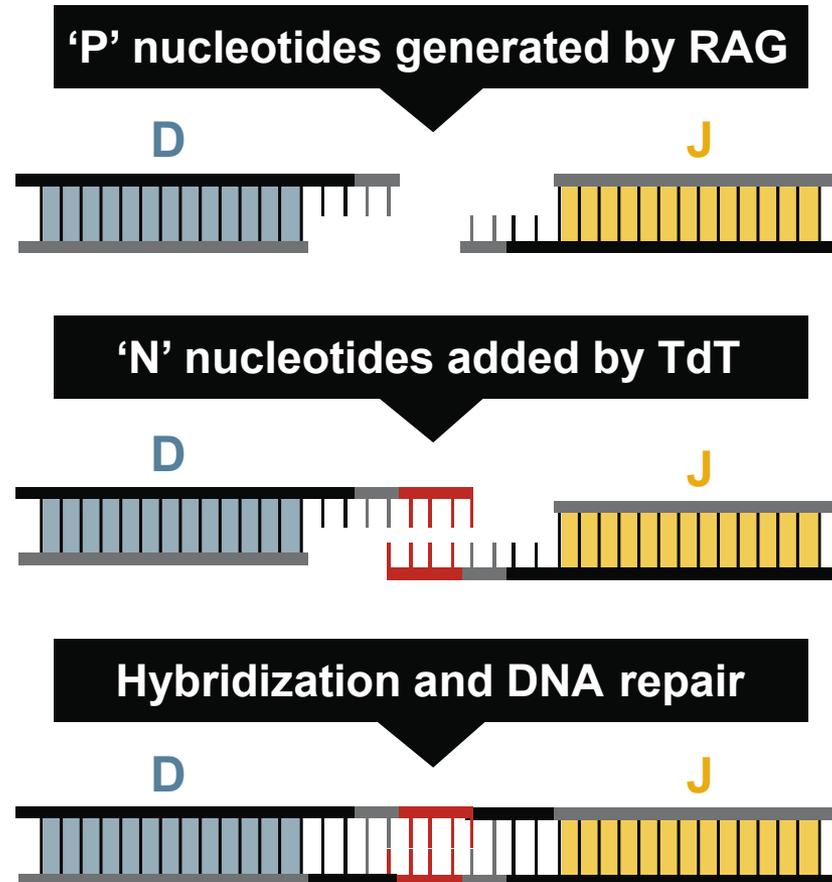
V(D)J gene sequences mapped to CDRs
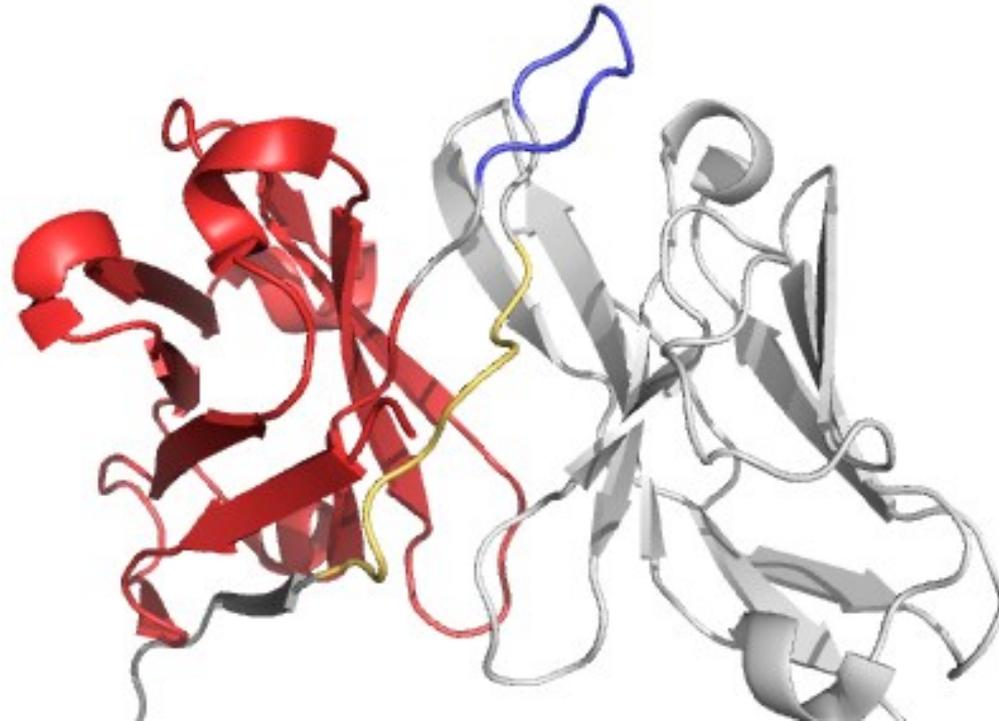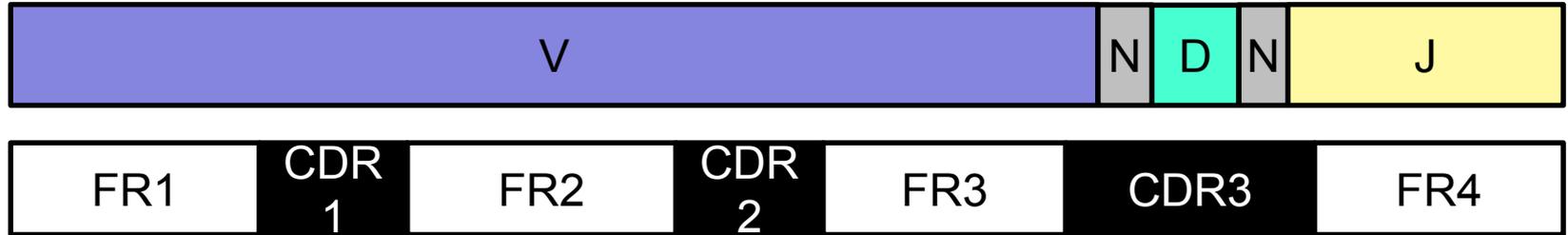
Heavy/light chain pairing
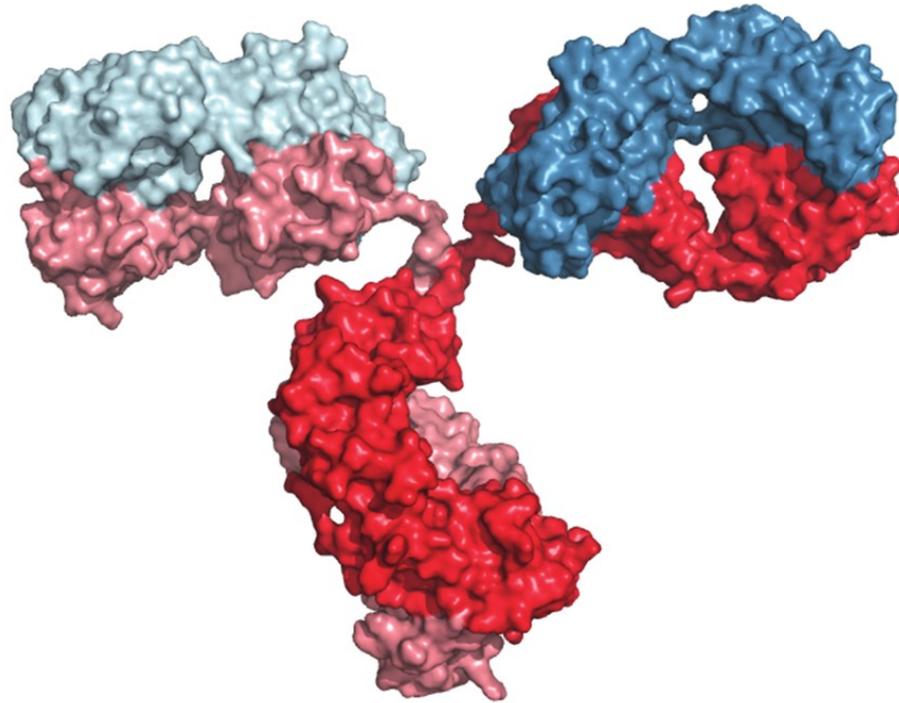
Heavy Chain   Light Chain

Affinity maturation
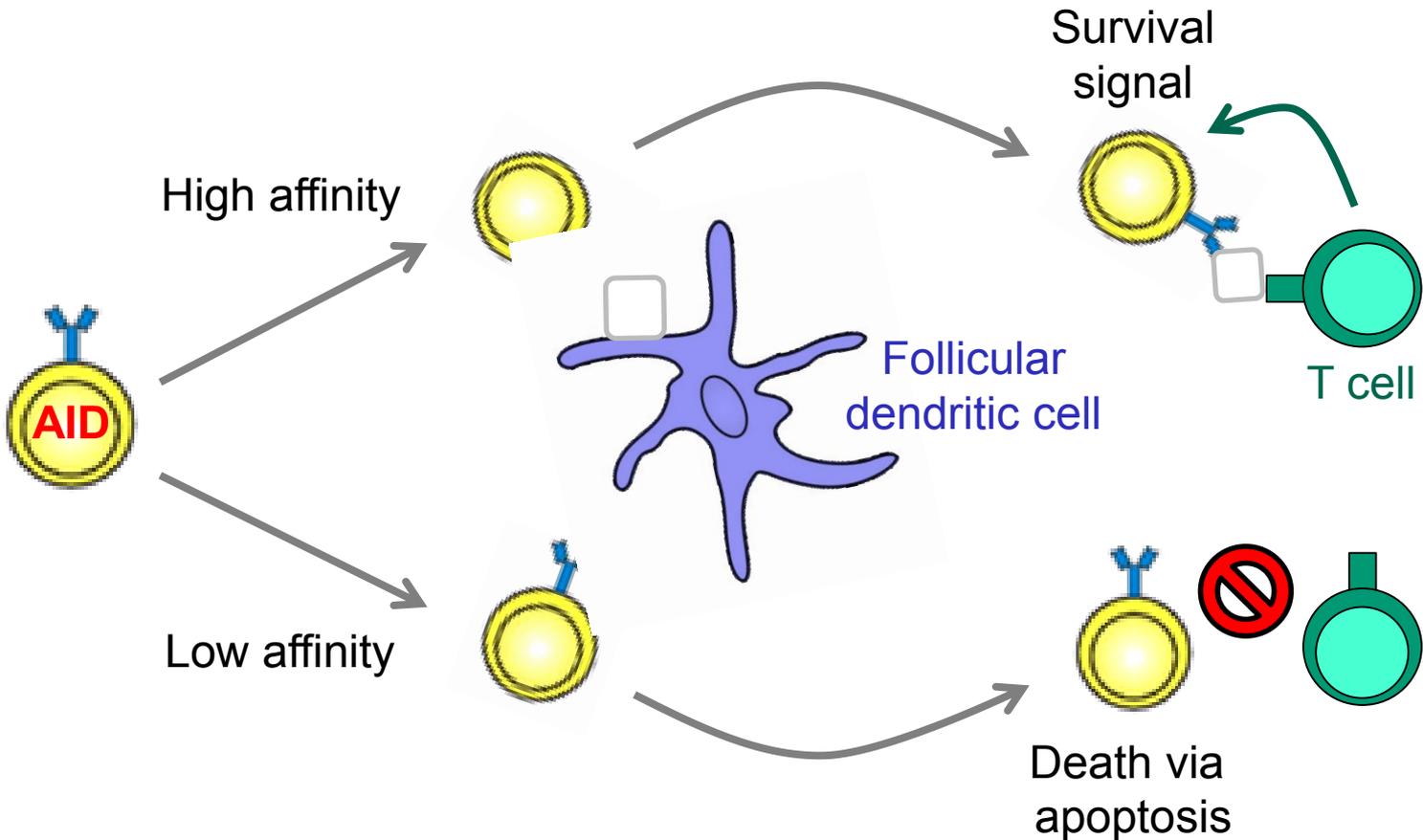
Humanized antibodies
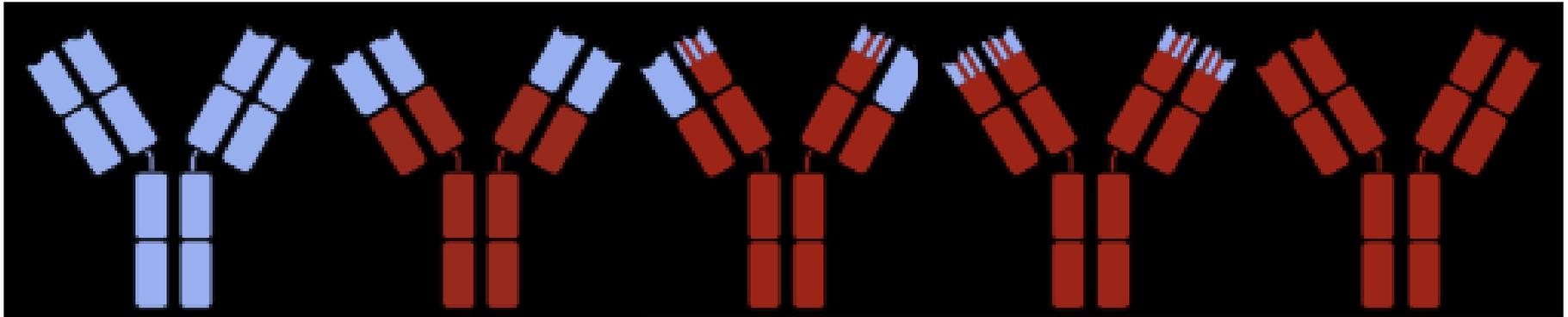
Mouse Antibody   Chimeric Antibody   Chimeric/ Humanized Antibody   Humanized Antibody   Human Antibody

Bispecific antibodies

Lewis, SM et al., Nat. Biotech., 2014
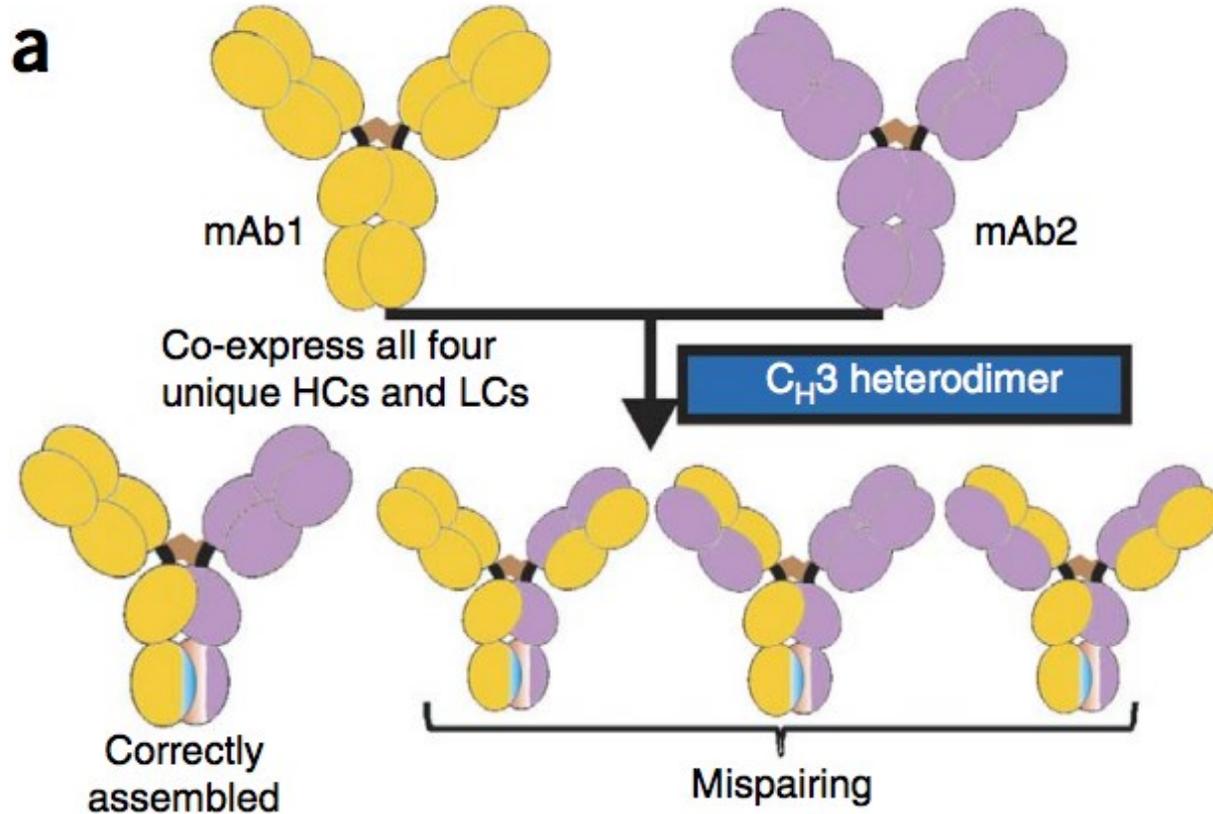
Resources

- Antibody structure:
  - North, Lehmann and Dunbrack, J Mol Bio 2011
  - Morea, Tramontano, Rustici, Chothia and Lesk, J Mol Bio 1998

- Sequence analysis web tools:
  - IMGT V-Quest
  - IMGT DomainGapAlign

- Antibody numbering guide:
  - AHo's Amazing Atlas of Antibody Anatomy