

(9/11) 7: Ab Structure & Function

Thursday, September 11, 2014
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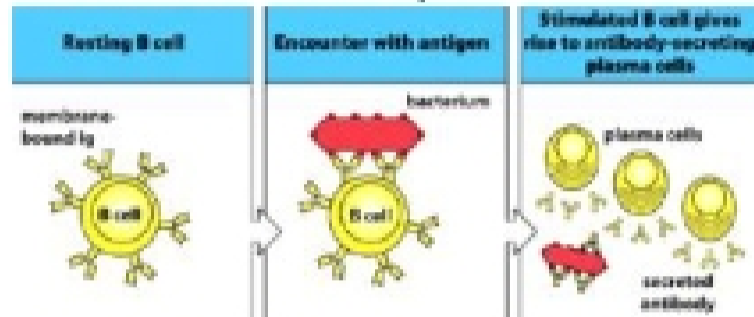
Lecture Outline:

- intro to B Cells, B cell receptor (BCR), & Ab
- B cell differentiation to Ab secreting plasma cells
- Ab structure
- Ab recognition of Ag (epitopes or antigenic determinants)
- 5 isotypes of Abs & their effector functions
- generation of monoclonal Abs (mAbs) & applications

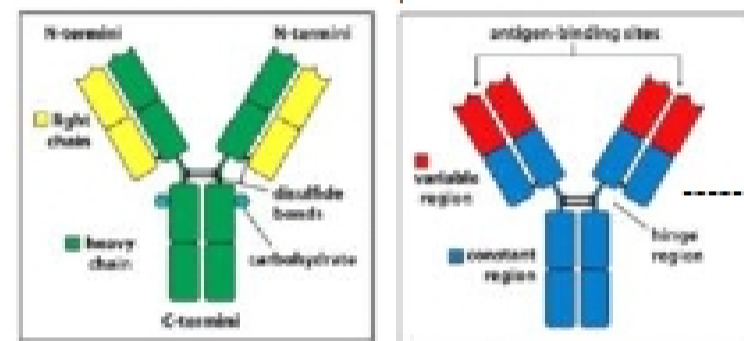
Adaptive Immune Cells: B/T

Innate Immune Cells: Mast, Dendritic, Macrophage, NK, Complement Protein, Granulocytes (Neutrophil, Eosinophil, Basophil)

PLASMA CELLS - secrete Abs in response to stimulated B-Cells

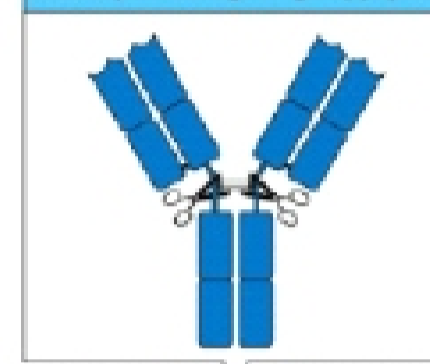


IgG - bound to B-Cell membrane; flexible

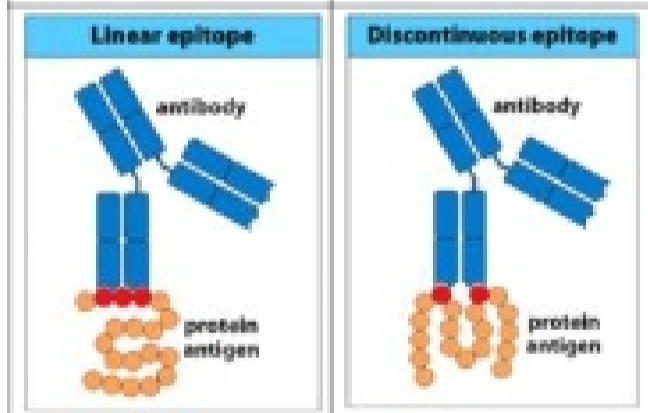
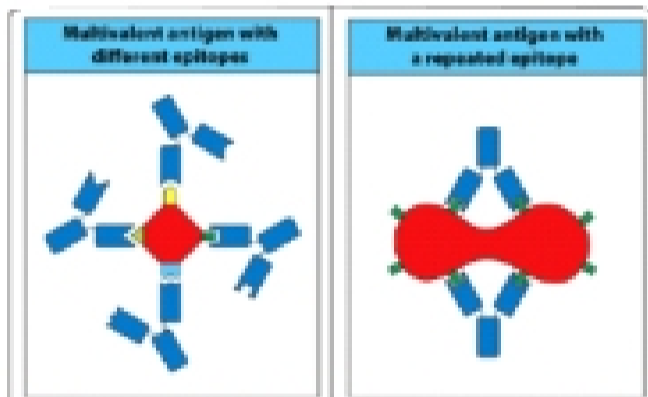
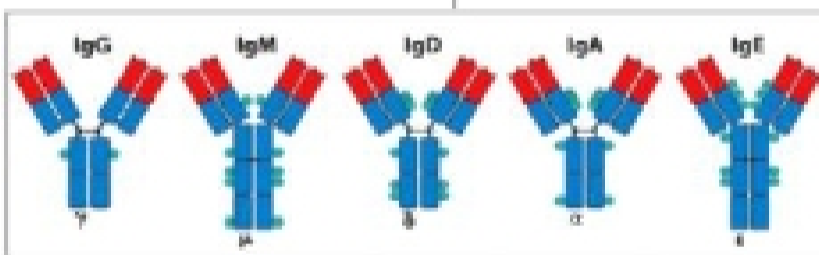
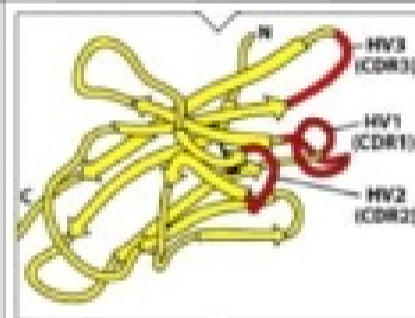
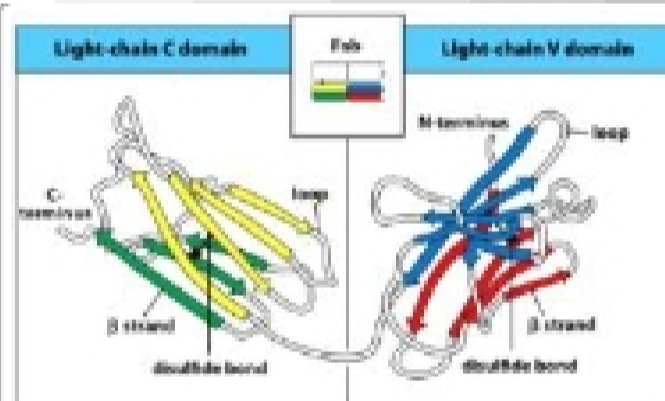
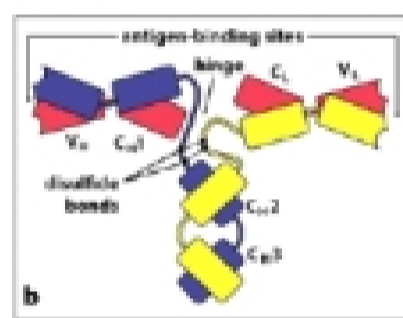
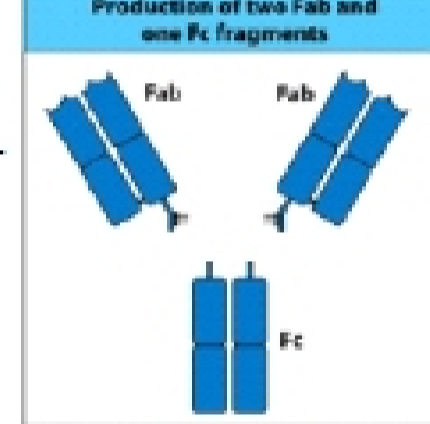


PROTEASE - cleaves IgG at hinge region

Proteolytic cleavage of IgG by pepsin



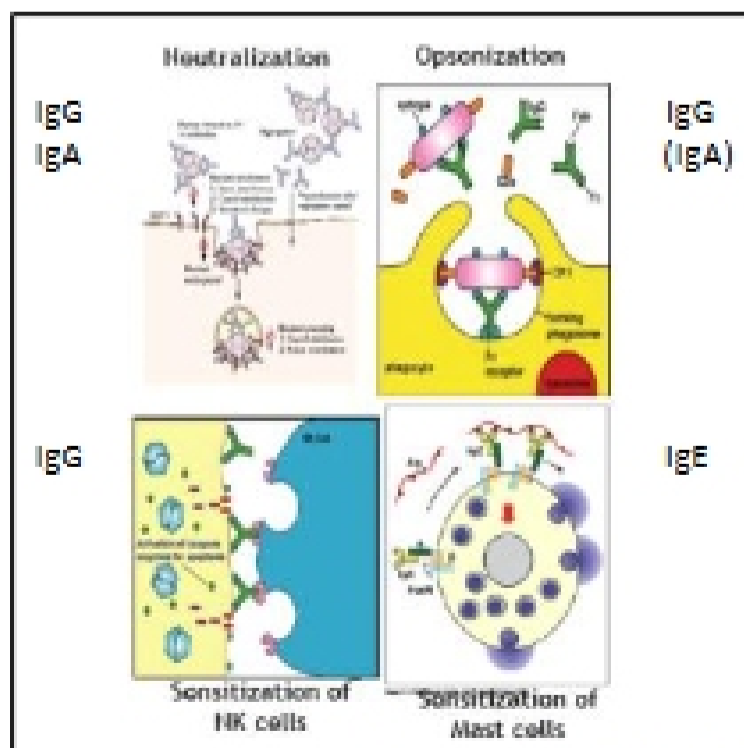
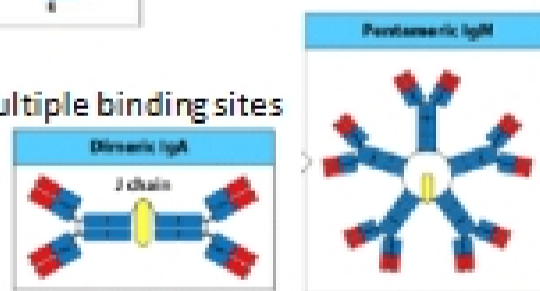
Production of two Fab and one Fc fragments



AVIDITY - overall strength of Ab binding to Ag w/ multiple binding sites

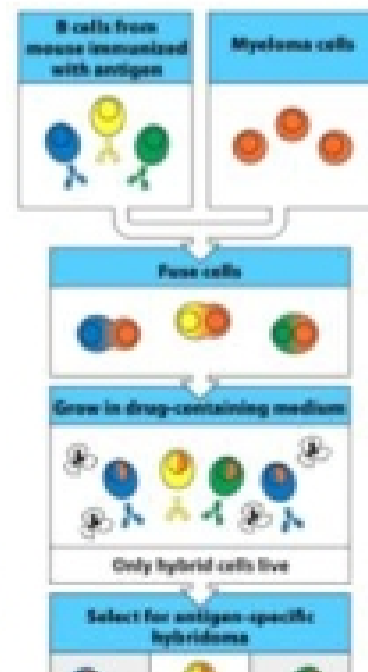
IgM - can form pentameric structure w/ J-Chain

IgA - can form dimeric structure w/ J-Chain



mAb - same parent cell, bind to same epitope (monovalent)

- FLOW CYTOMETRY - detects cells labeled with fluorescent Abs



mouse B-Cells Immunized w/Ag + Myeloma cells
↓
Hybridoma (only hybrids survive)
↓
clone Ag-specific Hybridoma



Function	IgM	IgD	IgG1	IgG2	IgG3	IgG4	IgA1	IgA2	IgE
Neutralization	+	-	+++	+++	+++	+++	+++	+++	-

Opsonization	-	-	+++	-	++	+	+	-
Sensitization for killing by NK cells	-	-	++	-	++	-	-	-
Sensitization of mast cells	-	-	+	-	+	-	-	+++
Activation of complement system	+++	-	++	+	+++	-	+	-



mouse	chimeric	humanized	human
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Summary:

- circulating Ab is soluble form of Ag-specific receptors on B-Cells
- the universe of Ag recognized by Ab is virtually limitless
- each Ab contains 2 Heavy Chains & 2 Light Chains
- each Ab chain has a V & C region
- each Ab has 2 Fab & 1 Fc regions
- V regions of both chains are required for formation of Ab-binding site
- C region is unique for every class of Ab
- 5 major classes of Ab: IgM, IgD, IgG, IgA, IgE (all have different effector functions)
- Application of Ab: mAbs, Flow Cytometry, Therapeutic Abs