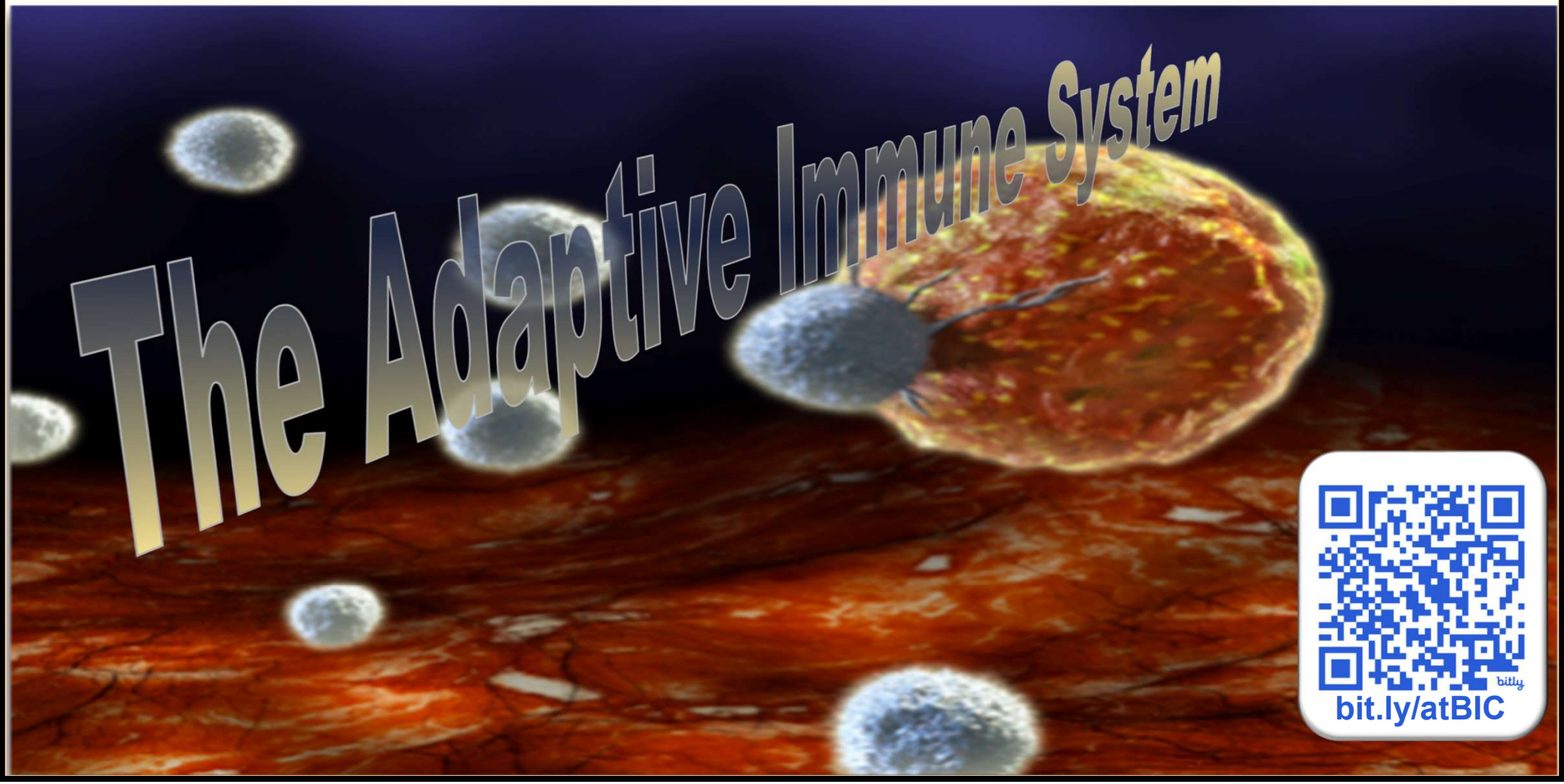
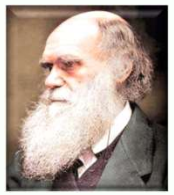
lecture 15



until now

- Class Book
  - Floreano, D. and C. Mattiussi [2008]. *Bio-Inspired Artificial Intelligence: Theories, Methods, and Technologies*. MIT Press.
    - Chapters 1, 2, 4, **5,** and 7
- Lecture notes
  - Chapter 1: What is Life?
  - Chapter 2: The logical Mechanisms of Life
  - Chapter 3: Formalizing and Modeling the World
  - Chapter 4: Self-Organization and Emergent Complex Behavior
  - Chapter 5: Reality is Stranger than Fiction
  - Chapter 6: Von Neumann and Natural Selection
  - Chapter 7: Modeling Evolutionary Systems
    - posted online @ http://informatics.indiana.edu/rocha/i-bic
- Papers and other materials
  - Optional
    - Nunes de Castro, Leandro [2006]. *Fundamentals of Natural Computing: Basic Concepts, Algorithms, and Applications*. Chapman & Hall.
      - Chapter 2, 7, 8
      - **Chapter 3, sections 3.1 to 3.5**



exploring similarities across nature

- self-similar structures
  - Trees, plants, clouds, mountains
    - morphogenesis
  - Mechanism
    - Iteration, recursion, feedback
- dynamical systems and unpredictability
  - From limited knowledge or inherent in nature?
  - Mechanism
    - Chaos, measurement
- self-organization, collective behavior, emergence
  - Complex behavior from collectives of many simple units or agents
    - cellular automata, dynamical networks, morphogenesis, swarms, brains, social systems
  - Mechanism
    - Parallelism, multiplicity, multi-solutions, redundancy
- evolution
  - Adaptation, learning, social evolution
  - Mechanism
    - Reproduction, transmission, variation, selection, Turing's tape
- Collective behavior derived from many inseparable sources
    - Multi-level selection, swarm intelligence, immune system, anticipatory systems, brain-body-environment-culture, embodiment, epigenetics, culture
  - Mechanism
    - Network causality, modularity, control, hierarchy, connectivity, stigmergy, redundancy

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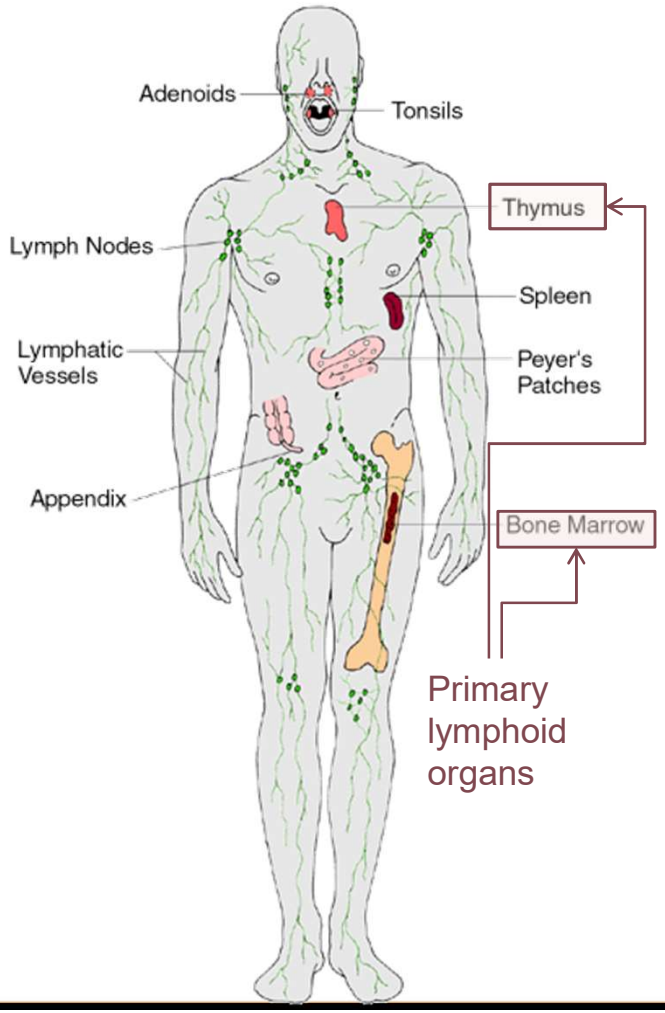
function



- maintain homeostasis
  - in concert with other bodily systems
- ***identification*** (detection) and ***elimination*** of non-self (≈external) elements and malfunctioning self elements
  - protect body from threats
    - toxic substances and pathogens
    - self from non-self detection
  - minimize harm to body
    - detect harmful non-self from everything else
  - choose appropriate elimination process
    - the right effectors for particular pathogen

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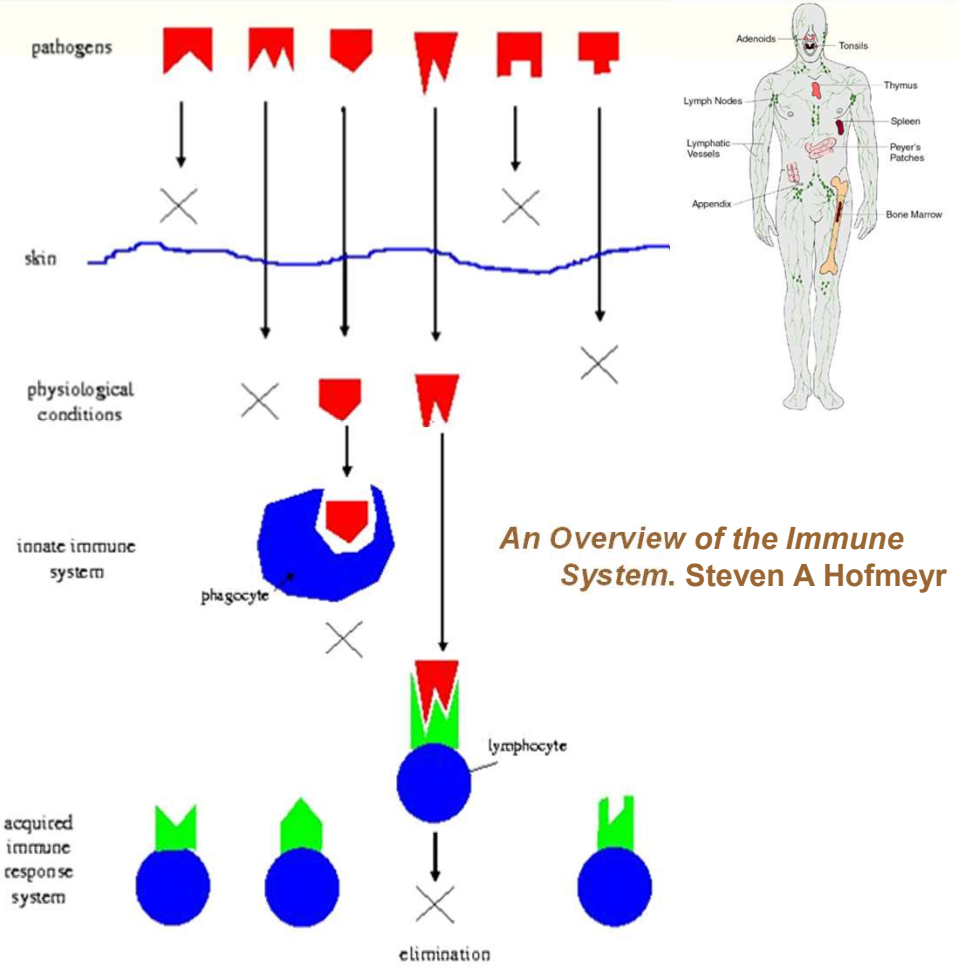
multilayers

- Skin
  - Blocks most pathogens
- Physiological conditions
  - Temperature, PH
- Innate immune system
  - Scavenger cells (e.g. phagocytes)
    - Engulf pathogens and other substances
- Adaptive immune system
  - Lymphocytes
    - Adapt to previous pathogens to eliminate them
- Chemical bonding
  - Mechanism for identification/detection and elimination for both innate and adaptive immune system
    - Receptors in cell surfaces bind to pathogens or to other immune system cells or molecules for ***signaling***



An Overview of the Immune System. **Steven A Hofmeyr**

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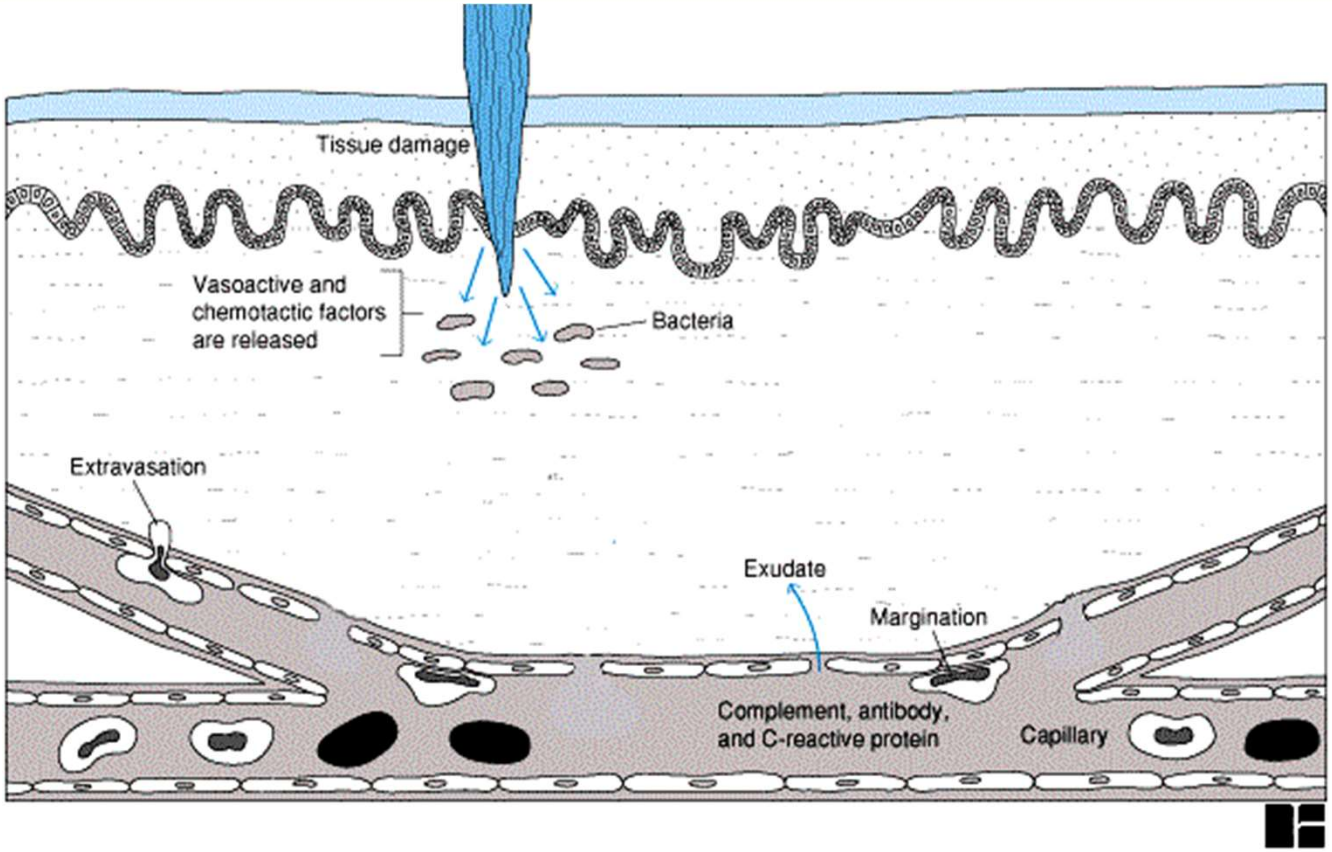
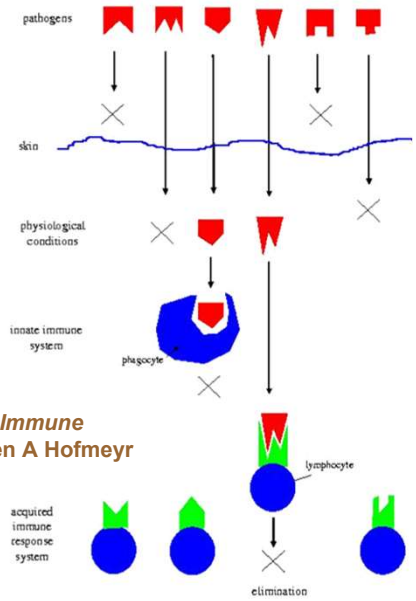
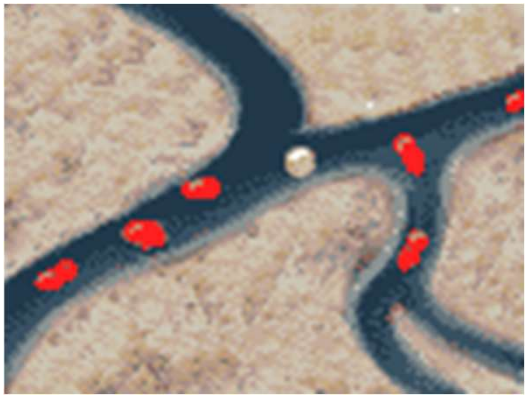
basic mechanisms



From Paul Bugl



An Overview of the Immune System. Steven A Hofmeyr



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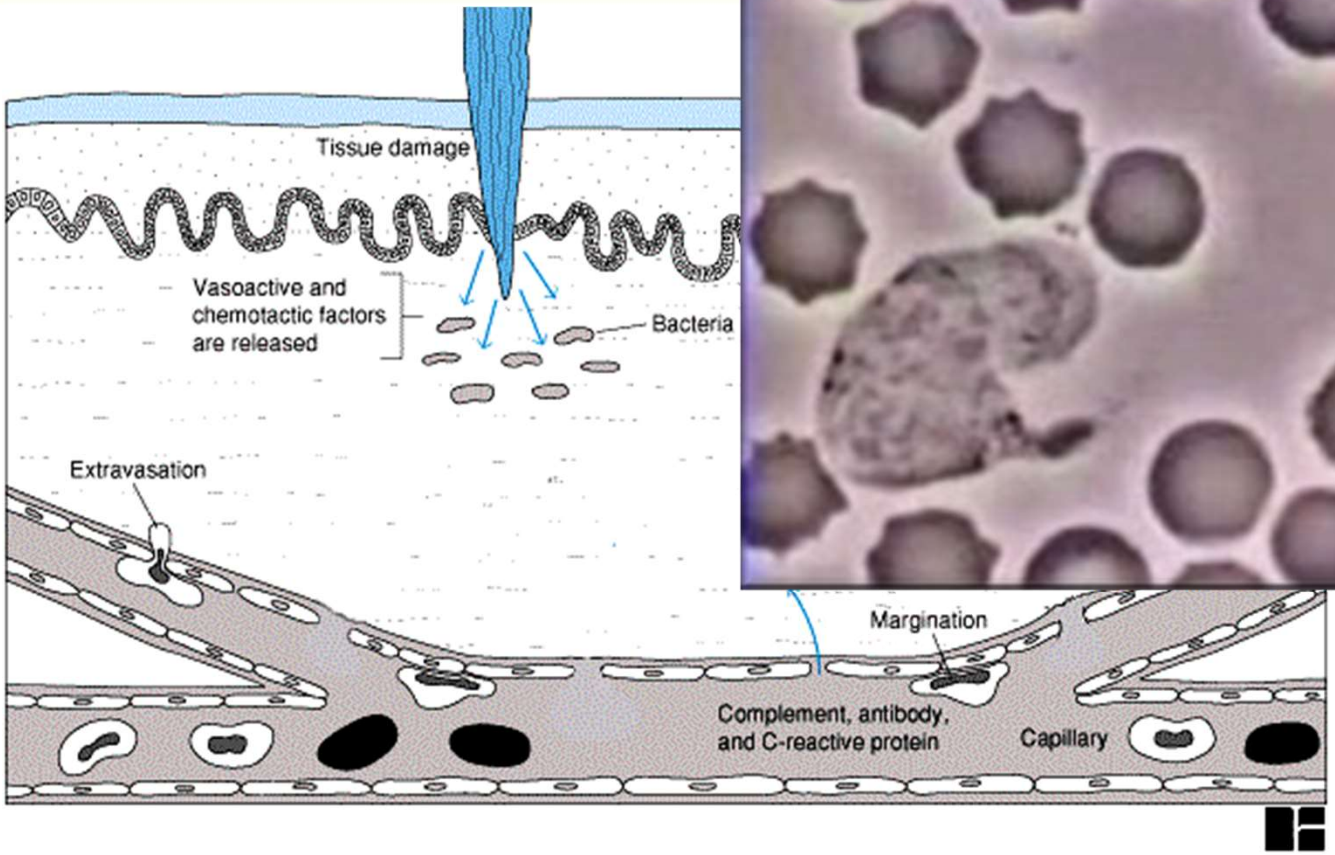
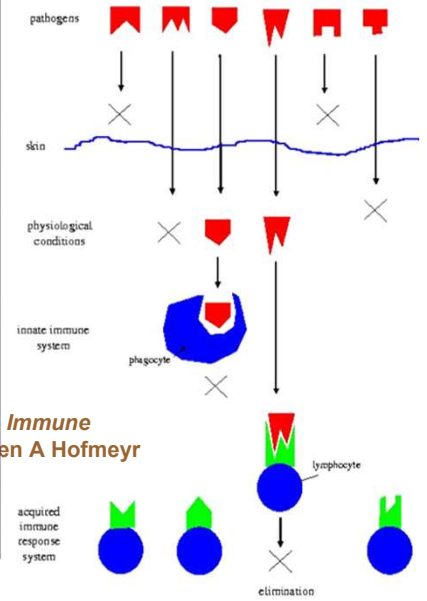
basic mechanisms





Immune
en A Hofmeyr

From Paul Bugl

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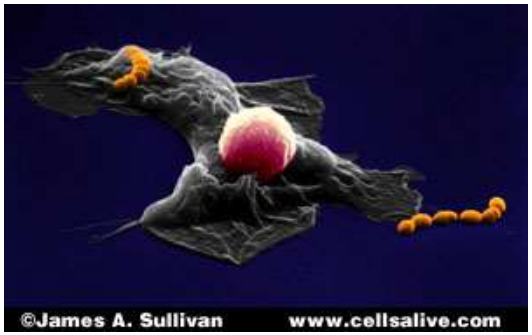
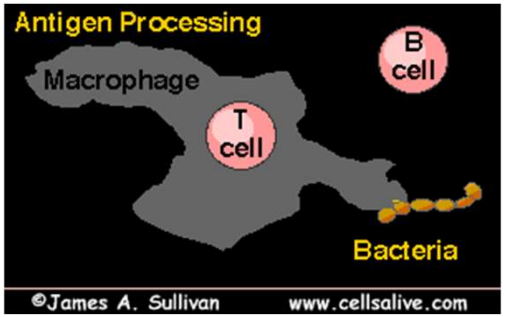
molecular memory defense (in vertebrates)

- **Learns** to recognize ***specific*** types of pathogens
  - Primary response
    - To new pathogens
      - Slow
    - Retains memory of pathogens
  - Secondary response
    - Quicker, based on **memory** of primary response
- Lymphocytes:T, B, or NK Cells (in innate system)
  - Detection and elimination of pathogens via **collective behavior**
    - Trillions of detectors with no centralized control
      - Interacting through simple, localized rules
- Antigen-presenting cells (APC)
  - Phagocytes ("eating cells") from the innate immune system which are also used to present antigen epitopes on their surface (on MHC and other receptors) to T-Cells
    - Macrophages, dendritic cells, etc





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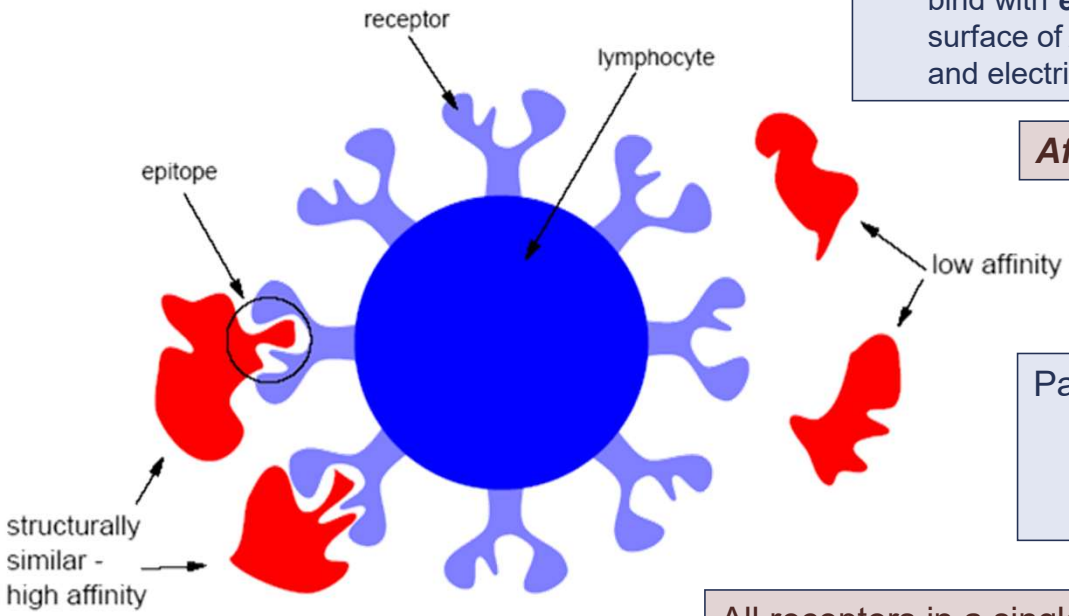
chemical bonds as generalized detectors



Lymphocyte recognition occurs when its ***receptors*** bind with ***epitopes*** from pathogens on the surface of APCs (by complementary structure and electrical charge)

Affinity: strength of bond

Pathogens may have many different epitopes: many lymphocytes may be specific to a single pathogen

All receptors in a single lymphocyte are identical and can only recognize similar epitopes: ***monospecificity***

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Aprox 10^5 receptors per lymphocyte: ***estimates*** affinity and quantity of pathogens as the number of binding receptors increases with affinity and quantity. ***Activation*** (detection event) occurs after a threshold of binding receptors

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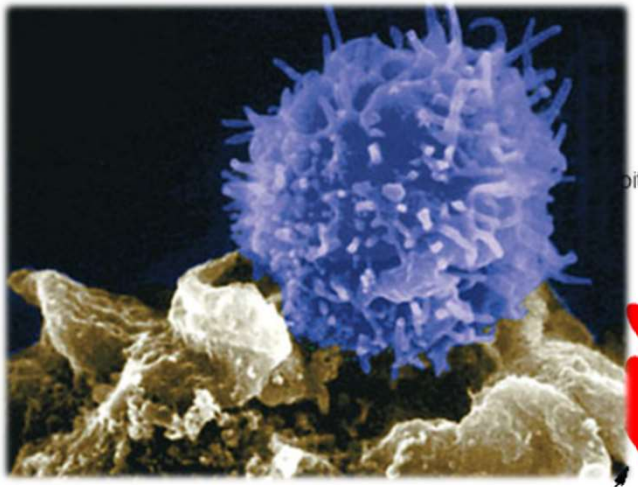
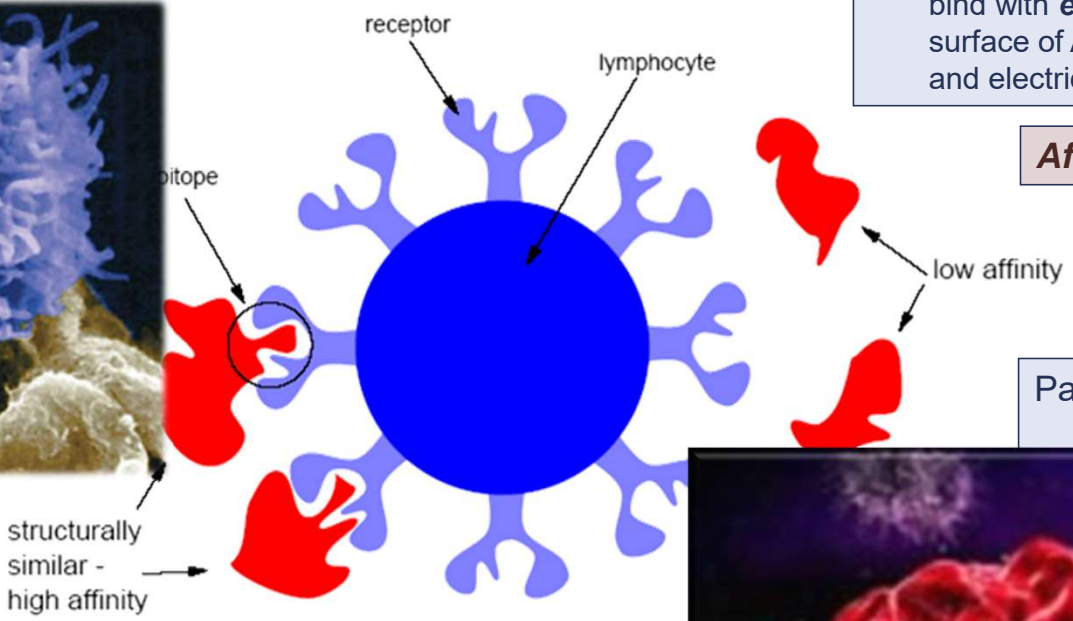
chemical bonds as generalized detectors

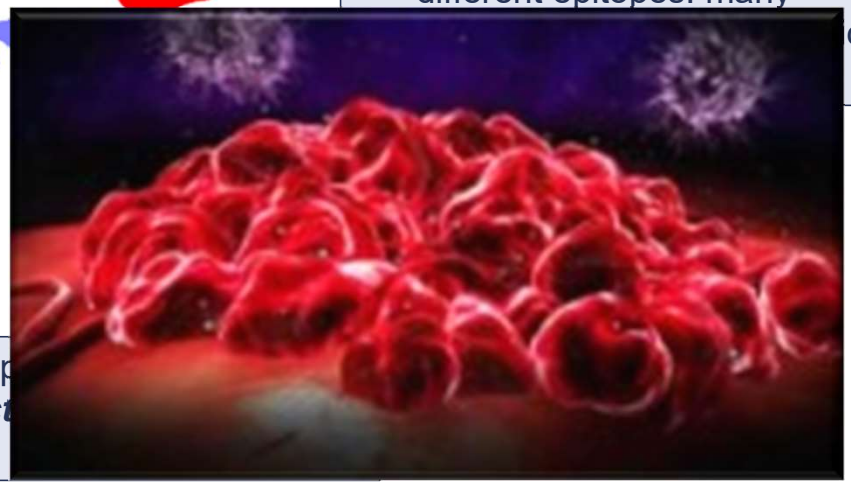




Lymphocyte recognition occurs when its ***receptors*** bind with ***epitopes*** from pathogens on the surface of APCs (by complementary structure and electrical charge)

Affinity: strength of bond

Pathogens may have many different epitopes: many



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Aprox 10^5 receptors per lymphocyte: ***estimates*** affinity and quantity of p
number of binding receptors increases with affinity and quantity. ***Act***
event) occurs after a threshold of binding receptors

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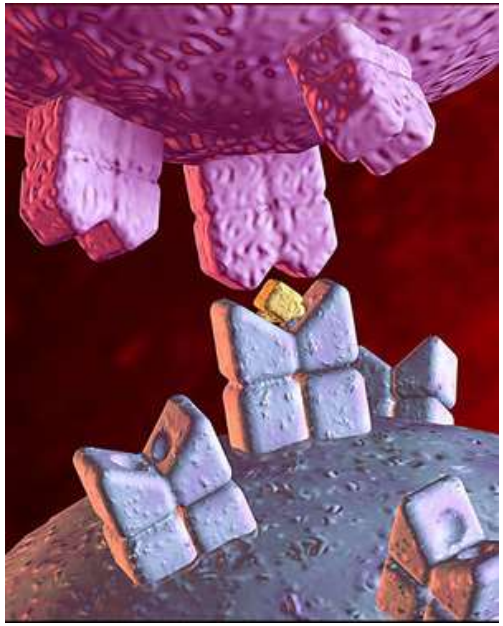
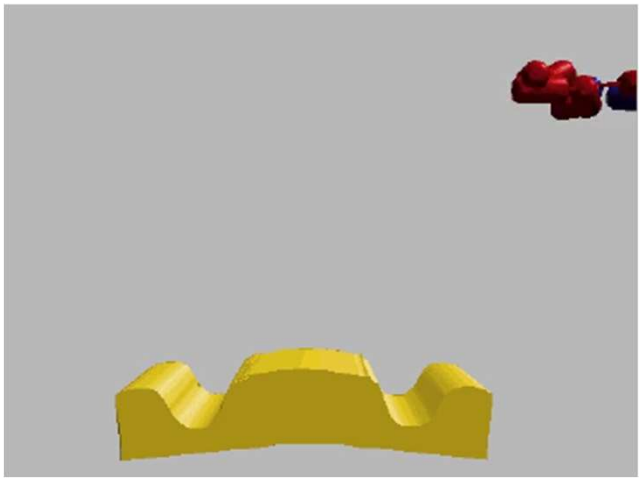
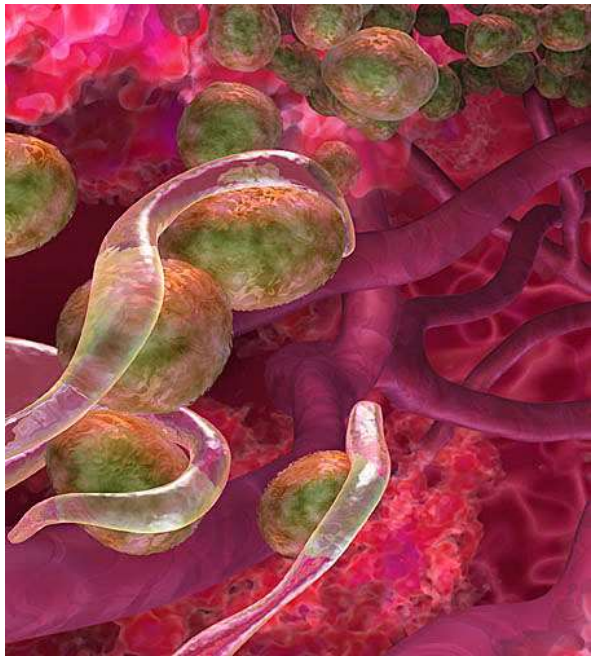
renderings



Antigenic Activation: T-cell binds to antigen presenting cell





Phagocytic Embrace

From Gary Carlson

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molecular pattern matching

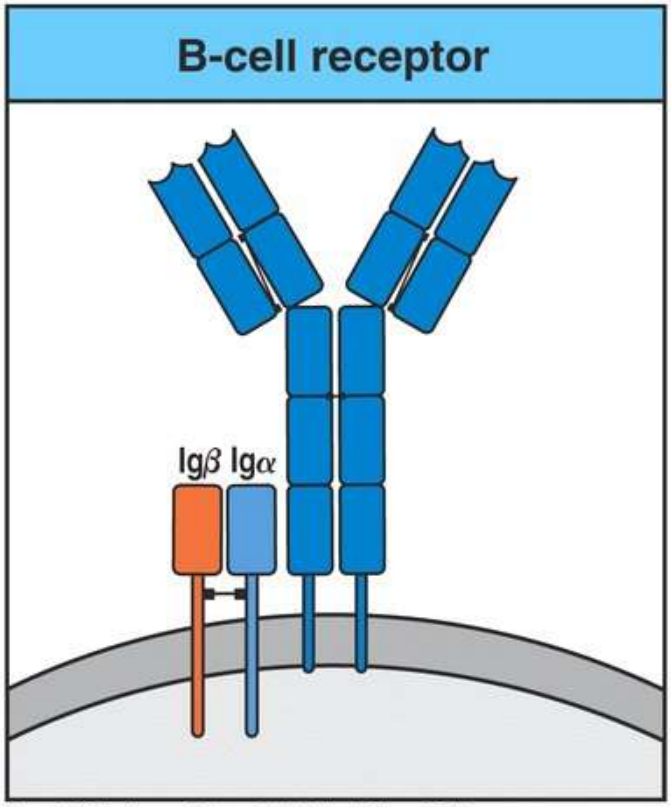
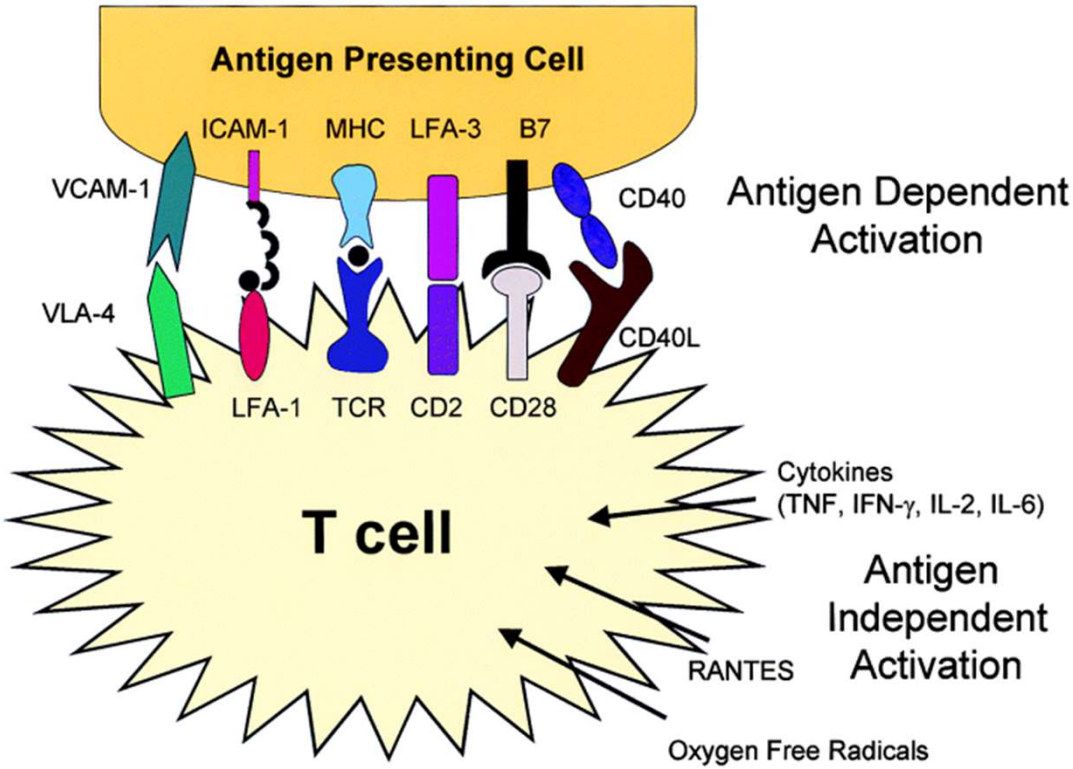


Figure 2-23 The Immune System, 2/e (© Garland Science 2005)



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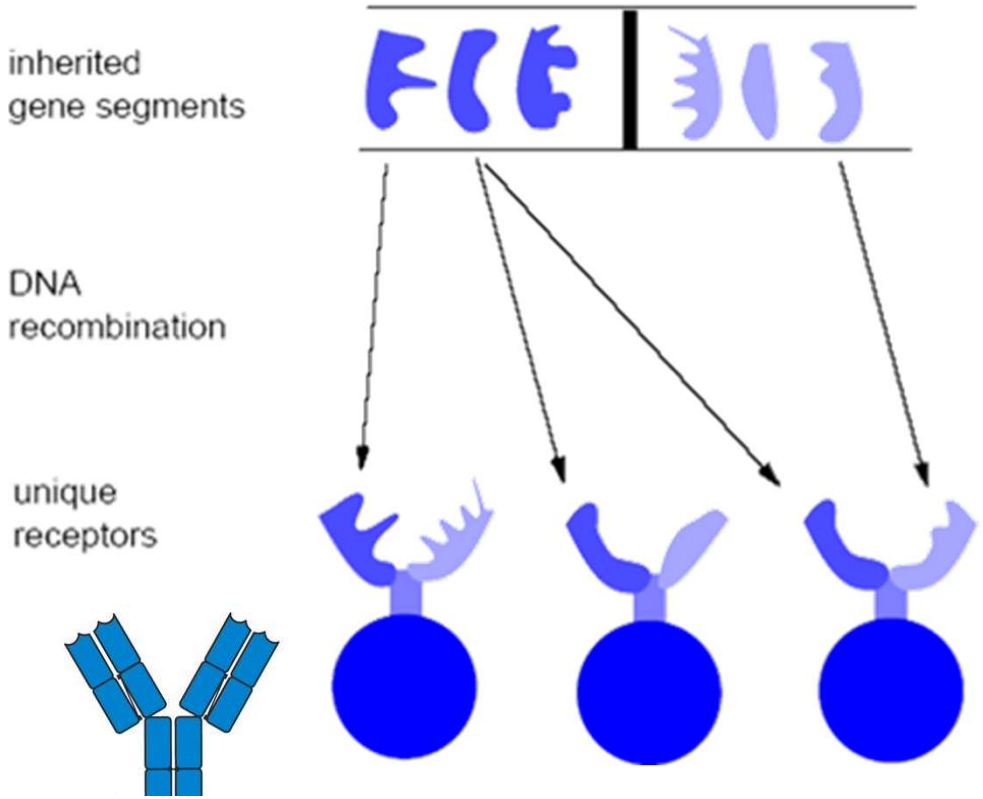
Building up the response repertoire

generating receptor diversity (from DNA memory banks)



Receptors are generated via DNA recombination

At any given time there are an estimated 10^8 varieties of receptors, but there are potentially 10^{16} epitope varieties

Dynamic protection: turnover of lymphocytes. 10^7 new lymphocytes generated each day!

10 days to generate a new repertoire

With dynamic protection and *immune memory*, protection is increased against enormous size of potential pathogens

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generating receptor diversity (in B Cells)

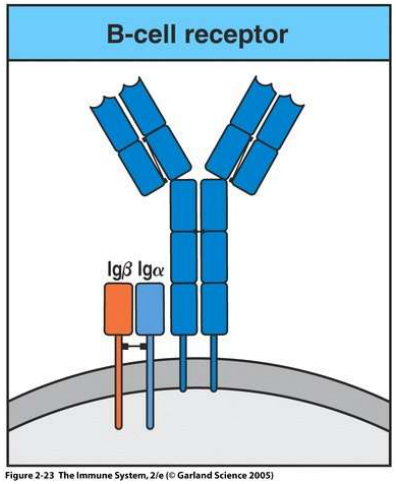
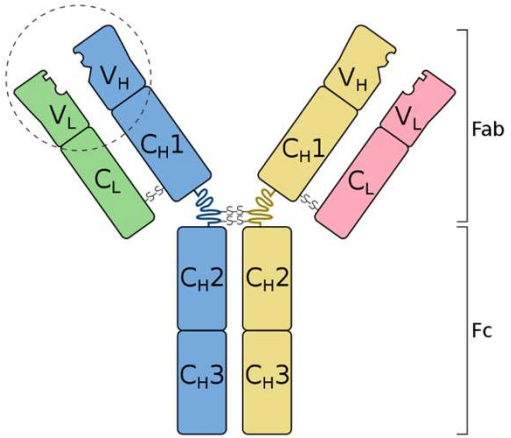
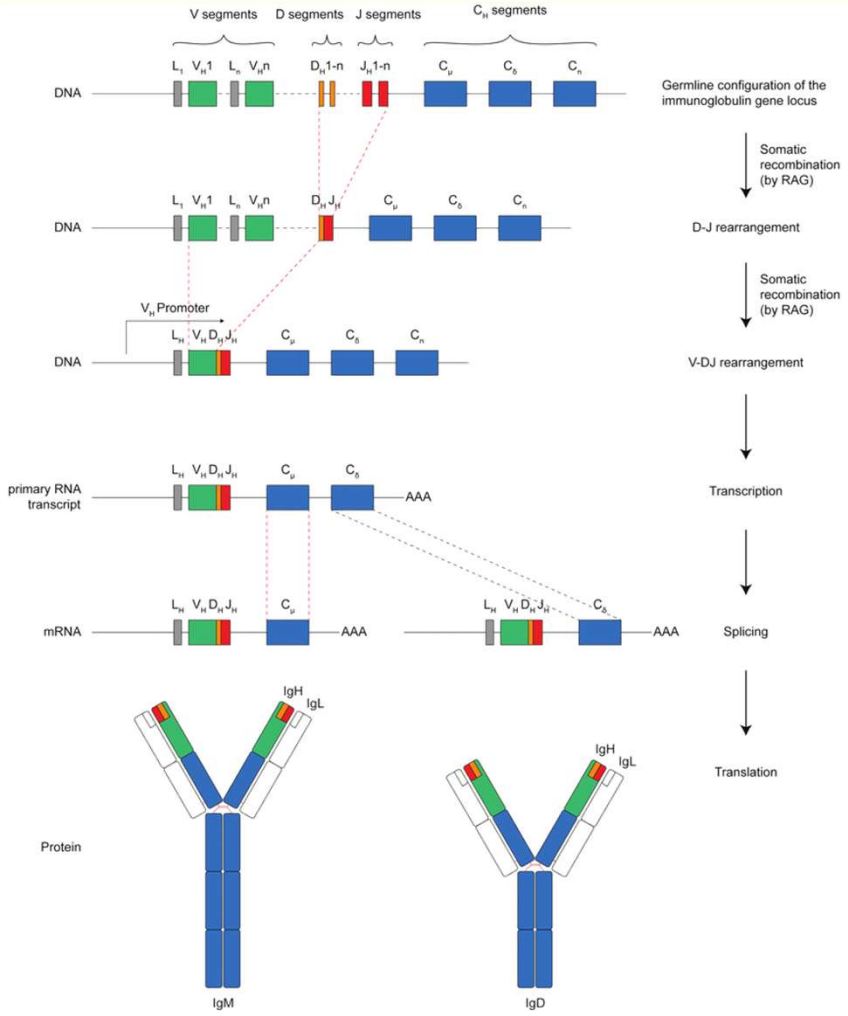


Figure 2-23 The Immune System, 2/e (© Garland Science 2005)





receptors: **antibody** (**Ab**), also known as an **immunoglobulin (Ig)**, is a Y shaped protein

V(D)J or Somatic Recombination: (nearly) random generation of gene segments (variable, diverse, and Joining)

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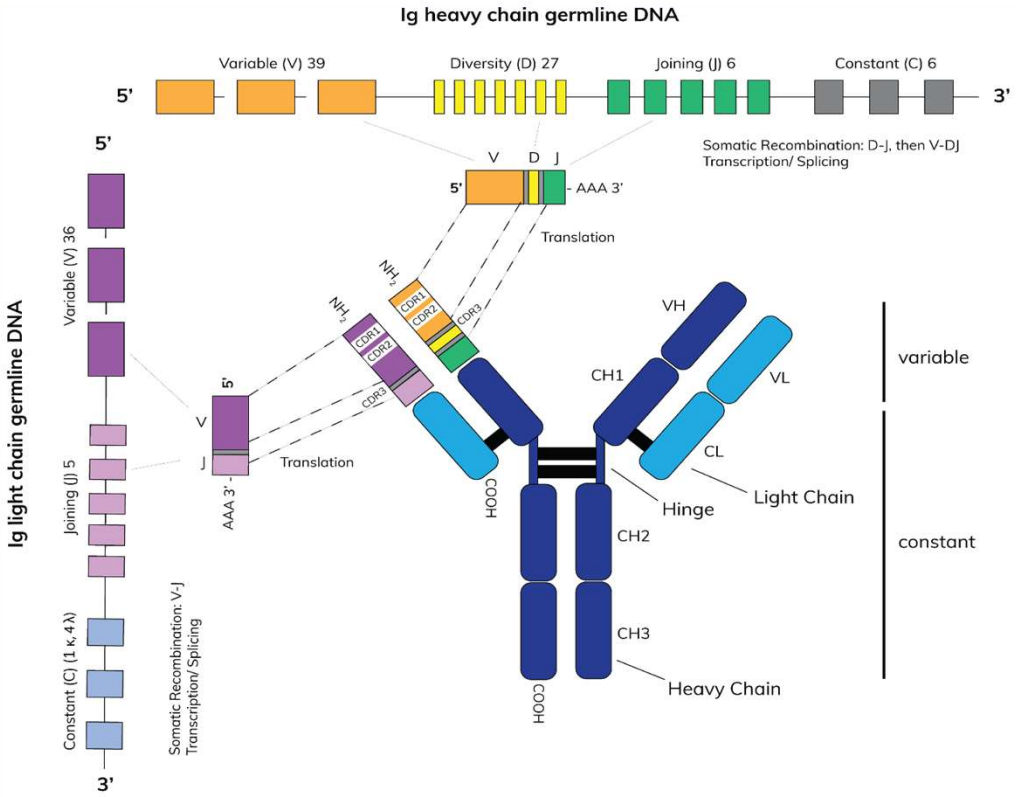
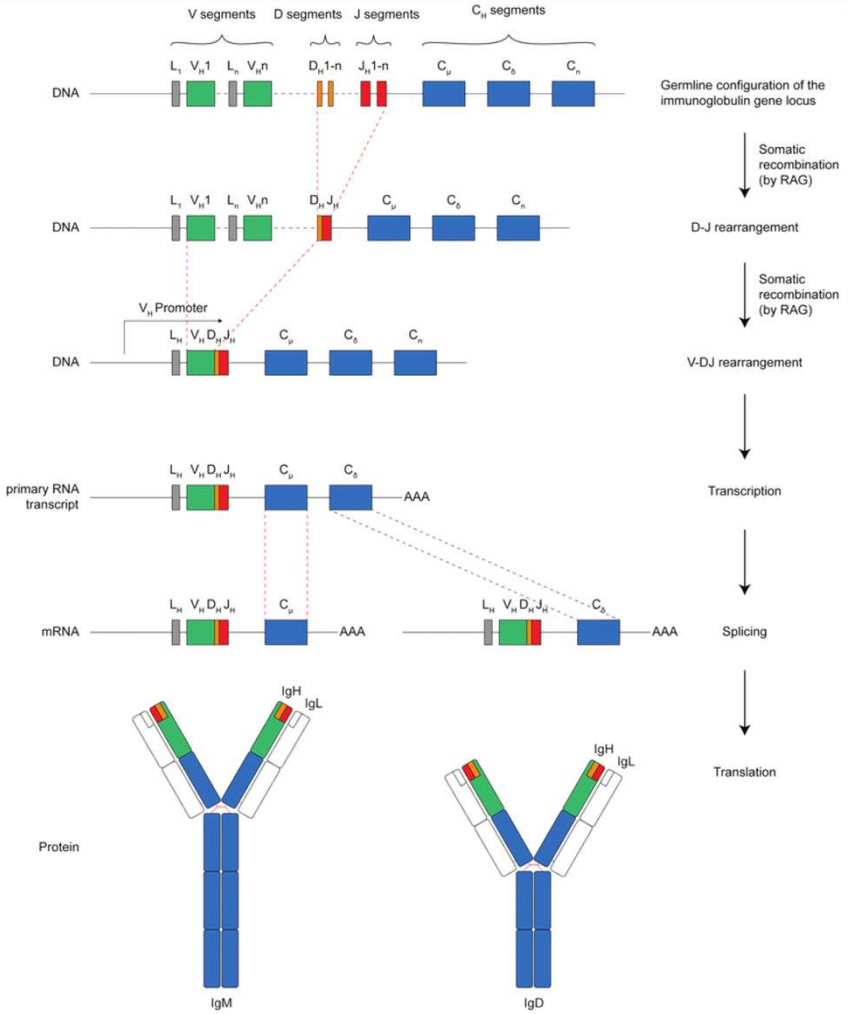
generating receptor diversity (in B Cells)





V(D)J or Somatic Recombination: (nearly) random generation of gene segments (variable, diverse, and Joining)

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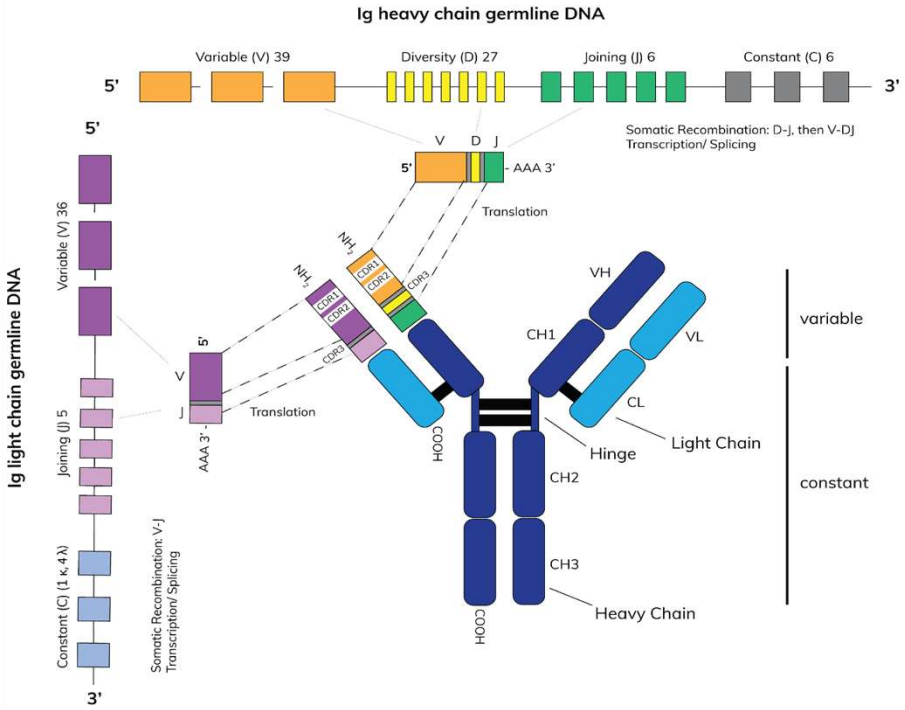
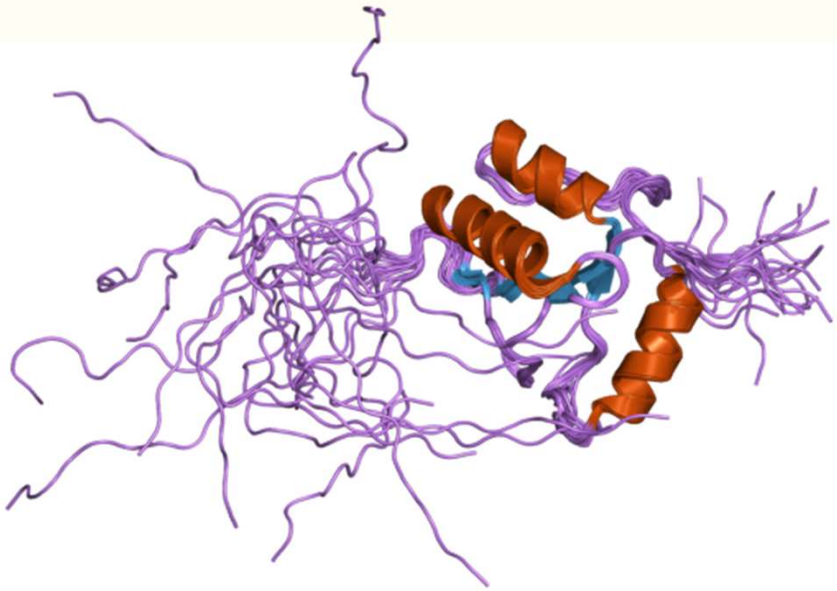
mechanism of receptor diversity





TdT: Terminal deoxynucleotidyl transferase or terminal transferase, adds nucleotides (without a template) to VDJ exons

Controlled, private Natural Selection

"randomizer" of DNA (Turing) tape

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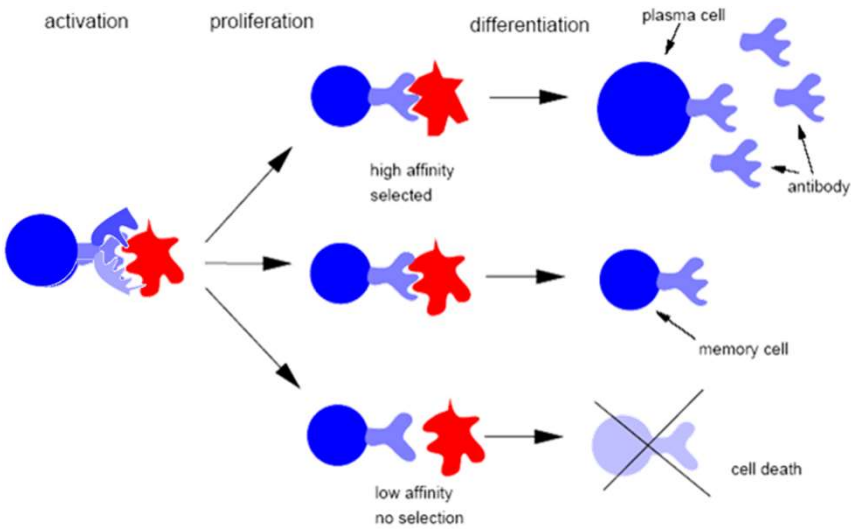
learning specific pathogens



Learning and remembering implemented by lymphocytes: ***B Cells***

If activated, migrate to ***lymph nodes***: gland where adaptive response develops

proliferation: B cell produces many short-lived clones (cell division) under ***somatic hypermutation*** (9 orders of magnitude higher than normal mutation)

Generate different receptor structures/epitope affinities

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Steven A Hofmeyr

If clones do not bind to pathogenic epitopes in lymph nodes, they die. If binding occurs, they leave the lymph node and differentiate into ***plasma*** or ***memory*** B cells. Due to limited resources, Darwinian selection occurs

Controlled, private Natural Selection

Antibodies (immunoglobulin): soluble form of receptors that bind to pathogen epitopes (opsonize and neutralize)

Humoral response (fluid)

antigen: anything that causes antibody generation:

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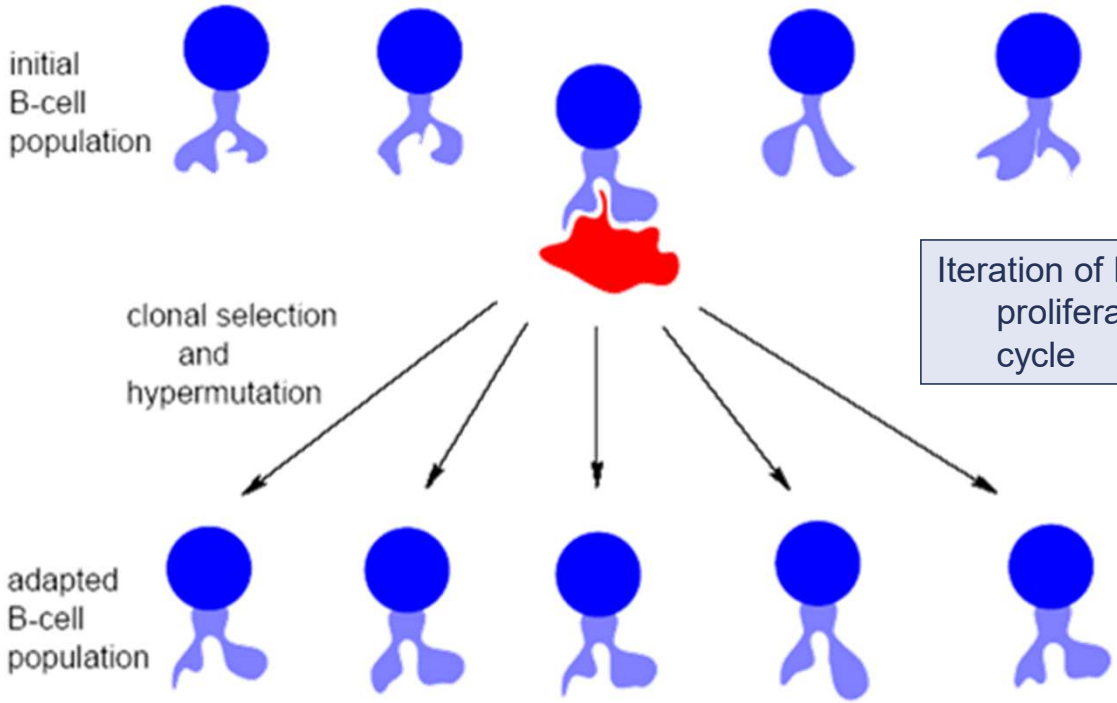
Via Darwinian variation and selection



Iteration of B-cell activation-proliferation-differentiation cycle

Clonal selection and hypermutation:

Controlled, private Natural Selection

Clones "compete" for pathogen epitopes. Higher affinity implies greater rate of reproduction (fitness)

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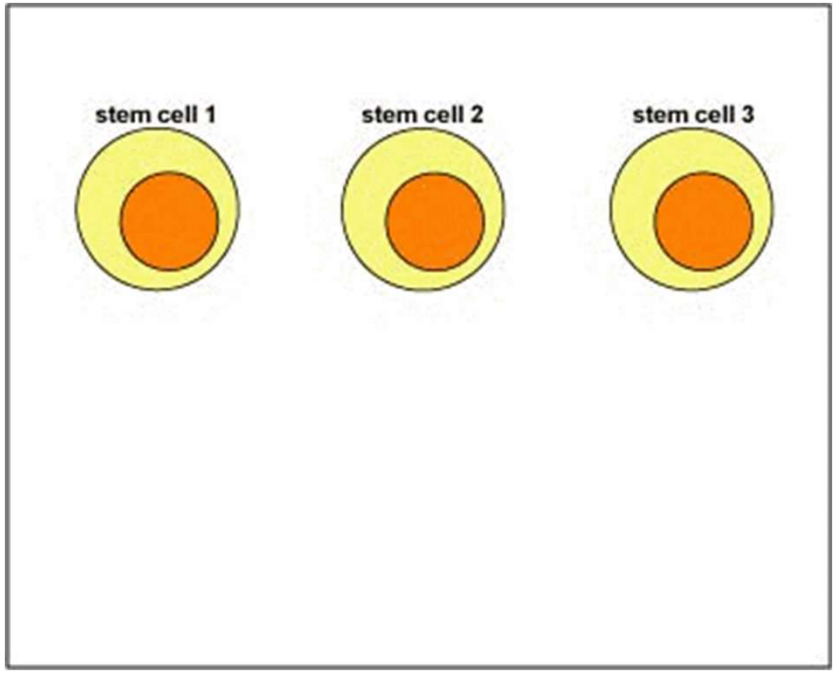
Of B-Cells



From: Doc Kaiser's Microbiology Home Page

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readings

- Class Book
  - Floreano, D. and C. Mattiussi [2008]. *Bio-Inspired Artificial Intelligence: Theories, Methods, and Technologies*. MIT Press.
    - Chapters 5 and 6
- Lecture notes
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- Papers and other materials
  - Optional
    - Nunes de Castro, Leandro [2006]. *Fundamentals of Natural Computing: Basic Concepts, Algorithms, and Applications*. Chapman & Hall.
      - Chapter 5, 7.7, 8.3.1, 8.3.6,