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Antibody Structure and Function

Monday, February 11, 2008
10:00 AM

- Antibody Structure
  - Derived from monoclonal antibodies secreted by plasmacytomas
  - All antibodies made of two identical heavy chains and two identical light chains
  - Constant Region
    - Located in carboxy part of chain
    - Light chains: numbered 108-214, κand λ
    - Heavy chain: α, γ, δ, ε, μ
      - γ1, 2, 3, 4
      - α 1 and 2
      - Subclasses have exactly same sequence
  - Variable Region
    - AA sequence in amino terminal part never the same for two immunoglobulins
    - Light chain residues 1-107
    - Variability = number of different amino acids at a residue/frequency of the most frequent amino acid
    - Hypervariable regions w/in a variable region have variability from 15-100
    - Hypervariable regions come together to form antigen binding site = complemtarity determining region (CDR)
    - Framework regions are clusters of amino acid residues btwn HV regions w/ variability of 1-20; form scaffold upon which variable region is built
    - Domains have 110 amino acid units with disulfide bridge btwn two cysteines
  - Folding of the Immunoglobulin
    - Variable and constant regions fold the same and are independent of each other
      - Parallel β-pleated sheets perpendicular to the cys-cys bond
      - HV residues clustered near each other and form the antigen binding pocket
    - Not every HV region contacts antigen
- Antibody Function
  - Antibody Classes
    - IgM: 4 constant region domains, 1.5 mg/ml in serum; fixes complement, opsinin
    - IgG: 3 constant region domains, proline rich hinge, 13.5 mg/ml in serum; opsinin, some subclasses fix complement, some cross placenta
    - IgA: 3 constant region domains, proline rich hinge; secreted at mucosal surface; only immunoglobulin that exits body
    - IgE: 4 constant region domains; binds mast cells, allergies
    - IgD: 3 constant region domains, proline rich hinge; cell surface only
  - Individual immunoglobulin has either κ or γ light chain
  - Opsinins are antibodies that enhance phagocytosis
  - Hinge is 20-30 aa region that is proline rich
  - IgA includes attached secretory piece which protects against proteolysis
  - Not all secreted as individual molecules
    - IgM secreted as pentamer w/ J chain in middle
    - IgA secreted as dimers w/ J chain
  - Fragments created by limited digestion of antibodies w/ proteolytic enzymes; each class or subclass of heavy chain has a different amino acid sequence and hence a different Fc region
  - Different effecter functions of different classes and subclasses of antibodies are mediated by binding to specific Fc receptors
    - Fc(ε)RI on mast cells, eosinophils
    - Poly Ig receptor on mucosal epithelia - IgA

        - Fc(γ) receptor on macrophages, neutrophils, eosinophils
        - Opsinins bind go IgG
    - b/c each subclass has a different constant regions different Fc receptors bind different classes and subclasses of Ig
        - Each subclass of Ig has specific set of effecter fxns
        - All antibodies can use same variable regions
        - But with different constant regions, way pathogen is handled after binding is different for each subclass