Final Exam Review

20.106 Systems Microbiology

Fall 2006

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Early Life, Origin of Microbes

- Early life
  - Necessities for life
  - Theories of microbial beginnings
- Timeline
  - Important events
  - Evidence
- Isotope ratios
  - Calculate
  - Examples (useful elements & how occur)

Structural Features of Bacteria

- **Capsule**
  - **Composition**
    - Capsules typically consist of a surface polysaccharide layer ('smooth' bacteria)
  - **Purpose**
    - Physically prevent ingestion by phagocytic cells in pathogenic bacteria
- **Peptidoglycan**
  - **Composition**
    - Cross-linked by peptides between NAM residues on adjacent chains
  - **Purpose**
    - Maintains shape of cell
- **LPS & LTA**
  - **Composition**
    - Lipid chains that vary from bacteria to bacteria, plus polysaccharide (gram-, LPS)
    - Lipid chains, plus techoic acid (gram$^+$, LTA)
  - **Purpose**
    - Stabilizes cell membrane
- **Pili**
  - **Composition**
    - Straight projections composed of pilin protein subunits with molecule-specific proteins on pilus tip
  - **Purpose**
    - Adherence to surfaces
    - Exchange of DNA via conjugation
- **Flagella**
  - **Composition**
    - Filament (flagellin monomers), hook and motor (H^+ driven motor)
  - **Purpose**
    - Motility

Gram-negative Cell wall

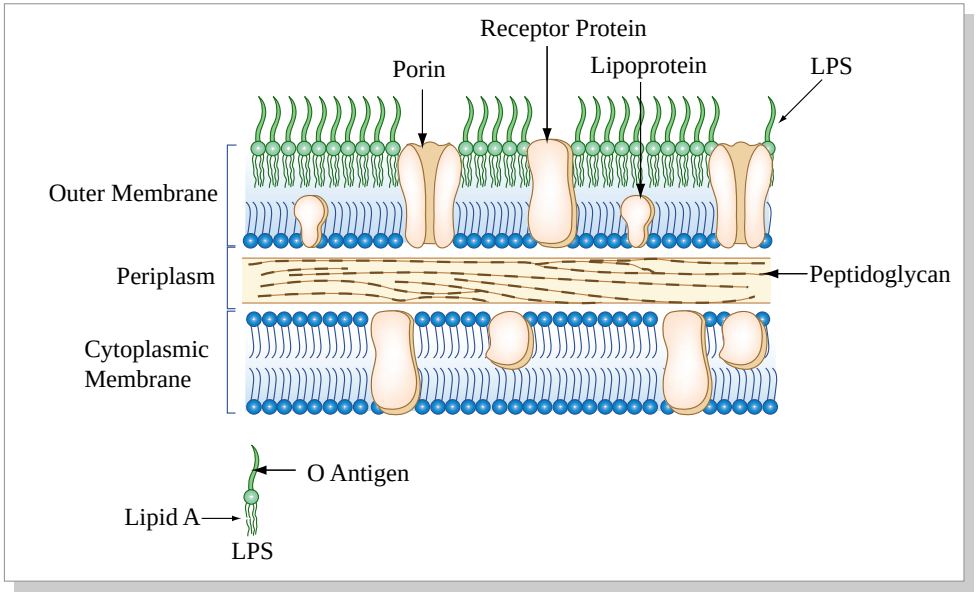


Figure by MIT OCW.

Gram-positive Cell wall

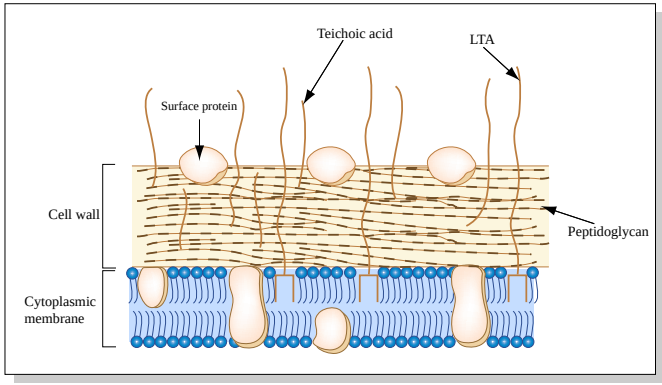


Figure by MIT OCW.

Motility

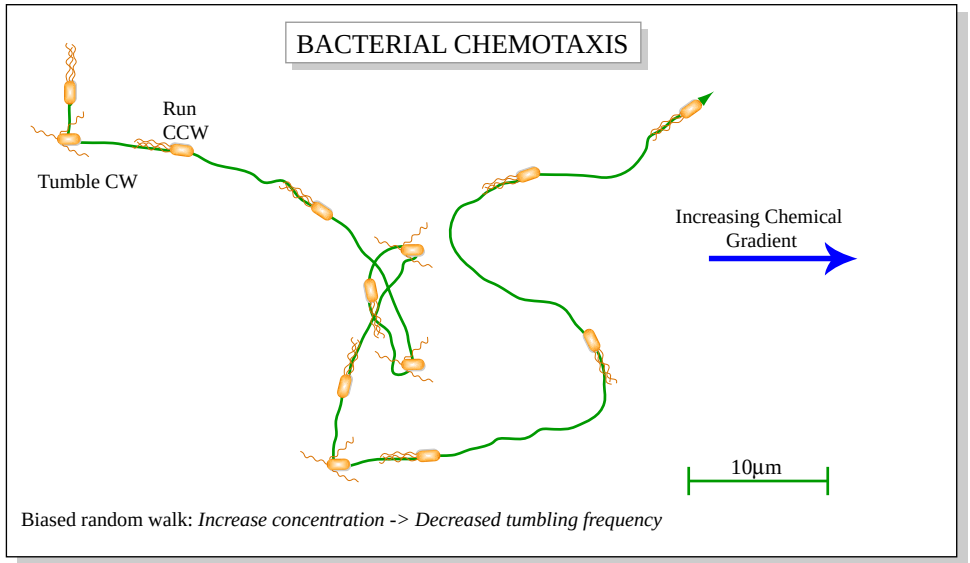
How at low Reynolds numbers?

- Only force at moment matters-no inertia
- Reciprocal motion useless
- Must be circular, corkscrew motion

Flagellar movement

- Random-walk pattern for environmental sampling
- Chemotaxis towards nutrients/niche

Image of a bacterium with long rotating flagella removed due to copyright restrictions.



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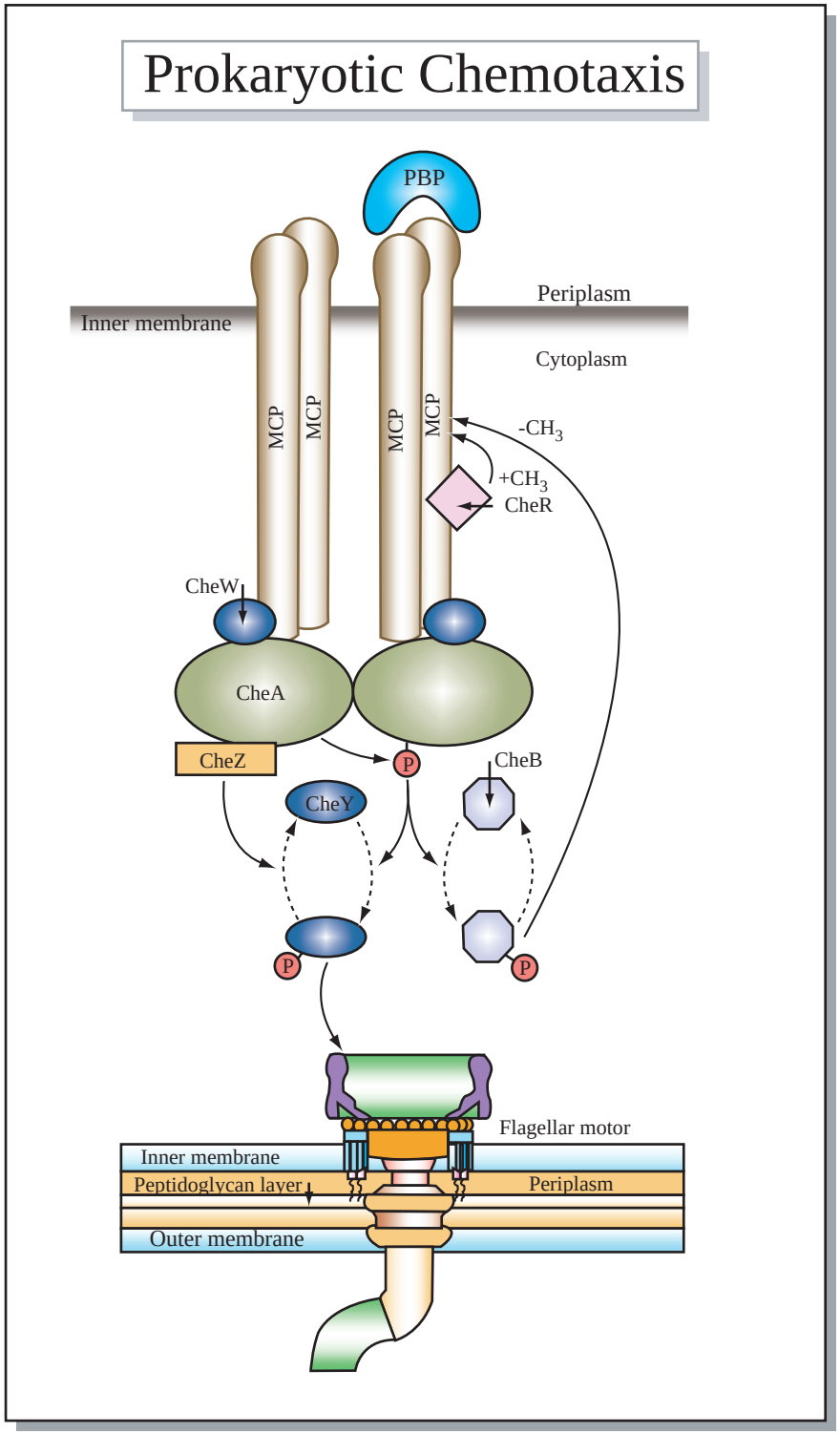


Prokaryotic Chemotaxis

Figure 2 | **Schematic diagram of the chemosensory system of *Escherichia coli*.** Two dimeric chemoreceptors — methyl-accepting chemotaxis proteins (MCPs) — are shown, one of which is interacting with a periplasmic binding protein (PBP). In addition, two chemotaxis protein (Che)W monomers and a CheA dimer are shown interacting with the highly conserved signalling domain of the MCPs in the cytoplasm. It should be noted that, given the packing within MCP clusters and the calculations of the number of chemosensory proteins, the actual arrangement will be different. One CheA monomer will probably not interact with one MCP dimer, and instead a CheA dimer might span several receptors. A decrease in attractant concentration induces *trans*-autophosphorylation of the CheA dimer, which phosphorylates the response regulator CheY. Phosphorylated CheY then binds to the flagellar motor to bring about a change in direction. Phosphorylated CheA also phosphorylates another response regulator — the methylesterase CheB. Phosphorylated CheB competes with a constitutive methyltransferase, CheR, to control the degree of methylation of specific glutamates in the MCPs. This resets the signalling state of the receptors and allows them to adapt to the present concentration of attractant and to sense subsequent changes. The dephosphorylation of phosphorylated CheY is accelerated by the phosphatase CheZ. P, phosphoryl group.

Figure by MIT OCW.

Mobile Elements and Lateral/Horizontal Gene Transfer

- Resistance plasmids
- Incompatibility groups
  - Two very similar plasmids will NOT co-exist in one bacteria
- Cloning (cloning vectors)
  - Plasmids
  - Phage
  - Cosmids
  - Bacterial Artificial Chromosomes (BAC)

Horizontal Gene Transfer: Transformation

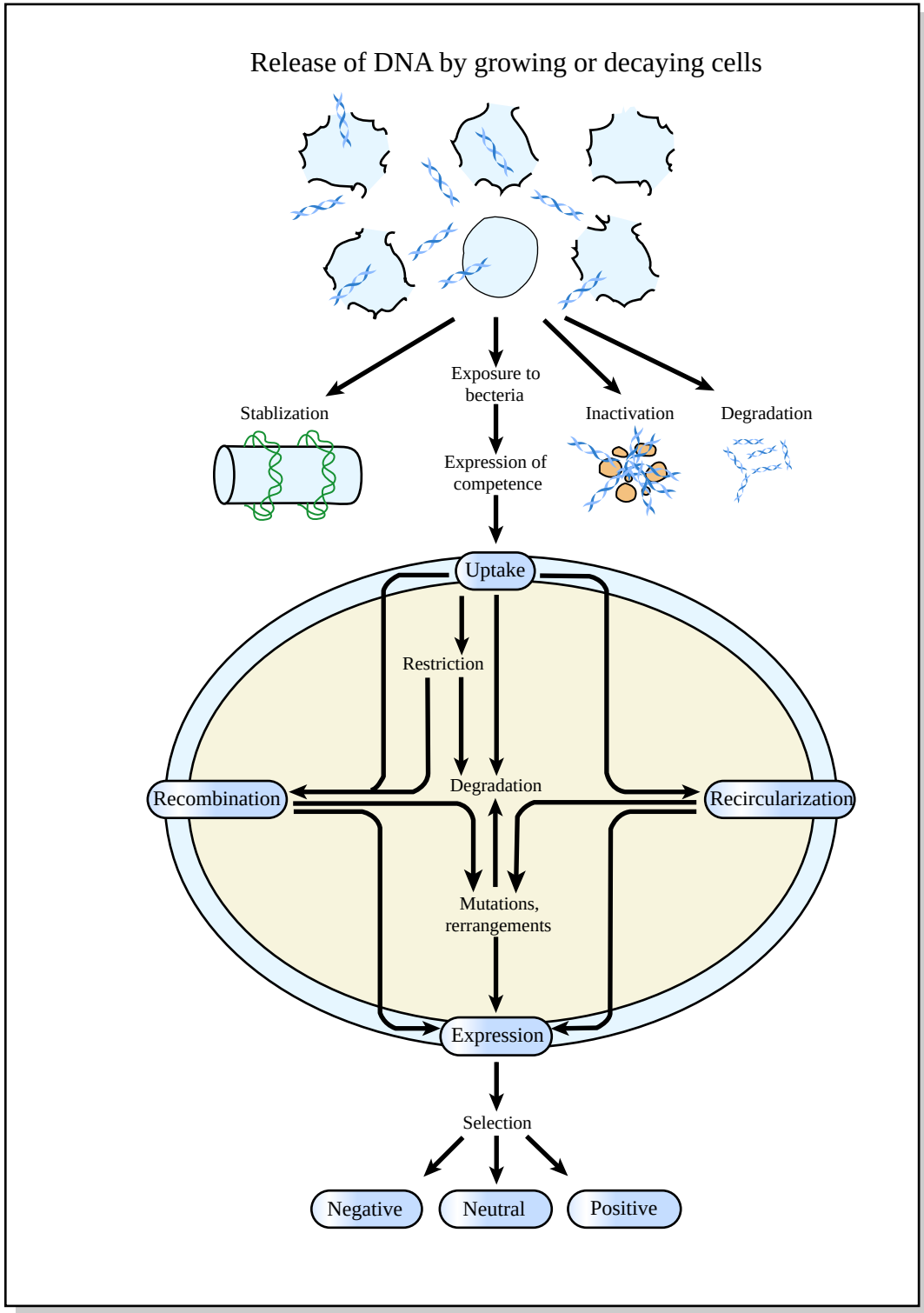


Figure by MIT OCW.

Horizontal Gene Transfer: Conjugation and Transduction

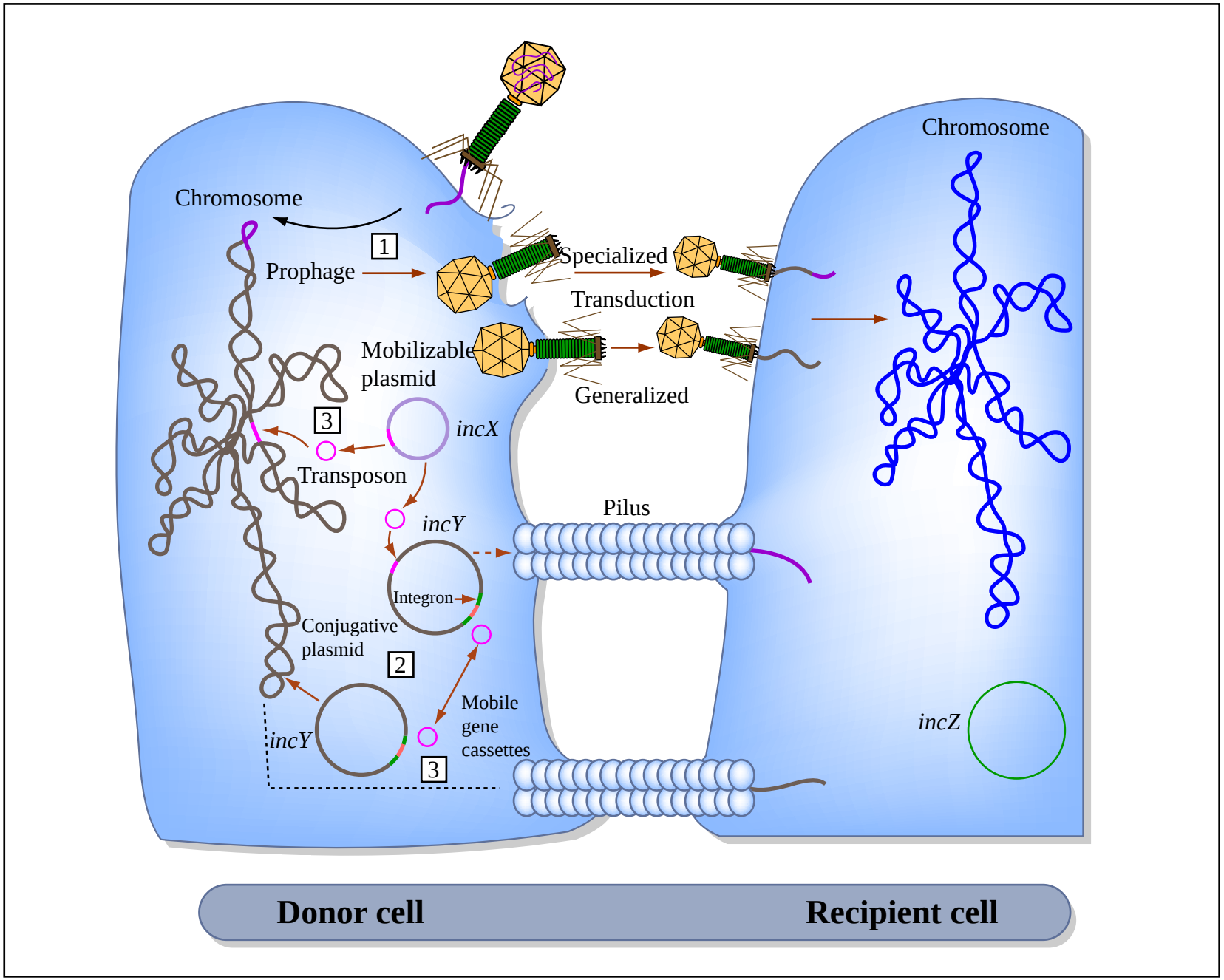


Figure by MIT OCW.

Metabolic Diversity

Basic needs

- Carbon source
  - Organic molecules (heterotrophs)
  - Inorganic molecules (autotrophs)
- Energy source
  - Chemical rxns (chemotrophs)
  - Light (phototrophs)
- Electron donor
  - Organic molecules (organotrophs)
  - Inorganic molecules (lithotrophs)
- Electron acceptor
  - Oxygen (aerobic)
  - SO_4, NO_3, FeIII (anaerobic)

Nitrogen Cycle

Important Reactions

- ✓ Nitrogen Assimilation
- ✓ Deamination
- ✓ Nitrification
- ✓ Denitrification
- ✓ N_2 Fixation

Rhizobium

- Free-living are aerobic, not N_2 fixers
- When symbiotic
  - *Rhizobium* turn on plasmid-based *Nod* genes
  - Become anaerobic N_2-fixing, bacteroid form
  - Legumes form nodules to control symbiotic relationship

Images of free-living Rhizobium and bacterioids in nodule removed due to copyright restrictions.

Symbiosis and Genome Reduction

- *Buchnera aphidicola* from two aphids *Schizaphus graminum* (Sg) and *Acyrthiosiphon pisum* (Ap)
- 70 million years
  - No chromosomal rearrangements
  - Sequence divergence (9^{-9} synonymous substitutions/yr
  - 1.65^{-9} non-synonymous substitutions/yr
- *E. coli* and *Salmonella* spp. (closest free-living relatives) 2000x more liable

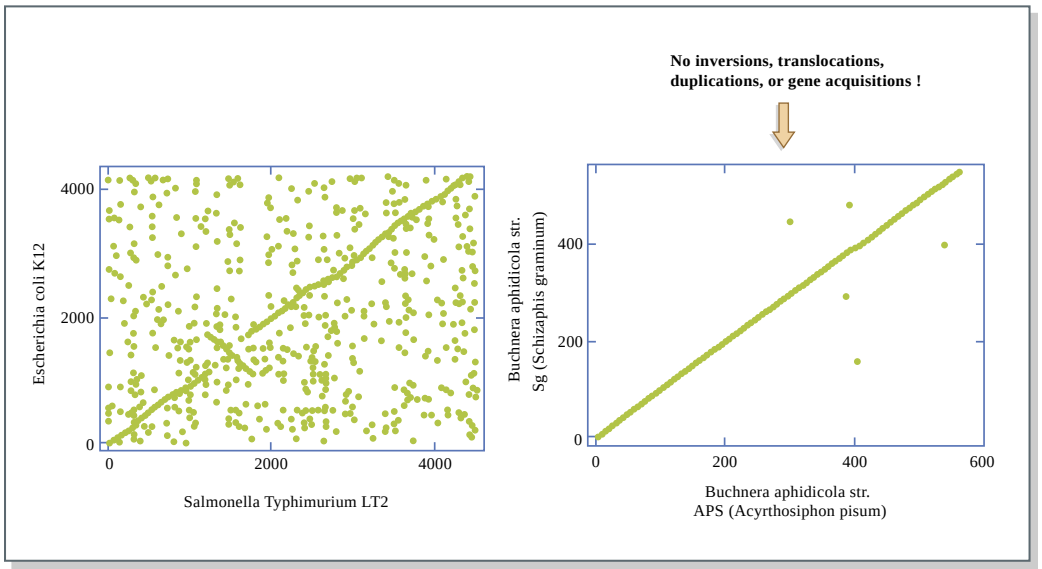


Figure by MIT OCW.

50 Million Years of Genomic Stasis in Endosymbiotic Bacteria

Ivica Tamas,[1*] Lisa Klasson,[1*] Björn Canbäck,[1] A. Kristina Näslund,[1] Ann-Sofie Eriksson,[1] Jennifer J. Wernegreen,[2] Jonas P. Sandström,[1] Nancy A. Moran,[2] Siv G. E. Andersson[1†]

SCIENCE 296:2376 (2002)

Genome Dynamics in *Buchnera*

Obligate endosymbiont

- Substantial sequence divergence
- Prominence of pseudogenes
- Loss of DNA repair mechanisms
- Stable genome architecture HOW??
  - Gene transfer elements reduced/eliminated
    - Reduced phage
    - Reduced exhange w/other genomes
    - Fewer repeat sequences
    - Fewer transposons
  - Lack of recombination mechanisms (no recA, recF)
  - Lower frequency of recombination

Agrobacterium

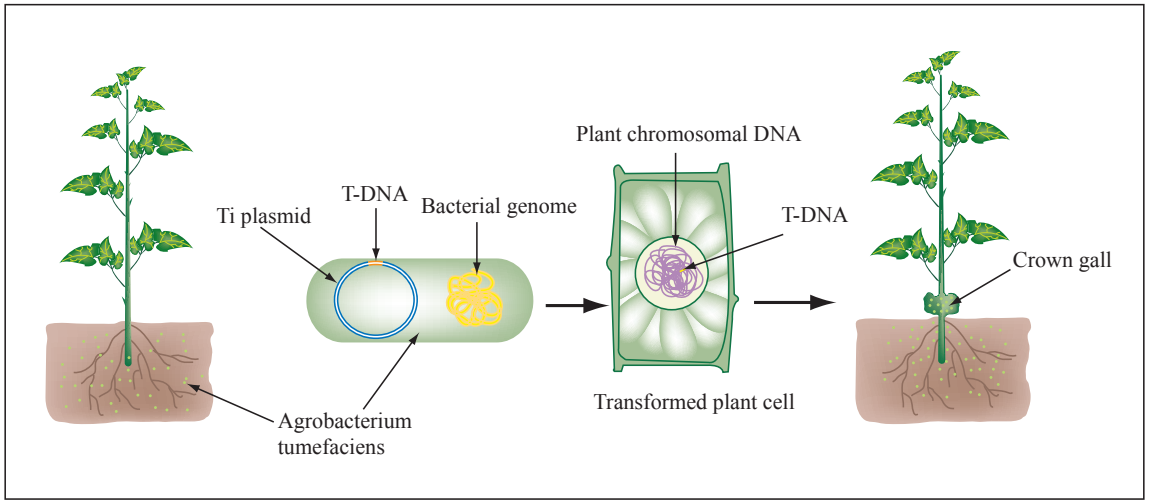
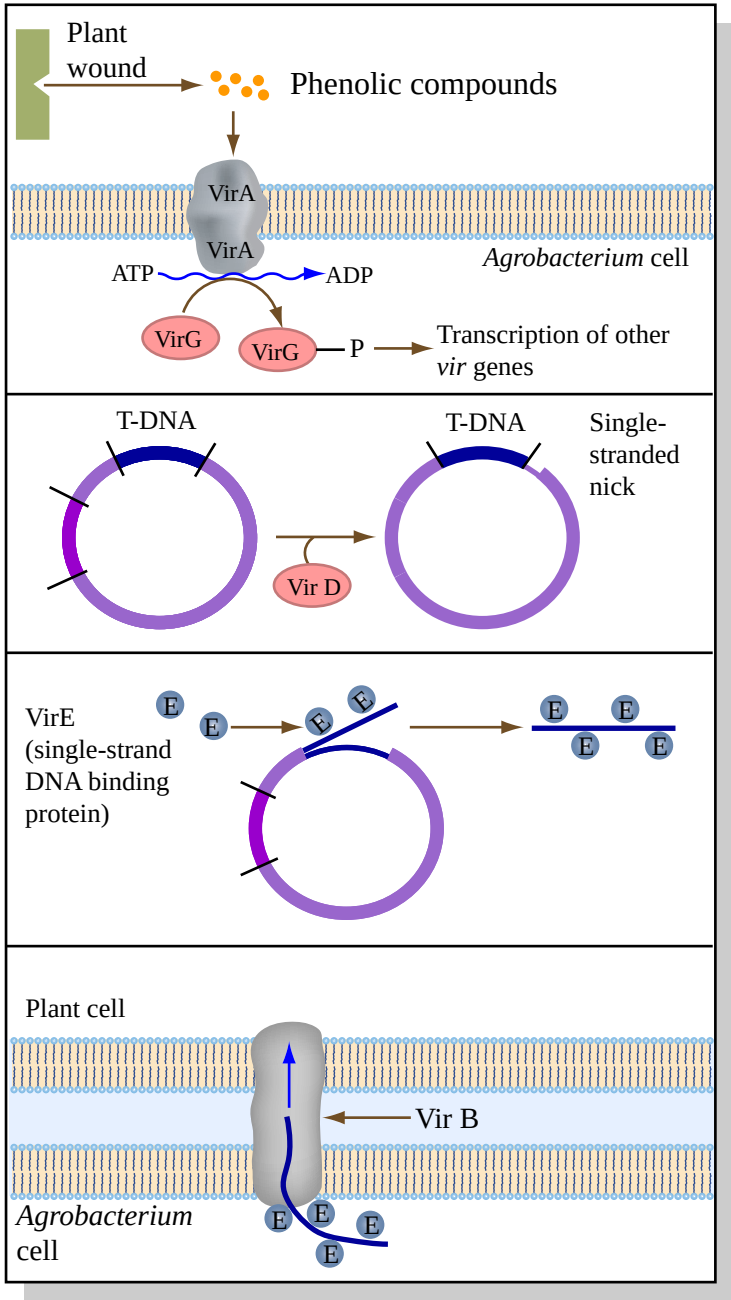


Figure by MIT OCW.

- Ti plasmid & crown gall disease
  - A portion of the Ti plasmid is inserted into the plant chomosome causing the formation of the tumor or gall.

Figure by MIT OCW.



Fundamentals of Regulation

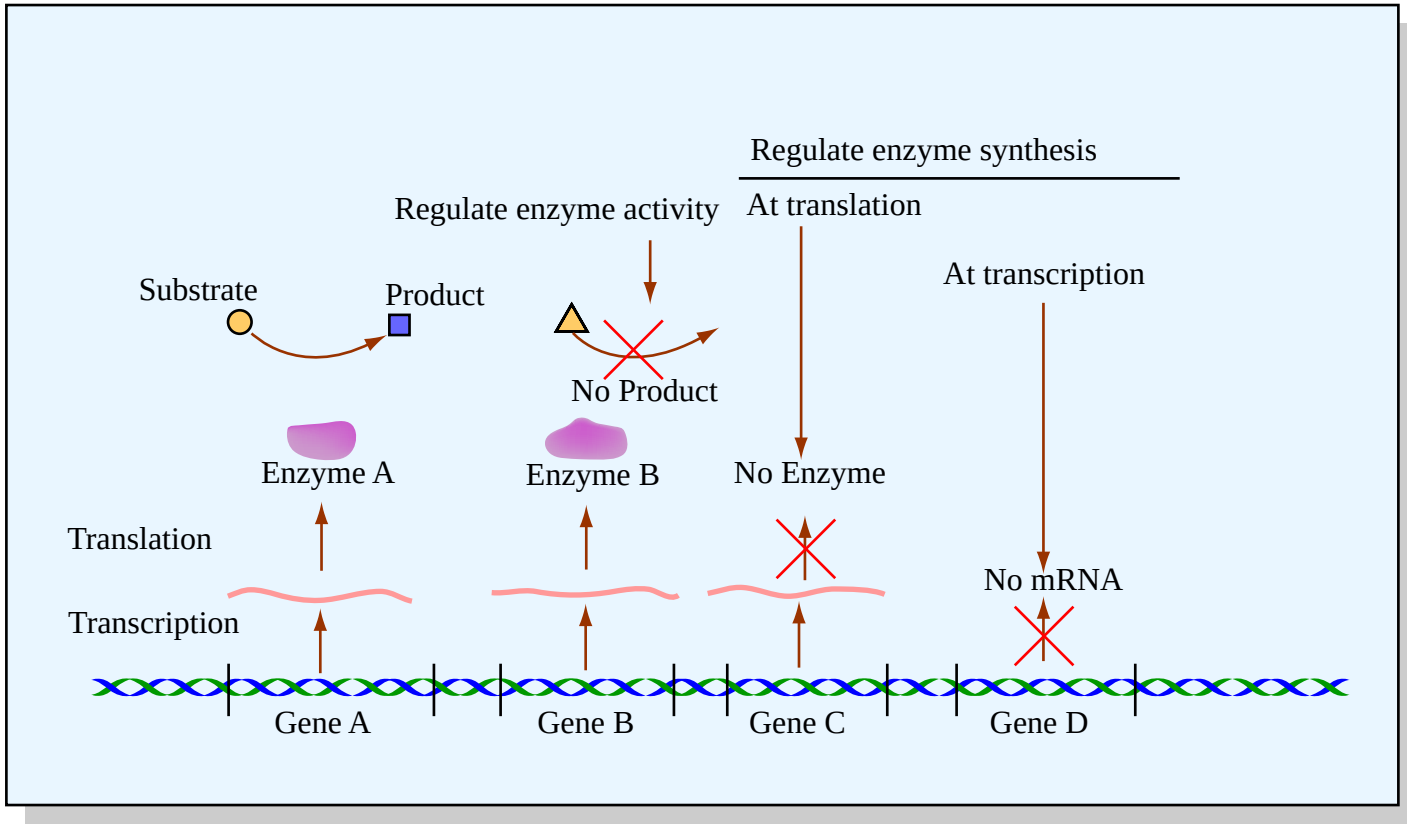


Figure by MIT OCW.

Prokaryotic Gene Regulation

1. Single-celled organisms with short doubling times must respond extremely rapidly to their environment.

2. Half-life of most mRNAs is short (on the order of a few minutes).

3. Coupled transcription and translation occur in a single cellular compartment.

Therefore, transcriptional initiation is usually the major control point.

Most prokaryotic genes are regulated in units called operons (Jacob and Monod, 1960)

Operon: a coordinated unit of gene expression consisting of one or more related genes and the operator and promoter sequences that regulate their transcription. The mRNAs thus produced are "polycistronic'—multiple genes on a single transcript.

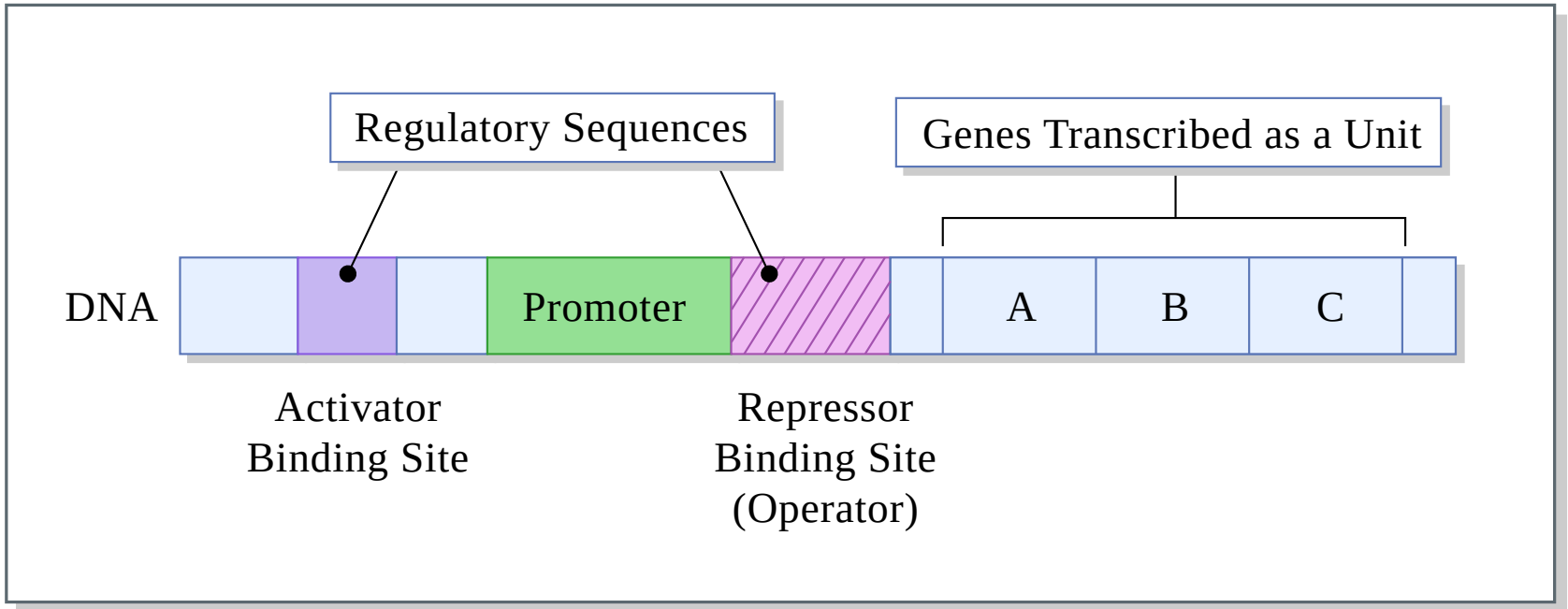


Figure by MIT OCW.

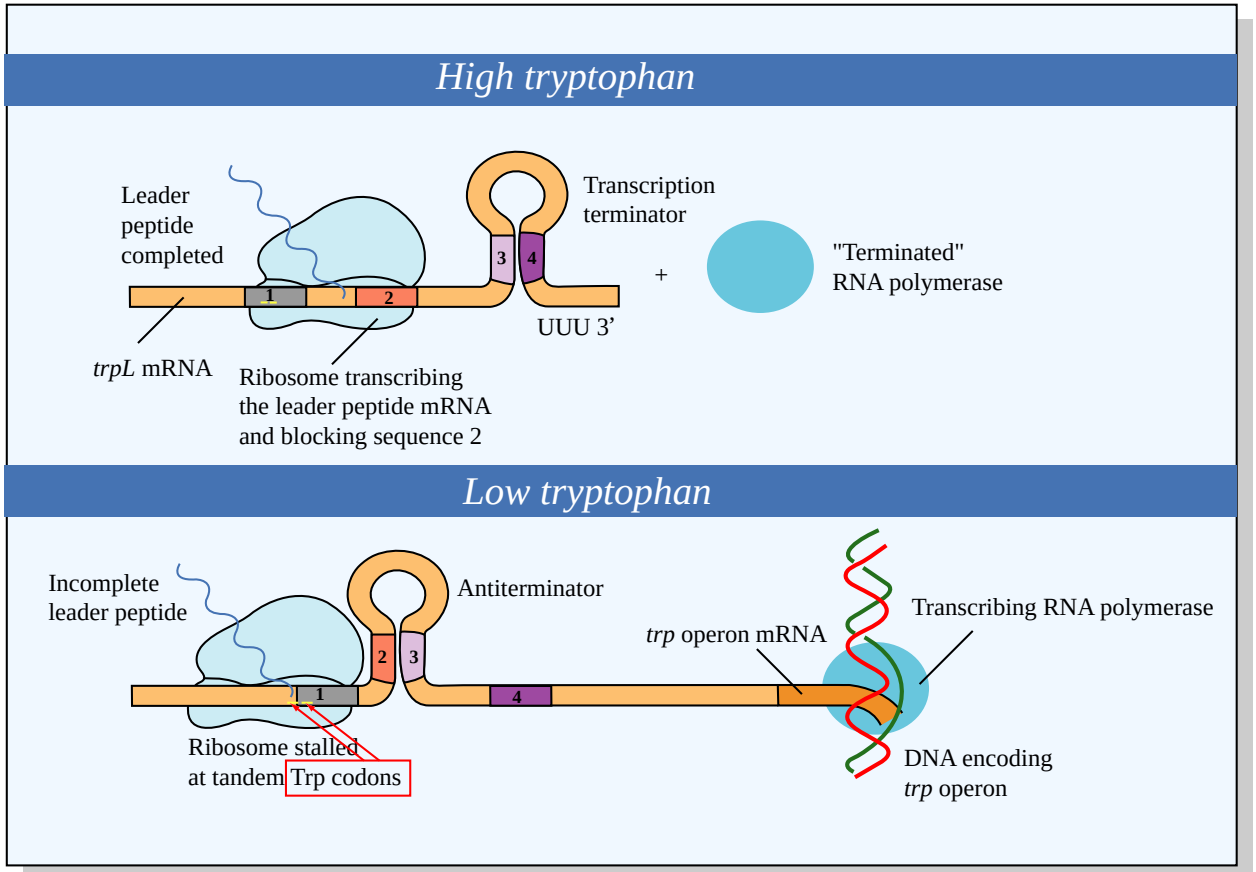
Transcriptional Regulation

- Sigma Factors
  - Some required for binding of RNA polymerase to promoter
  - Others present under different environmental signals
- Transcription Factors
  - DNA binding proteins
  - Interact with regulated promoter to increase (activator/inducer) or decrease (repressor) transcription speed
- Transcriptional Termination
  - RNA polymerase reaches termination site, released from DNA
  - Attenuator sequence--leader peptide produced when aa is present, speeds up translation causing loop in mRNA that ends translation and transcription

Attenuation

Attenuation is mediated by the tight coupling of transcription and translation

- The ribosome translating the *trp* leader mRNA follows closely behind the RNA polymerase that is transcribing the DNA template.
- Alternative conformation adopted by the leader mRNA.



- The stalled ribosome is waiting for tryptophanyl-tRNA.
- The 2:3 pair is not an attenuator and is more stable than the 3:4 pair.

Figure by MIT OCW.

Translational Regulation

Ribosome binding site
Strength of ribosome binding to mRNA
"stringent" response
Shuts down translational machinery globally

Post-translational Regulation

Feedback inhibition
Covalent modifications
Affect protein activity

Cultivation, Isolation, and Identification of Microrganisms

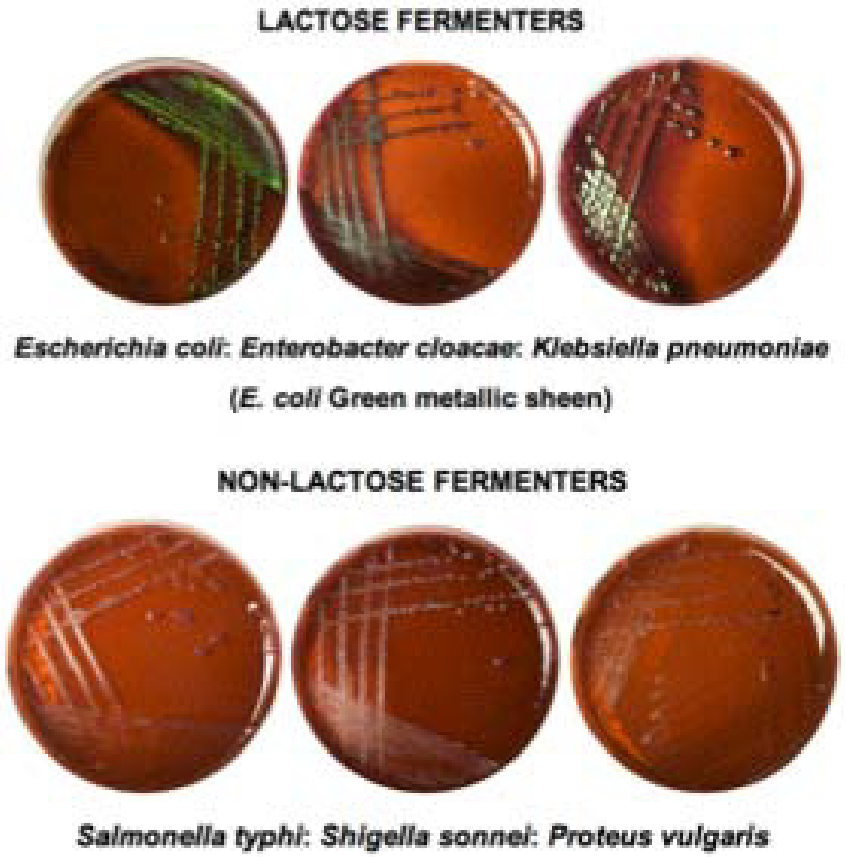
To go from a mixed population to a *pure culture...*

1. Establish permissive conditions for growth
2. Physically isolate the organism
3. Identify the organism

- **Microscopic examination**
  1. Presence of yeast
  2. Morphology of bacteria
- **Cultivation**
  1. Isolation (serial dilutions or streaking)
  2. Identification (Genus species)
     - ✓ Morphology
     - ✓ Metabolic characterization
- **DNA fingerprinting** (strain ID)

*viral identification need plaque assay and serology

Selective & Differential Media



Photograph of test tubes removed due to copyright restrictions. See Figure 24-7b in Madigan, Michael, and John Martinko. *Brock Biology of Microorganisms.* 11th Ed. Upper Saddle River, NJ: Pearson Prentice Hall, 2006. ISBN: 0131443291.

www.spiceisle.com/zross/Enteric%20Demo.htm

Courtesy of Dr. Z. Ross. Used with permission.

Growth Control

- Methods
  - Physical antimicrobial control
    - Filter
    - Radiation
    - Heat
  - Chemical control
    - Pathogenic vs non-pathogenic
    - Sterilants
    - Disinfectants
- Antimicrobials
  - Synthetics
  - Growth Factor analogs
  - Chemotherapeutics
- Antibiotics
  - Broad vs narrow spectrum
  - Different classes (macrolides, aminoglycosides, etc)
- Resistance
  - R plasmids
  - Other mechanisms (drug or target modification, pathway perturbations, etc)

Indigenous microbiota

- Microorganisms that inhabit body sites in which surfaces and cavities are open to the environment
- Skin, oral cavity, upper respiratory tract, gastrointestinal (GI) tract, and vagina
- Each habitat can be considered a separate ecosystem
- For every cell in human body (10^{13}) there are 10 viable indigenous bacteria in the GI tract
- The GI tract (10^{14}) harbors 100-fold more bacteria than the skin (10^{12})

Defining the GI microbiota

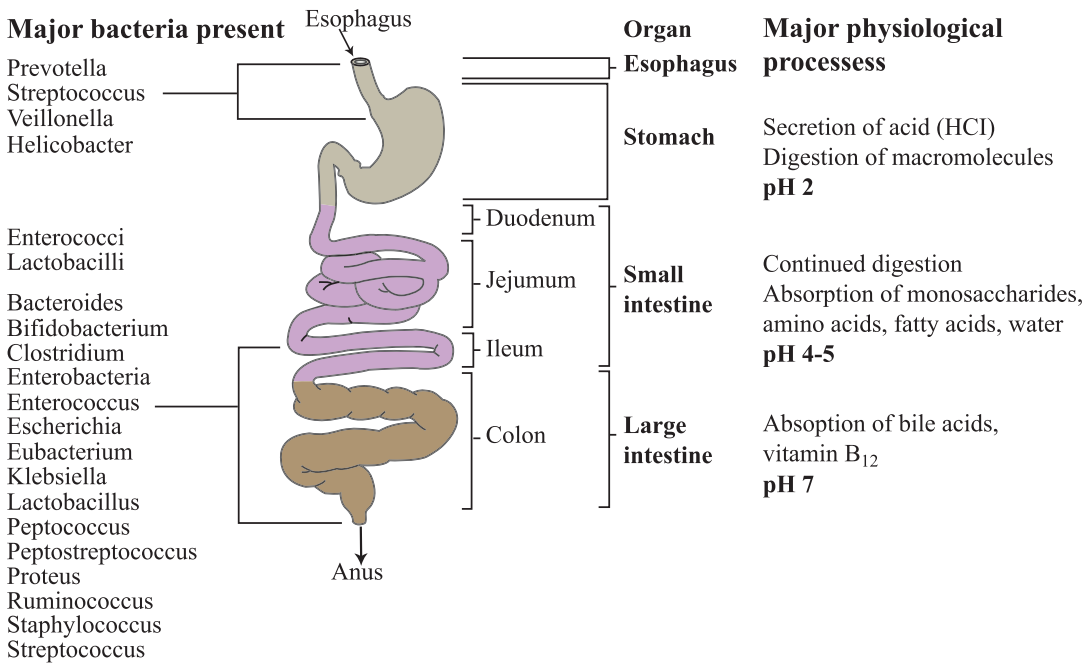


Figure by MIT OCW.

- Autochthonous microbiota
  - Present during the evolution of an animal and therefore present in every member of a species
- Normal microbiota
  - Common and perhaps even present in every individual in a given geographic area/community, but not in every member of the species
- True pathogens
  - Acquired accidentally and therefore not normally present in all members of a community of an animal species

Dubos et al. J Exp Med 122:67-76, 1965

Ecological principles

- In a stable GI ecosystem, all available habitats are occupied by indigenous microbiota
- Transient species derived from food, water, or even another part of the GI tract or the skin will not establish (colonize)
- Habitats are physical spaces in the GI tract normally occupied by a climax community of indigenous microbiota
- Population levels and species composition are stable and not easily disrupted

The indigenous GI microbiota

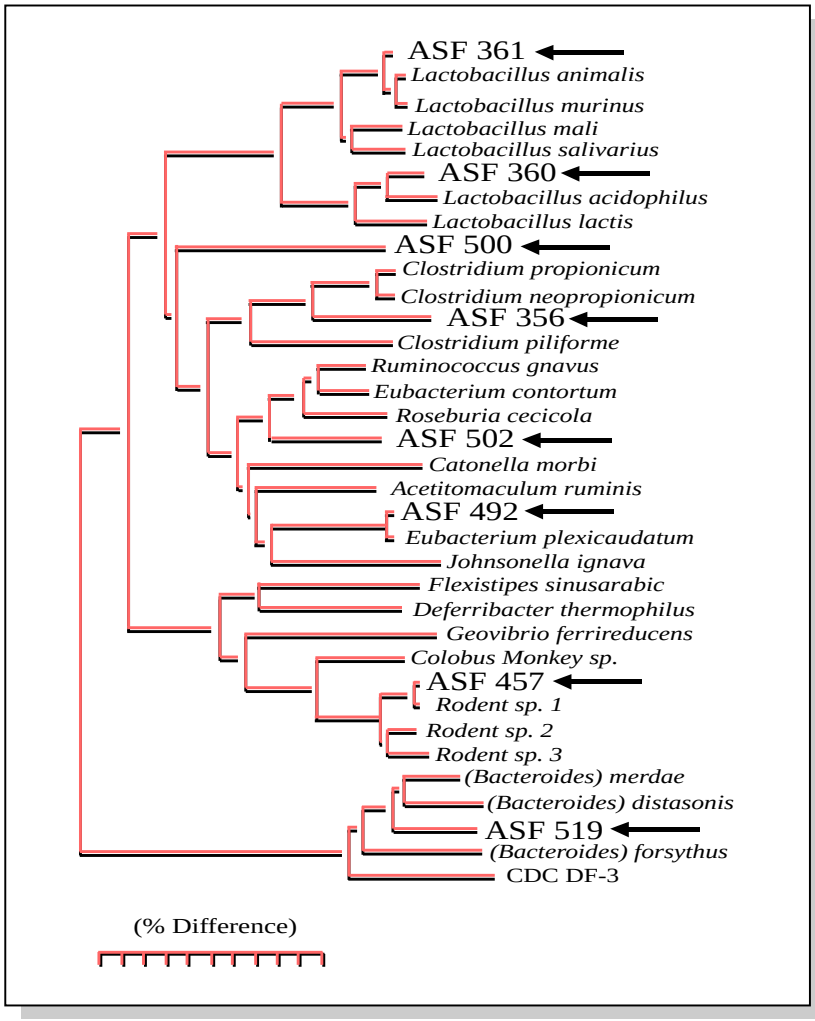
- Does not appear spontaneously in newborn humans or animals
- Certain microbes colonize particular habitats at certain times after birth that are characteristic of a given animal species (succession)
- Fetus is normally sterile in utero
- Becomes contaminated with heterogeneous collection of microbes at birth, but within days many of these are eliminated and the process of succession begins

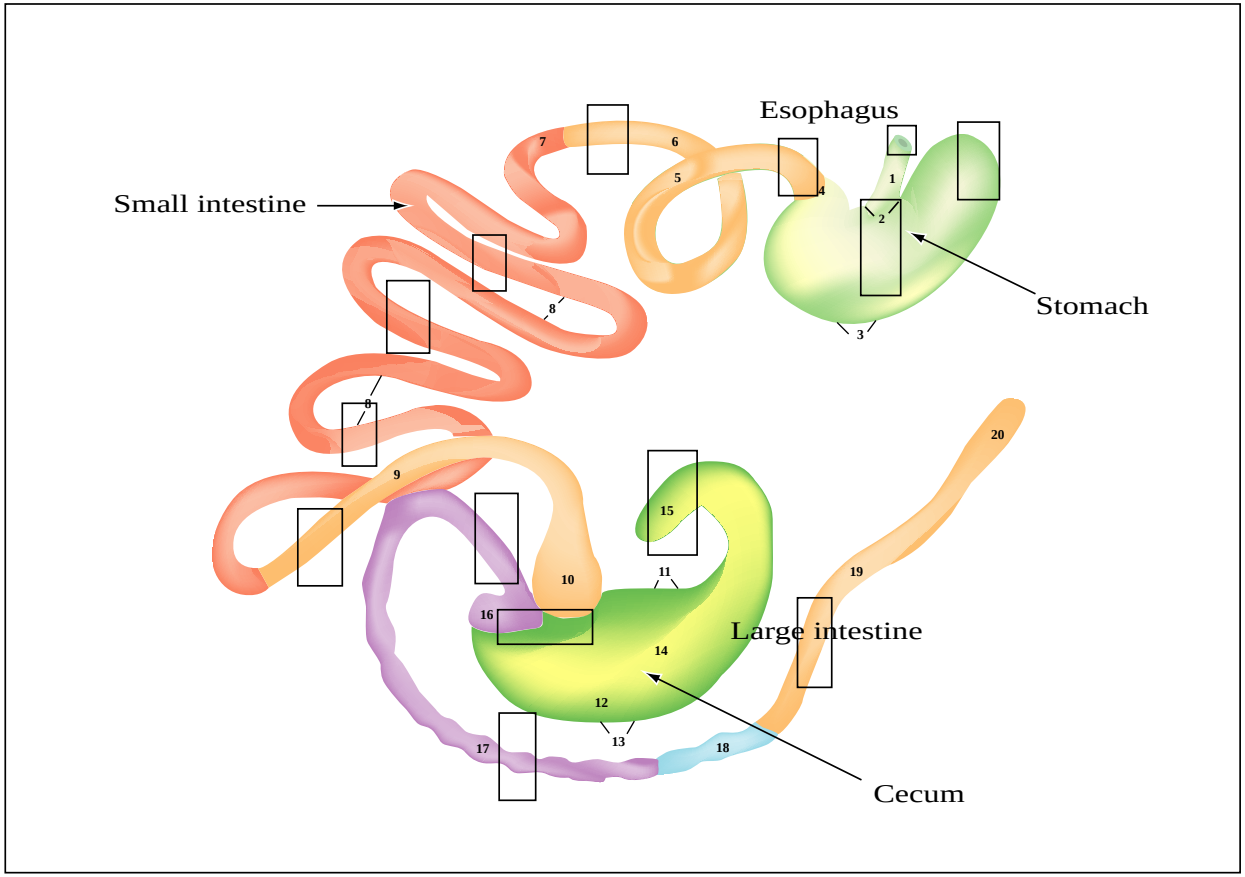
Succession & climax populations

- Lactic acid bacteria and coliforms predominate in infant human and animal GI tracts
- During weaning the microbiota changes drastically and obligate anaerobic bacteria become predominant
- The indigenous GI microbiota of adults consists of climax communities that are remarkably stable
- Each region of the GI tract has a characteristic population of microbes, in terms of complexity and population density

Colon microbiota as an organ

- Distinct cell lineages
- Consumes, stores, and redistributes energy
- Mediates physiologically important chemical transformations
- Maintains and repairs itself
- The "microbiome" has ≥ 100 times the genetic complement of our genome provides functional features that we have not had to evolve ourselves
- Traditionally viewed as commensal microbiota, but clearly a mutualistic relationship where both partners benefit





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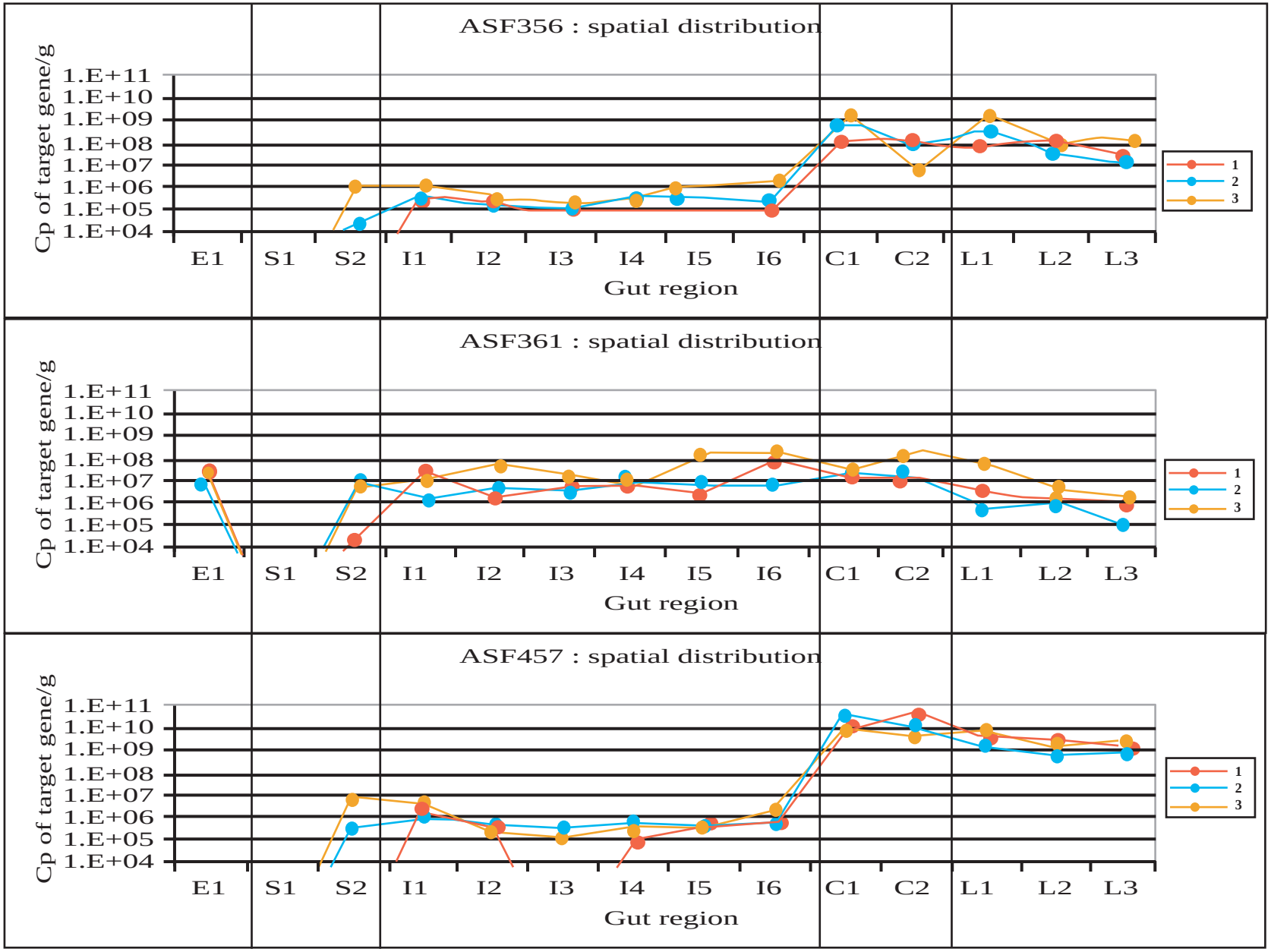

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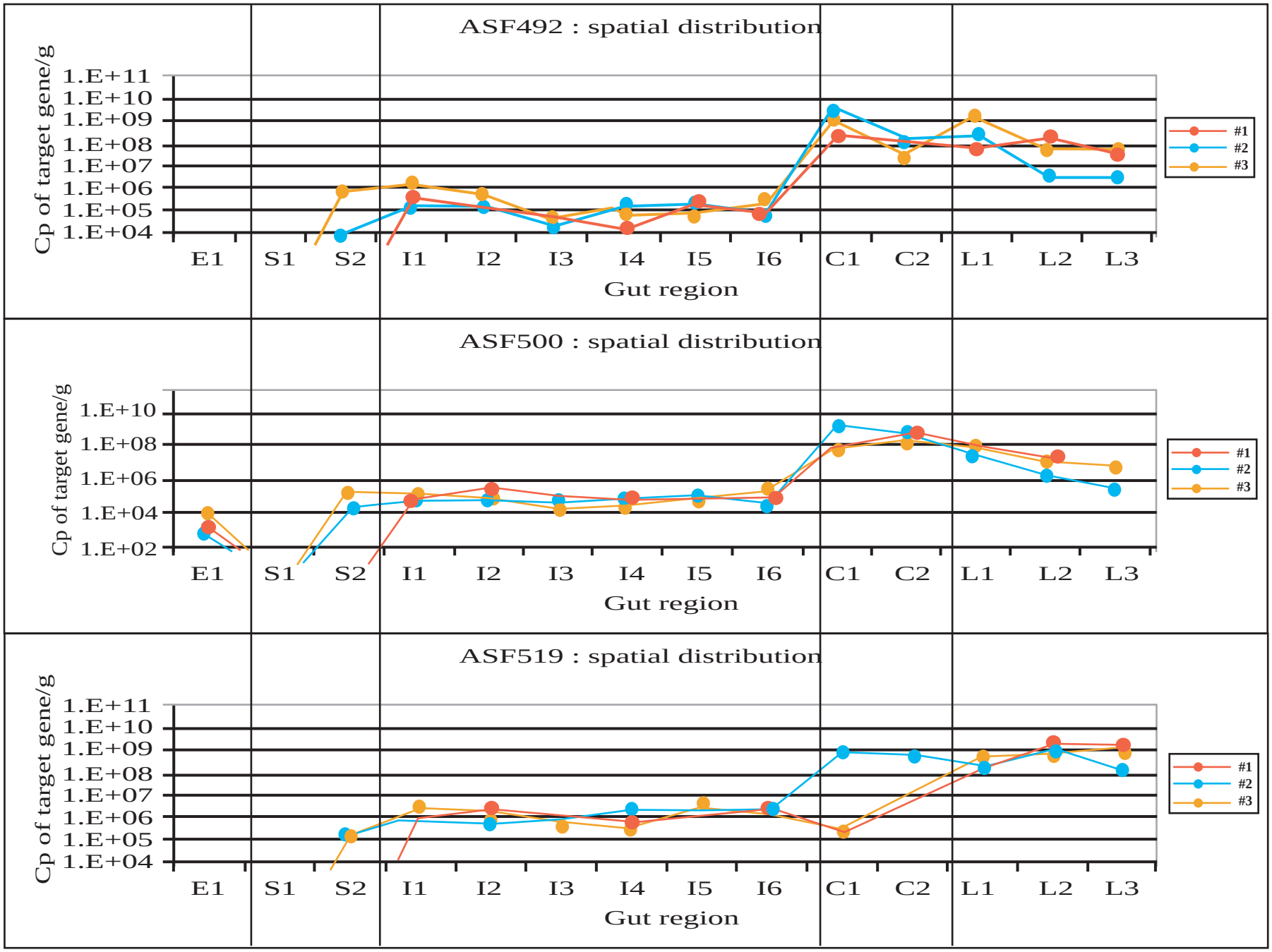


Figure by MIT OCW.

Human colonic microbiota

- Highest cell densities recorded for any ecosystem
- Diversity at the division level is among the lowest
- Only 8 of the 55 known bacterial divisions have been identified in colonic bacteria to date
- 2 division dominate
- Cytophaga-Flavobacterium-Bacteroides (CFB)
- Firmicutes (genera *Clostridium* and *Eubacterium*)
- Proteobacteria are common, but not dominant
- Compare to many soil communities, where ≥ 20 bacterial division can be present

Immune Responses

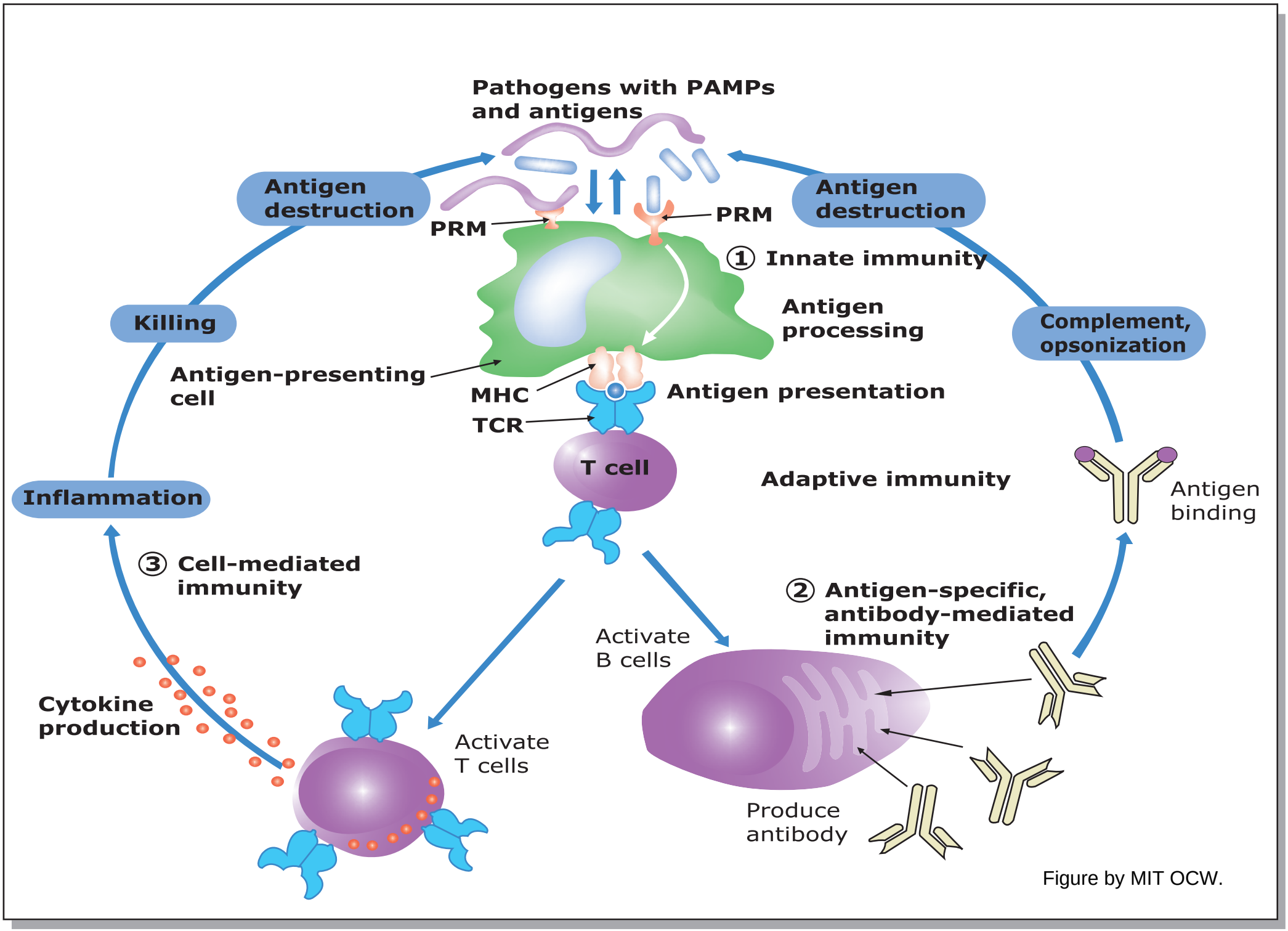


Figure by MIT OCW.

Cells of the Immune System

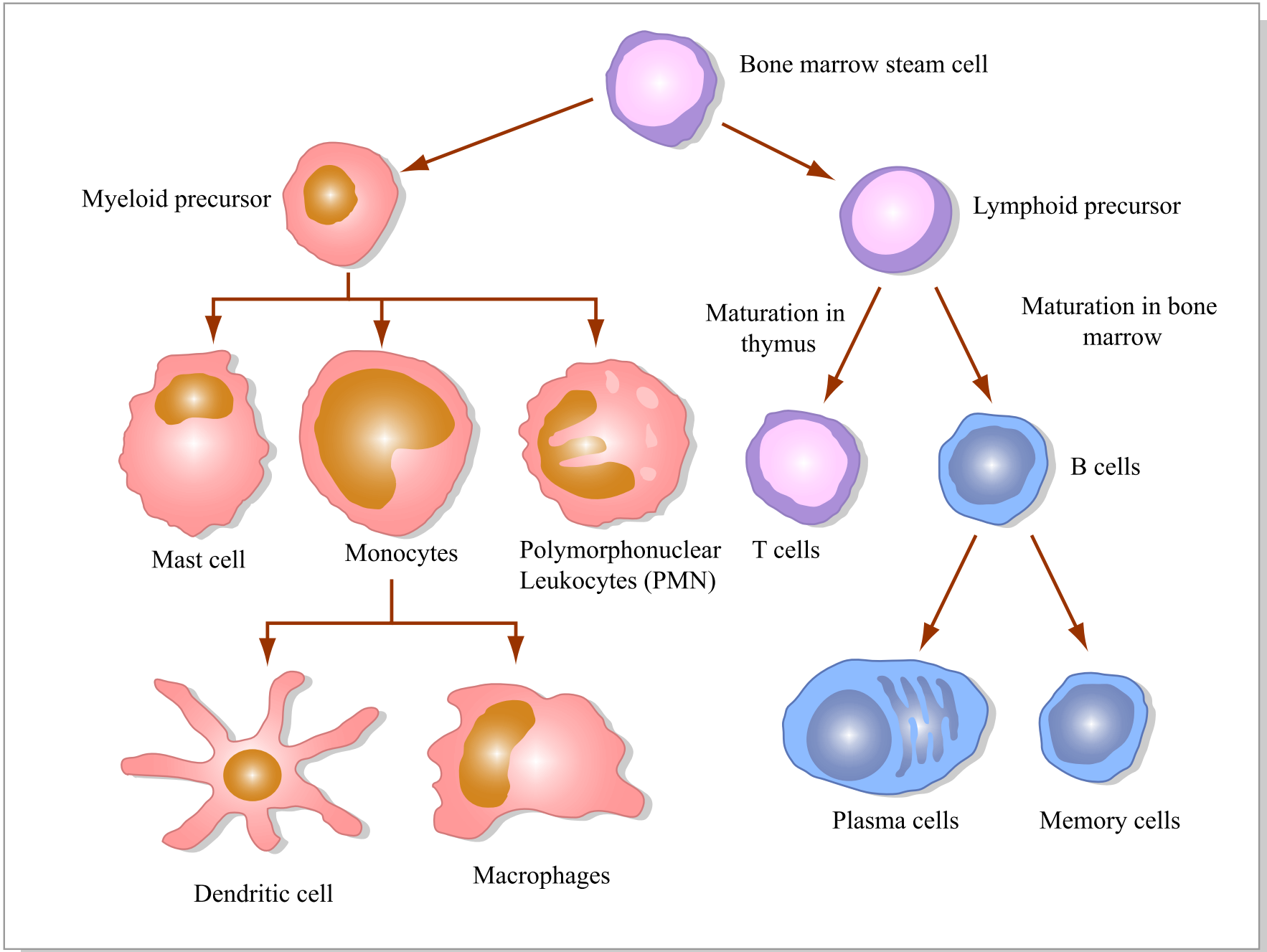


Figure by MIT OCW.

Activation of Phagocytes

PRRs

- Present before infection
- Evolved to recognize microbes
- PRRs interact with PAMPS shared by a variety of pathogens, activating complement and phagocyte effector mechanisms to target and destroy pathogens
- Activation of signaling cascade leads to production of chemokines and cytokine
- First discovered as the Toll receptors in *Drosophila* (the fruit fly), the evolutionarily and functionally related transmembrane proteins are called **Toll-like receptors (TLRs)** in mammals

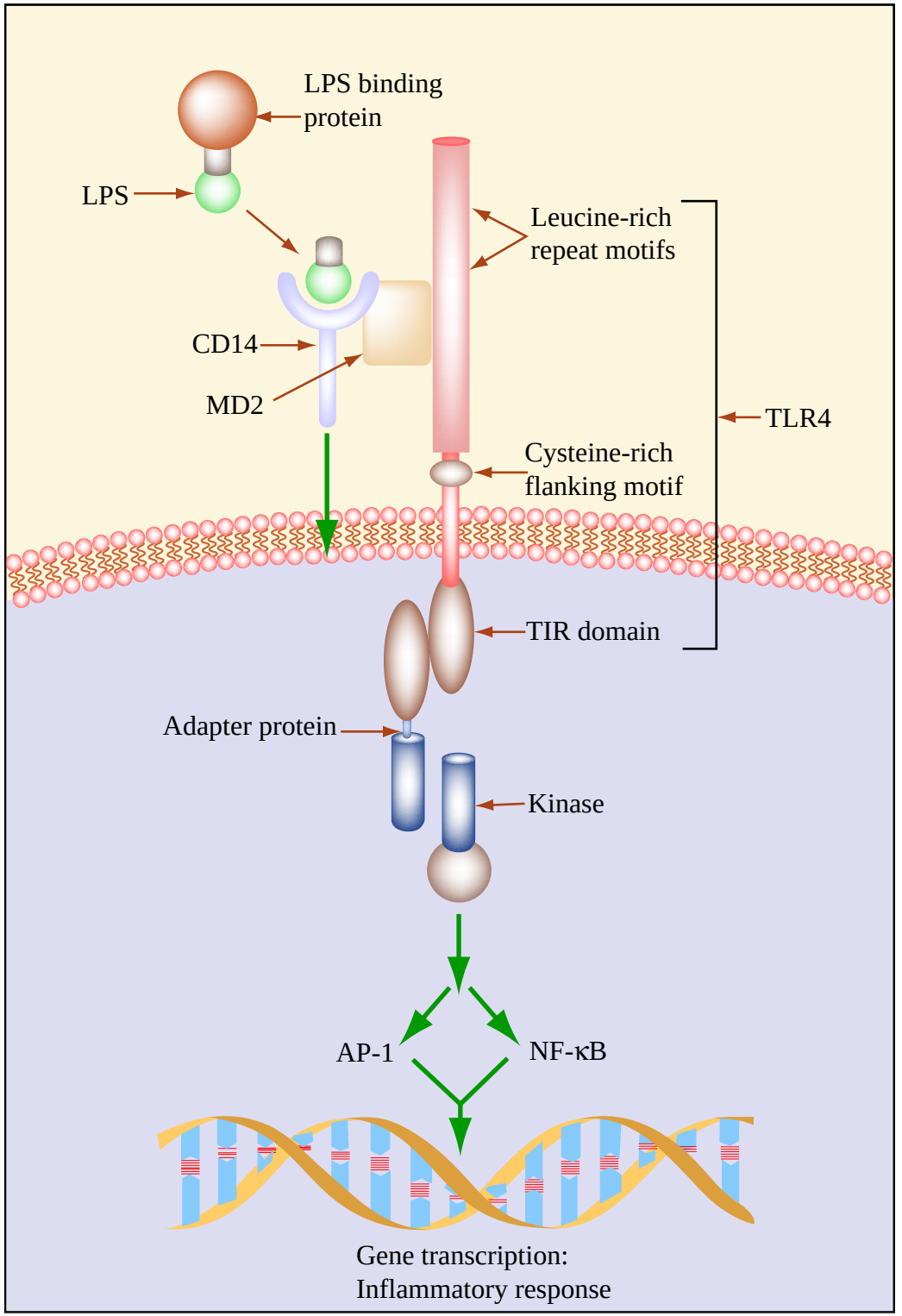
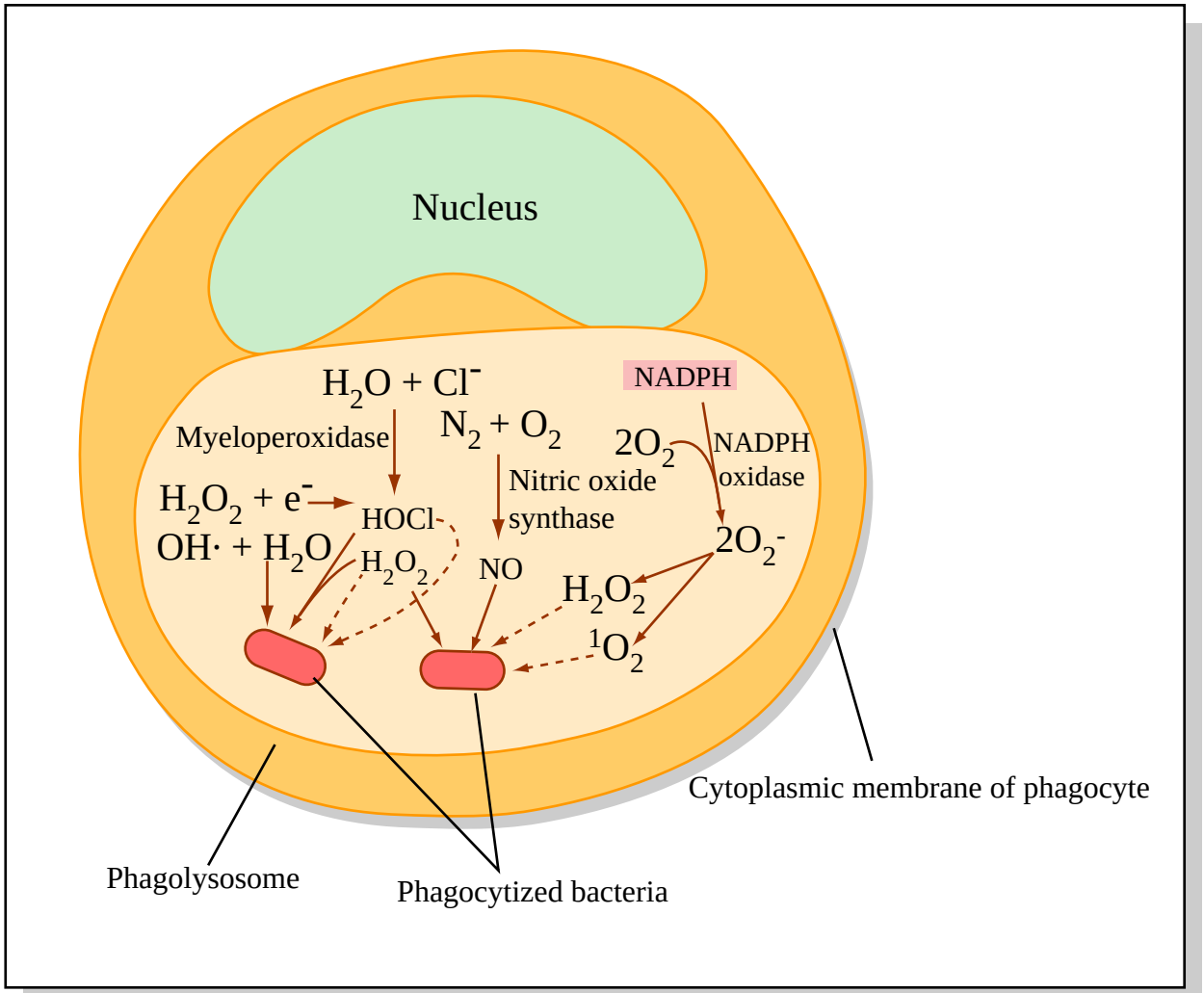


Figure by MIT OCW.

Phagocytosis

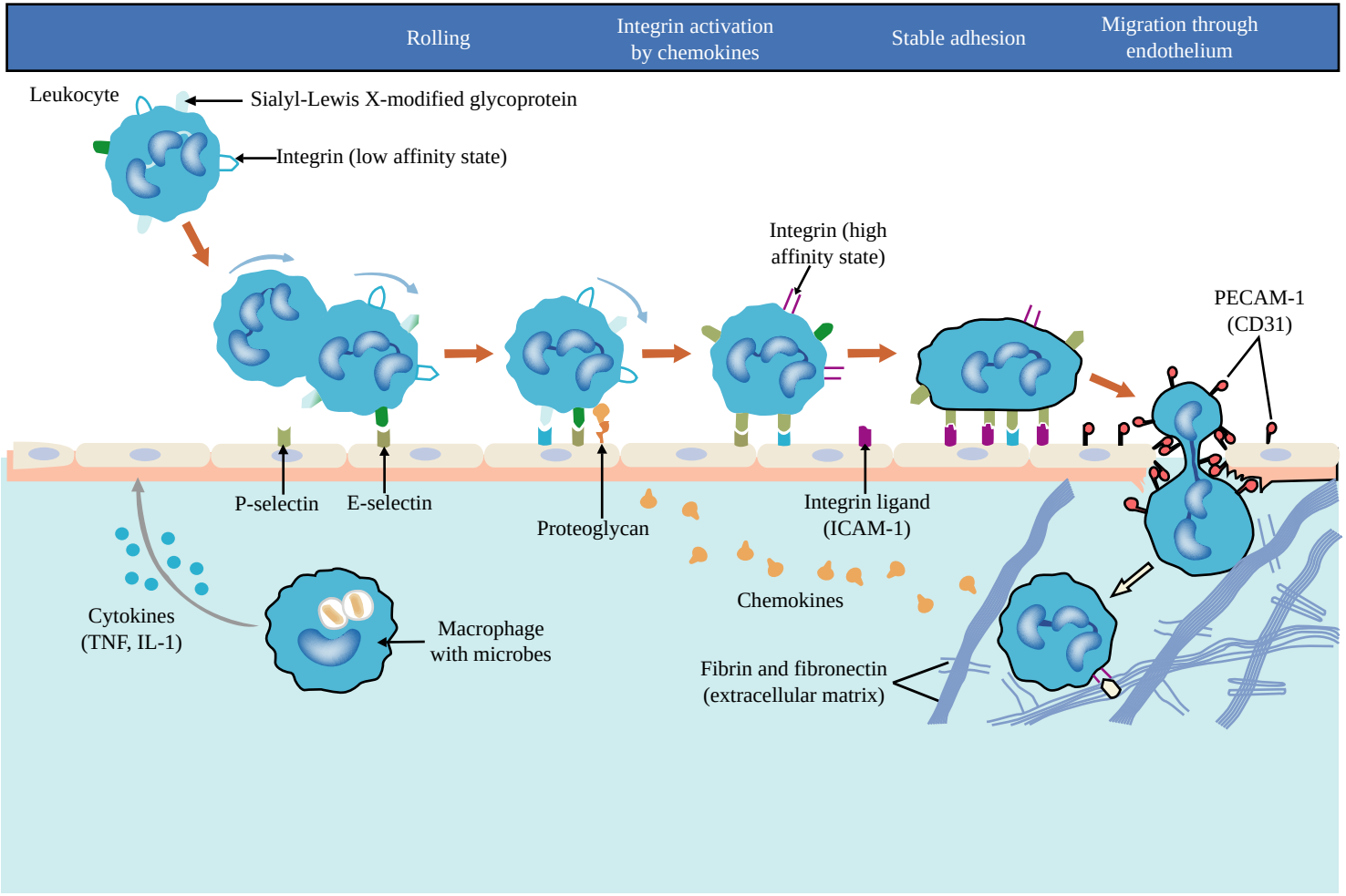


- Phagocytosis stimulates respiratory burst
- NADPH or phagocyte oxidase (Phox)
- PMNs produce myeloperoxidase that converts H_2O_2 to HOCl
- Efficient killing

Figure by MIT OCW.

Leukocyte Extravasation

1. Margination, rolling, adhesion
   - E-selectin, P-selectin, and L-selectin
   - ICAM-1, VCAM-1, and integrins LFA-1, MAC-1, $\alpha_4\beta_1$, and $\alpha_4\beta_7$
2. Transmigration across the endothelium (diapedesis)
3. Migration in interstitial tissues towards a chemotactic stimulus



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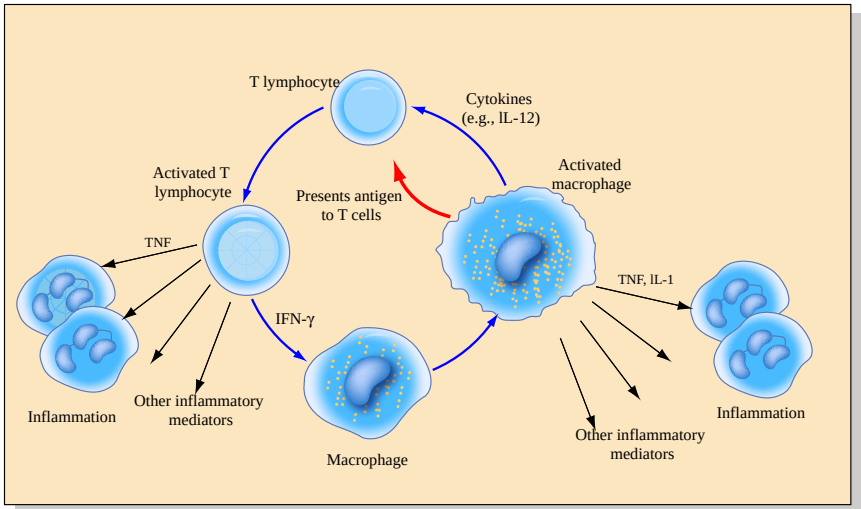

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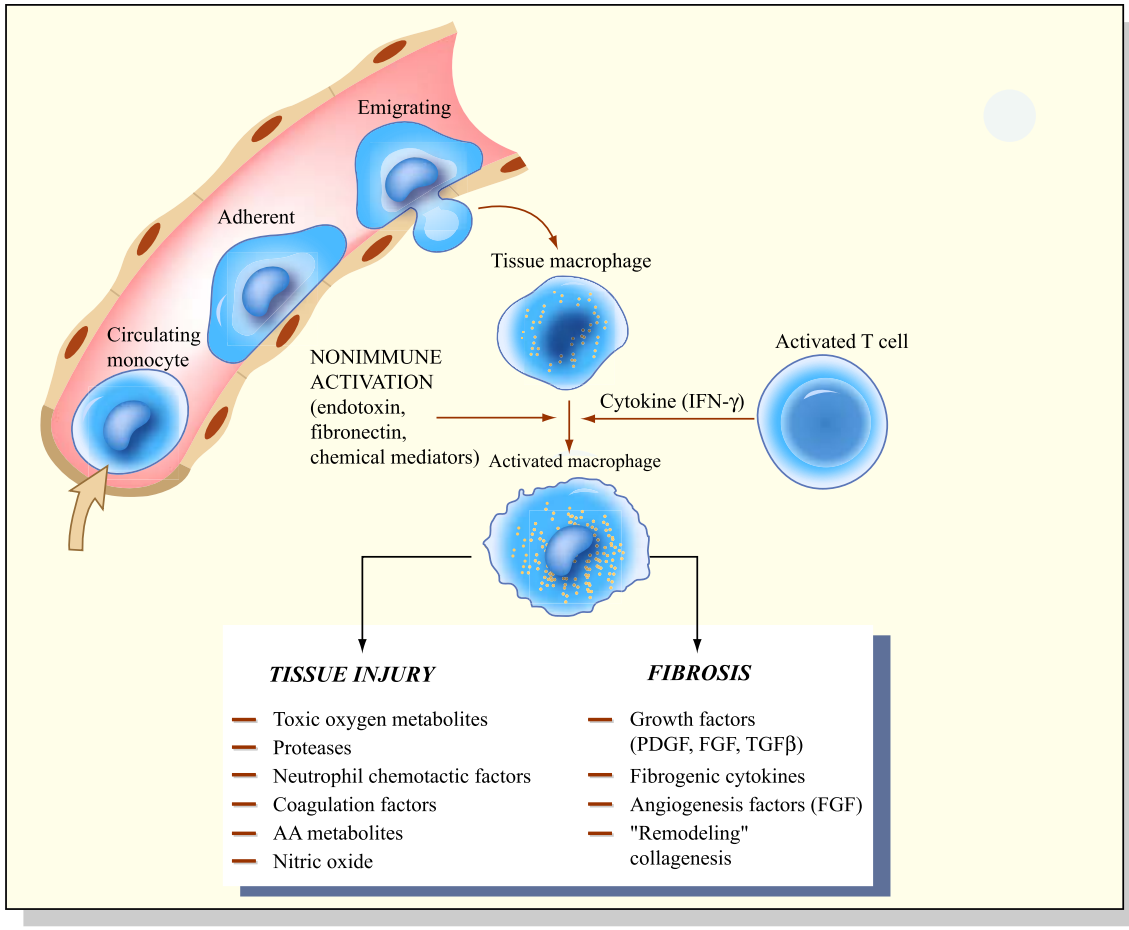

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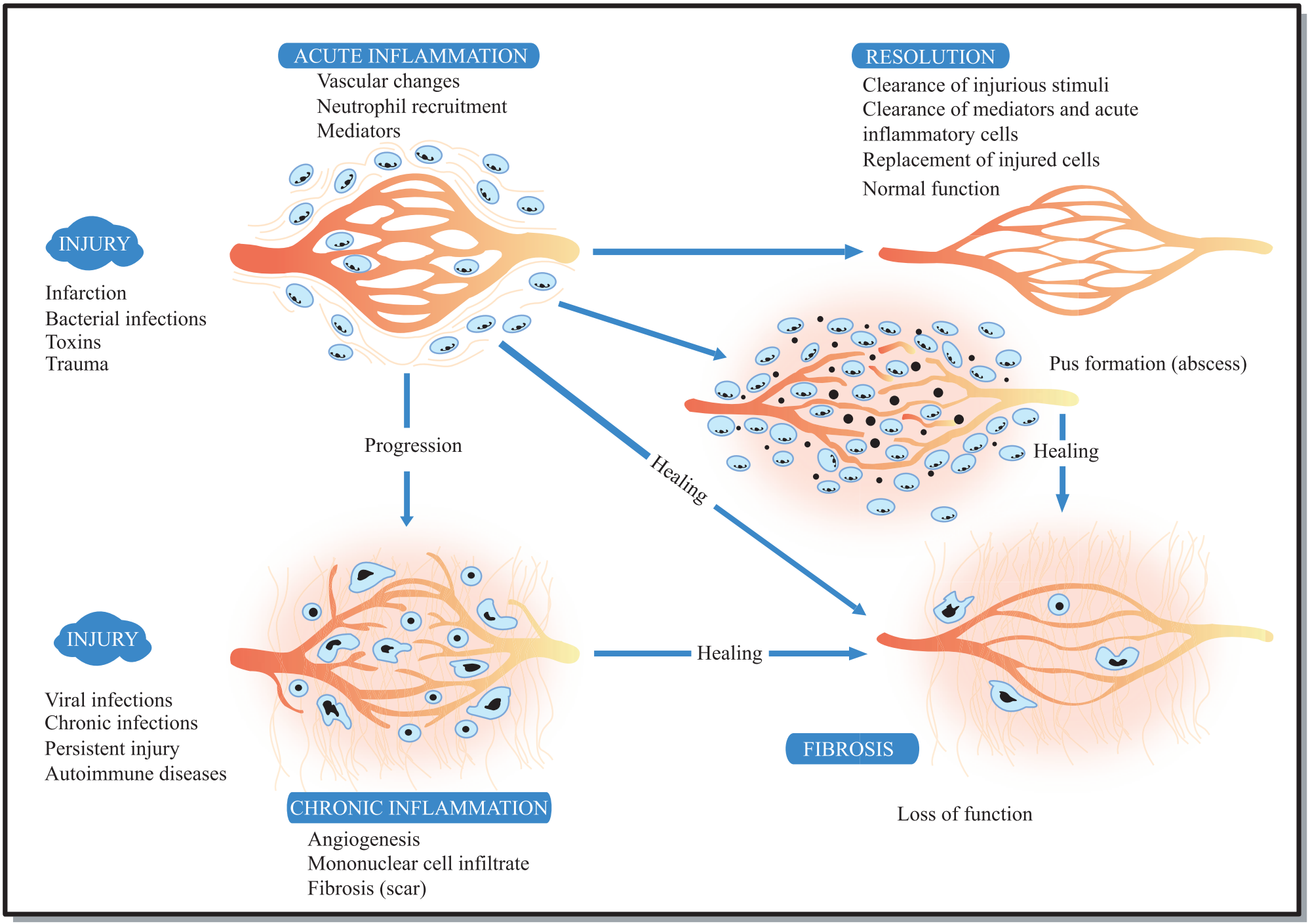


Figure by MIT OCW.

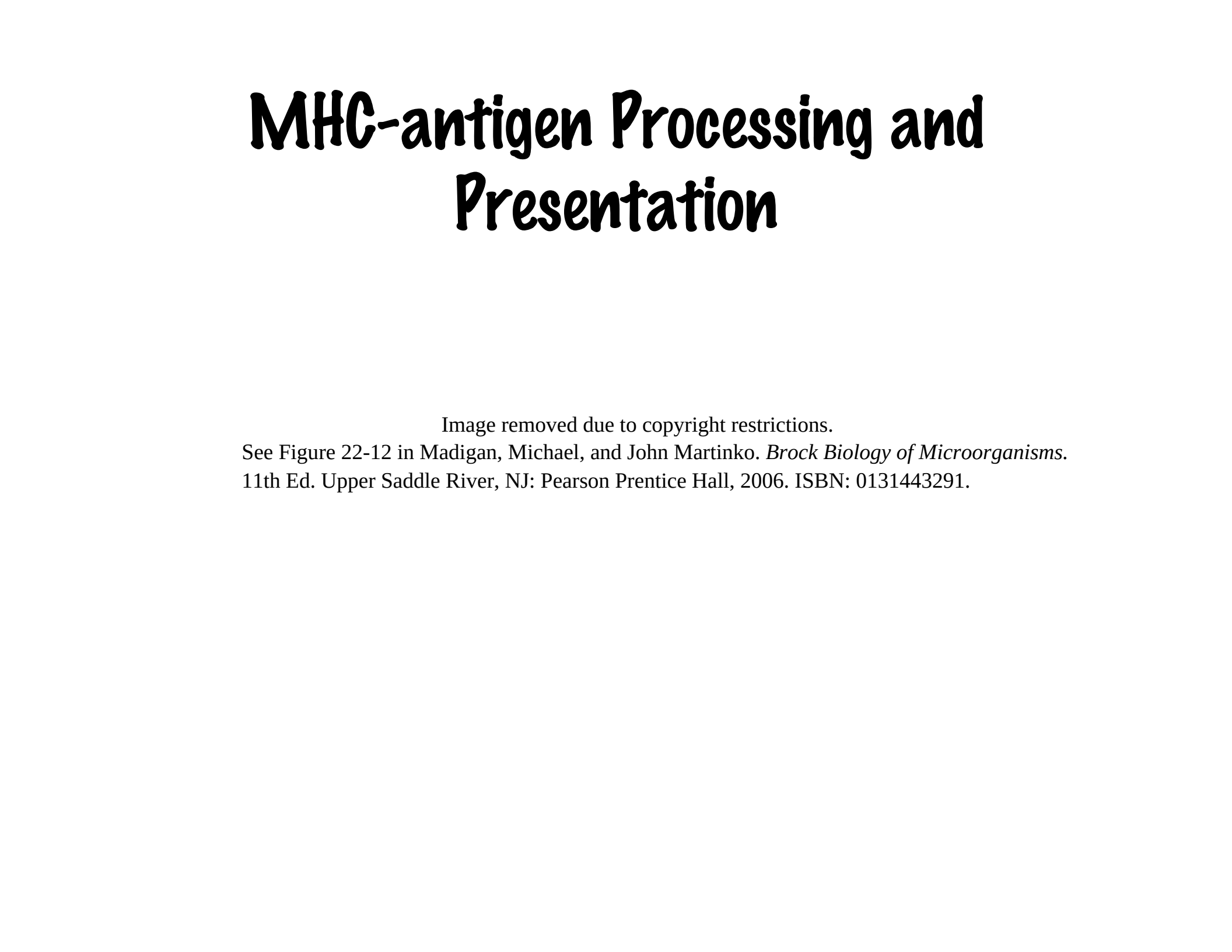
- **Antigens** are molecules recognized by antibodies or T-cell receptors (TCRs)
- **Antibodies** recognize conformational determinants
- **TCRs** recognize linear peptide determinants
- Antibodies and TCRs interact with a distinct portion of the antigen called an **antigenic determinant** or **epitope**

Immunoglobin Superfamily

Immunoglobin (Ig) gene superfamily encodes proteins that are evolutionarily, structurally, and functionally related to Igs (**antibodies**)

Images removed due to copyright restrictions
See Figures 22-9 and 23-1 in Madigan, Michael, and John Martinko. *Brock Biology of Microorganisms*. 11th Ed. Upper Saddle River, NJ: Pearson Prentice Hall, 2006. ISBN: 0131443291.

MHC-antigen Processing and Presentation



T cell Selection and Tolerance

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See Figure 23-9 in Madigan, Michael, and John Martinko. *Brock Biology of Microorganisms* 11th Ed. Upper Saddle River, NJ: Pearson Prentice Hall, 2006. ISBN: 0131443291.

T cell Activation

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See Figure 23-10 part 1 in Madigan, Michael, and John Martinko. *Brock Biology of Microorganisms.* 11th Ed. Upper Saddle River, NJ: Pearson Prentice Hall, 2006. ISBN: 0131443291.

Requires two signals

- Binding of TCR to MHC-antigen complex
- Binding of CD28 on T cell to B7 receptor on APC

Cytotoxic T cells (T_c)

- CD8 co-receptor to TCR, binds MHC-I protein during TCR-MHC-antigen interactions
- Recognize antigens mainly on virus-infected or tumor cells
- Antigen recognition triggers killing via release of perforins and granzymes

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See Figure 23-13a in Madigan, Michael, and John Martinko. *Brock Biology of Microorganisms.* 11th Ed. Upper Saddle River, NJ: Pearson Prentice Hall, 2006. ISBN: 0131443291

T_H1 T cells

- CD4 co-receptor to TCR, binds MHC-II protein during TCR-MHC-antigen interactions
- Recognize antigens mainly from intracellular as well as extracellular bacteria
- Antigen recognition triggers release of proinflammatory cytokines that further enhance phagocytosis

T_H2 T cells

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See Figure 23-14 in Madigan, Michael, and John Martinko. *Brock Biology of Microorganisms*. 11th Ed. Upper Saddle River, NJ: Pearson Prentice Hall, 2006. ISBN: 0131443291.

- CD4 co-receptor to TCR, binds MHC-II protein during TCR-MHC-antigen interactions
- Typically interacts with antigen presented via MHC-II on a B cell
- Activated T_H2 cells secrete cytokines to stimulate production and secretion of soluble antibodies by the B cell

Antibody Production/B cell Clonal Selection

1. Antigen is carried to the nearest lymph node
2. After initial antigen exposure, stimulated B cells multiply and differentiate into both antibody-secreting plasma cells and memory B cells
   - Plasma cells mainly produce IgM and last less than 1 week
   - More specific antibodies appear after a time lag
3. Upon second exposure to antigen, memory B cells immediately produce specific IgG
   - No requrrement for T cell help
   - IgG is main class of antibody produced (over IgM)

Image removed due to copyright restrictions
See Figure 23-8 part 2 in Madigan, Michael, and John Martinko. *Brock Biology of Microorganisms*. 11th Ed. Upper Saddle River, NJ: Pearson Prentice Hall, 2006. ISBN: 0131443291.

Antibodies

Purpose: bind to virus, toxins, pathogen surface markers to inactivate and mark for phagocytosis and destruction by other immune cells

- Immunoglobulins (Ig) collectively most abundant protein component in blood (~20%)
- Produced by B-cells (naïve or memory) once activated by BOTH antigen and helper T-cells
  - Surface bound (IgD, IgM) not very specific
  - Soluble (IgG, IgA, IgE) specific to peptide

Classes of antibodies

- **IgM-μ heavy chain**, first Ig produced, mainly surface bound, secreted upon activation in pentameric form (early infection)
- **IgD-δ heavy chain**, same antigen binding site as IgM, surface bound, only on *mature naïve* B-cells
- **IgG-γ heavy chain**, many isotypes, monomer, major class in blood, Fc regions bind Fc receptors on macrophages and neutrophils, only Ig able to breach placental barrier (Fc regions)
- **IgE-ε heavy chain**, monomer, very high affinity (K_A~10^{10}L/mole) Fc receptor on mast cells (tissue) and basophils (blood), also binds Fc receptors on eosinophils
- **IgA/sIgA-α heavy chain**, main Ig in secretory fluids, monomer in blood and dimer in secretions, Fc region binds Fc receptors on epithelial cells allowing for trans-membrane transport (inefficient transport of IgM, but occurs)

Roles of antibodies during infection

Opsonization

- Antibodies bind to antigen and Fc region to Fc receptors on phagocytic cells
- Antibody-dependent cell-mediated cytotoxicity (ADCC)
  - antibodies bind viral proteins on surface of host cells or large microbes
  - cells killed by secreted toxic compounds from phagolysosomes

Neutralization

- Antibodies bind toxins or viruses
- Blocks entry into cells via receptors

Activate complement cascade

- Cascade activated by microbial molecules or antibodies on microbes' surface

Prevent breach of epithelial barrier

- sIgA in mucin binds antigens and Fc region sticks to mucin components
- Microbes prevented from reaching epithelium

Four Types of Hypersensitivity

Hypersensitivity

Classification	Description	Immune Mechanism	Time of Latency	Examples
Type I	Immediate	IgE sensitization of mast cells	Minutes	Reaction to bee venom (sting) Hay fever
Type II	Cytotoxic*	IgG interaction with cell surface antigen	Hours	Drug reactions (penicillin)
Type III	Immune complex	IgG interaction with soluble or circulating antigen	Hours	Systemic lupus erythematosis (SLE)
Type IV	Delayed type	T_H1 inflammatory cells	Days	Poison ivy Tuberculin test

*Autoimmune diseases may be caused by Type II, Type III, or Type IV reactions.

Figure by MIT OCW.

Immediate Type I Hypersensitivity (Allergies)

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See Figure 22-25 in Madigan, Michael, and John Martinko. *Brock Biology of Microorganisms* 11th Ed. Upper Saddle River, NJ: Pearson Prentice Hall, 2006. ISBN: 0131443291.

Type IV Hypersensitivity--Delayed-Type Hypersensitivity (DTH)

- cell-mediated hypersensitivity
- characterized by tissue damage due to inflammatory responses (T_H1)
- Typical antigens
  - certain microorganisms
  - a few self antigens
  - several chemicals that bind covalently to the skin, creating new antigens.

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See Figure 22-26b in Madigan, Michael, and John Martinko. *Brock Biology of Microorganisms*. 11th Ed. Upper Saddle River, NJ: Pearson Prentice Hall, 2006. ISBN: 0131443291.

Immunologic Memory

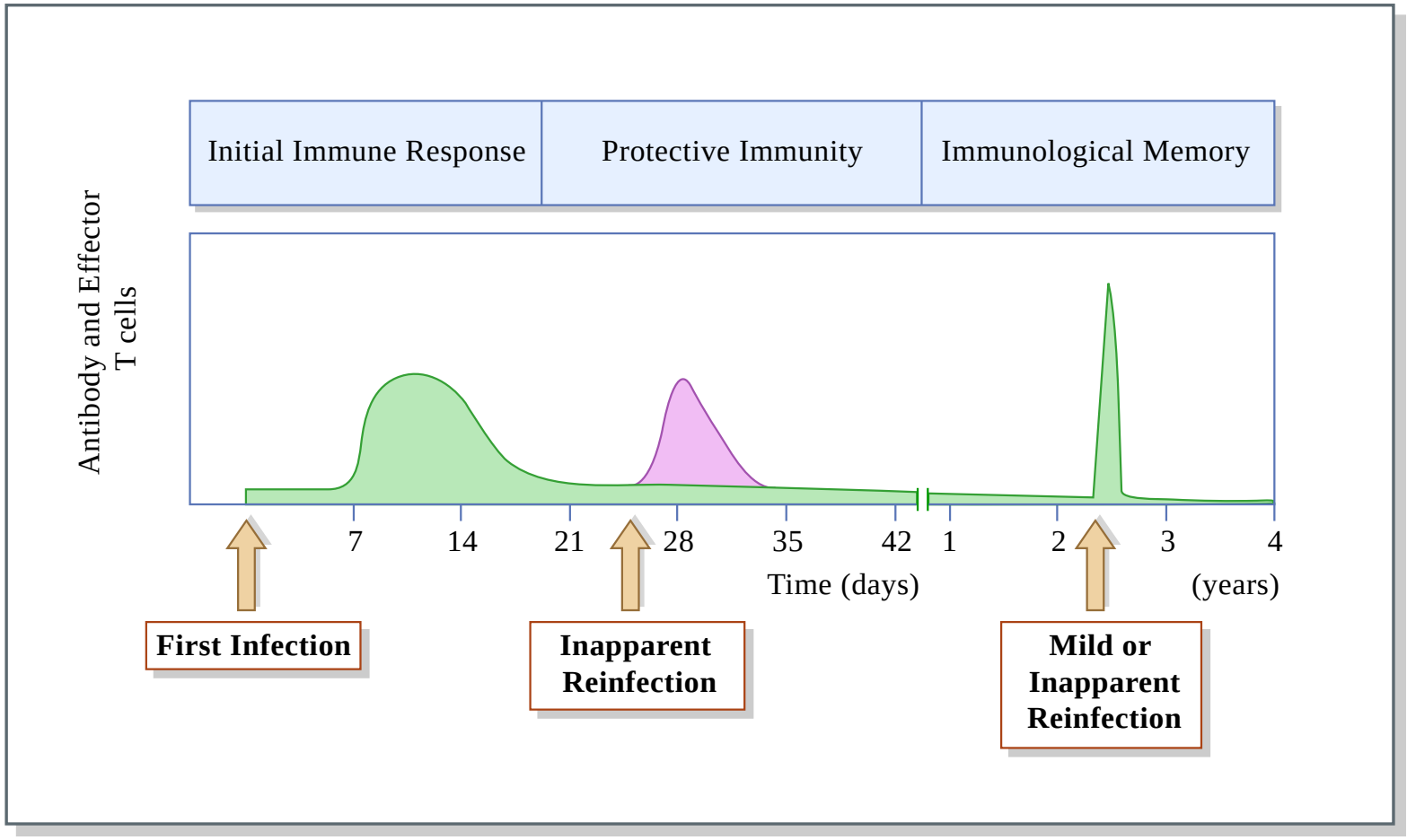

Figure by MIT OCW.

- Effector T-cells and antibody levels decline after primary infection
- Second exposure activates memory T-cells and B-cells to expand (faster clearance than primary), no need to activate DCs and naïve lymphocytes

GOAL of IMMUNIZATIONS

Induce pathogen-specific humoral and cell-mediated immune responses and immunologic memory to prevent or limit effects of re-infection

The Ideal Vaccine

- ✓ Effective at birth
- ✓ Single dose
- ✓ Oral or non-invasive administration
- ✓ Safe and efficacious when administered with other vaccines
- ✓ Temperature stability
- ✓ Low cost
- ✓ Global availability and accepted

- Cells required from immunization
  - Memory cytotoxic T-cells
  - Memory helper T-cells
  - Memory B-cells
- Down fall: not eliciting robust response and lack of appropriate cellular or humoral response
  - Multiple immunizations, sometimes with different administrations
  - Booster shots

Adjuvants

Substances that enhance immune response to an antigen typically by providing stimulation (second signal) to DCs

- Current adjuvants
  - Aluminum (widely used)
  - Ribi (monophophoryl lipid A w/mycobacterial cell walls)
  - MF59 (oil-surfactant emulsion)
  - polymers
- New ideas
  - Cytokines
  - Delivery systems (liposomes, microcapsules)
  - Bacterial toxins (*E. coli* heat-laible toxin, cholera toxin)

Types of Immunizing Agents

- Attenuated/related organism
  - Infection with weaker or related organism or lower inoculum
- Viral/bacterial vector
  - Carriers to deliver antigens from pathogens that are unsafe as attenuated
- Subunit vaccines
  - Purified components or known peptide motifs of antigen, toxoid vaccines
- Conjugate vaccines
  - Protein carrier/conjugate to present polysaccharide as antigen
- Nucleic Acid (DNA) vaccines
  - Bacterial plasmids encoding antigens
- Edible vaccines
  - Transgenic plants, produce antigenic proteins
- Mucosal vaccines
  - Nasal or oral delivery of antigens

Measuring Immune Responses

- Humoral Response
  - ELISPOT
    - Number of antibody secreting cells (B-cells) during culture with antigen
    - Measure different classes and isotypes (IgG)
  - ELISA
    - Amount of antibody in serum or mucosal secretions
    - Measure different classes and isotypes (IgG)
- Cell-mediated Response
  - Lymphocyte proliferation *ex-vivo*
    - ^{3}H-thymidine incorporation of immune cells upon culture with antigen
  - ELISPOT
    - Cytokines secreted by T-cells (CD8+, CD4+, total) or 'immune cells'

Toxins & Monoclonal Ig

- Enterotoxins
- Exotoxins
- Cytolytic Toxins
- Superantigens

Production of Monoclonal Antibodies

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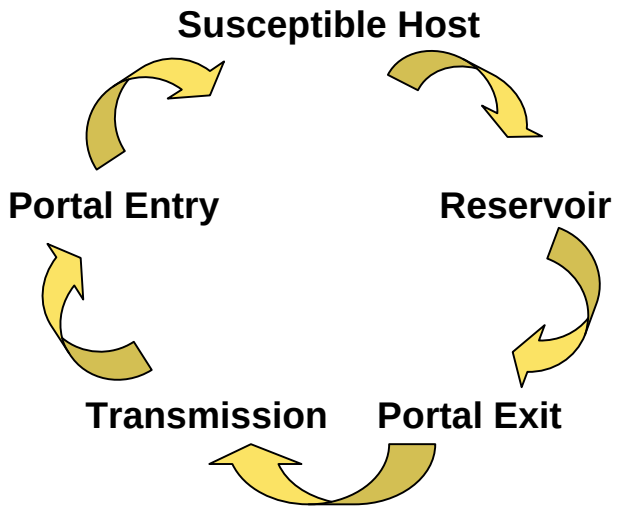
See Figure 22-12 in Madigan, Michael, and John Martinko. *Brock Biology of Microorganism.* 11th Ed. Upper Saddle River, NJ: Pearson Prentice Hall, 2006. ISBN: 0131443291.

Epidemiology



- Acute
- Chronic
- Carrier
- Reservoir
- Morbidity
- Mortality

- Direct Host-host transmission occurs when infected host transmits to susceptible host

- Indirect Host-host transmission occurs when pathogens are spread from infected host to susceptible host via a vector (arthropods or vertebrates), fomites (inanimate objects) or vehicle (food or water)

Classification of Disease Incidence

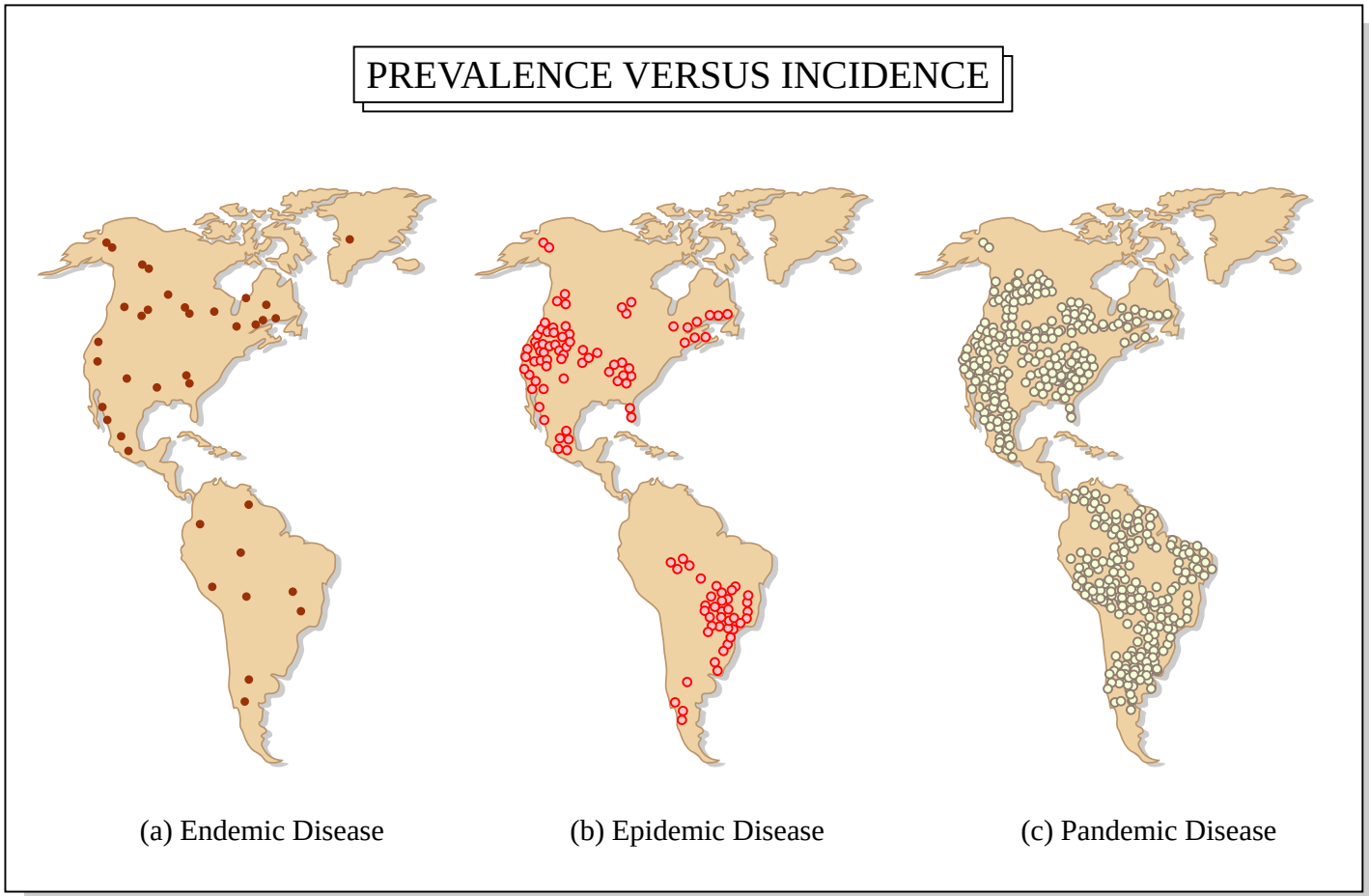


Figure by MIT OCW.

Outbreak: number of cases are observed in short period of time in area previously only having sporadic cases

- Common source epidemic
  - Infection of a large number of people from contaminated common source
- Host-to-host epidemic
  - May be started by one individual
  - Numbers of reported cases gradually, and continually rise

Eradication & Elimination

Control--*reduction of disease incidence, prevalence, morbidity or mortality to a* ***locally*** *acceptable level as a result of deliberate efforts; continued intervention measures are required to maintain the reduction.* i.e.. diarrheal diseases

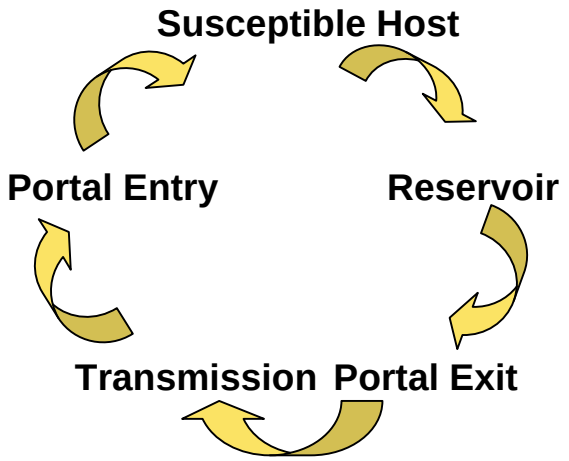
Elimination of disease--*reduction to zero of the incidence of a specified* ***disease*** *in a defined geographical area as a result of deliberate efforts; continued intervention measures are required* i.e.. neonatal tetanus

Elimination of infection--*reduction to zero of the incidence of* ***infection*** *caused by a specific agent in a defined geographical area as a result of deliberate efforts; continued measures to prevent reestablishment of transmission are required.* i.e.. Measles, poliomyelitis

Eradication--*permanent reduction to zero of the* ***worldwide*** *incidence of infection caused by a specific agent as a result of deliberate efforts; intervention measures are no longer needed.* i.e.. smallpox

Extinction--specific infectious agent no longer exists in nature or in the **laboratory**. i.e.. nothing

Control Measures



- Against reservoir
  - eliminate infection in domestic animals
  - No control over wild animals
  - Prevent contact or eliminate insect vectors
- Against transmission
  - Prevent contamination of vehicle (water, milk)
- Immunization
- Quarantine
  - Restrict movement and contact of infected individuals with general population
  - Time limit is longest period of communicability of the disease

  International required quarantine for smallpox, cholera, plague, yellow fever, typhoid fever and relapsing fever
- Surveillance
  - Observation, recognition, and reporting of diseases as they occur
  - Typically pathogens with potential for epidemic

Herd Immunity

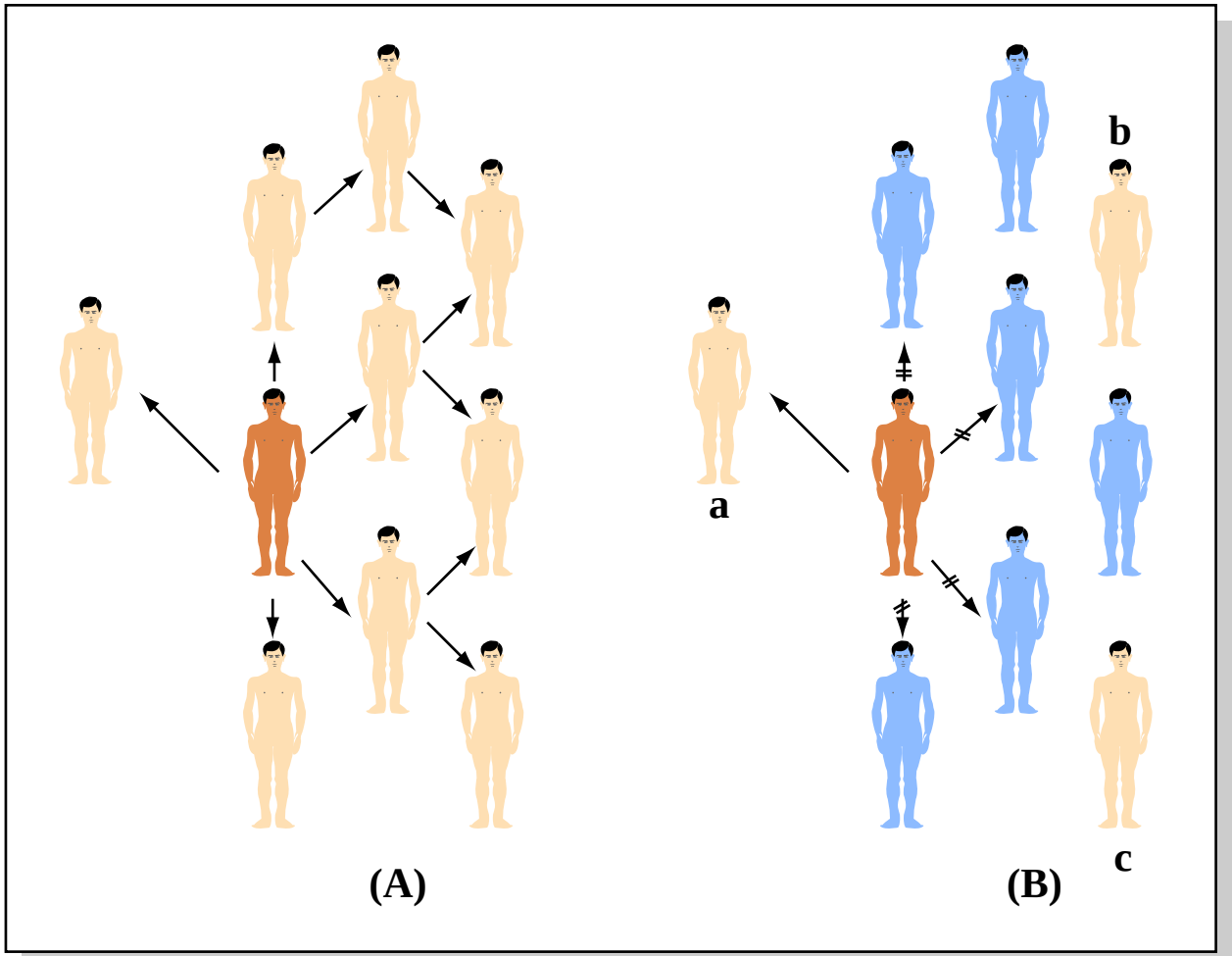


Figure by MIT OCW.

Resistance of a group to infection due to immunity of a high enough proportion of the members of the group.

Typically >70% of population must have protective immunity

Highly infectious agents require up to 95% protection

Protective immunity, not solely immunization

Emergence Factors

1. Demographics
2. Technology and industry
3. Economic development and land use
4. International travel and commerce
5. Microbial adaptation and change
6. Breakdown of public health measures
7. Abnormal natural occurrences

Questions?

ELISA and ELISPOT

BD ELISPOT Assay Procedure

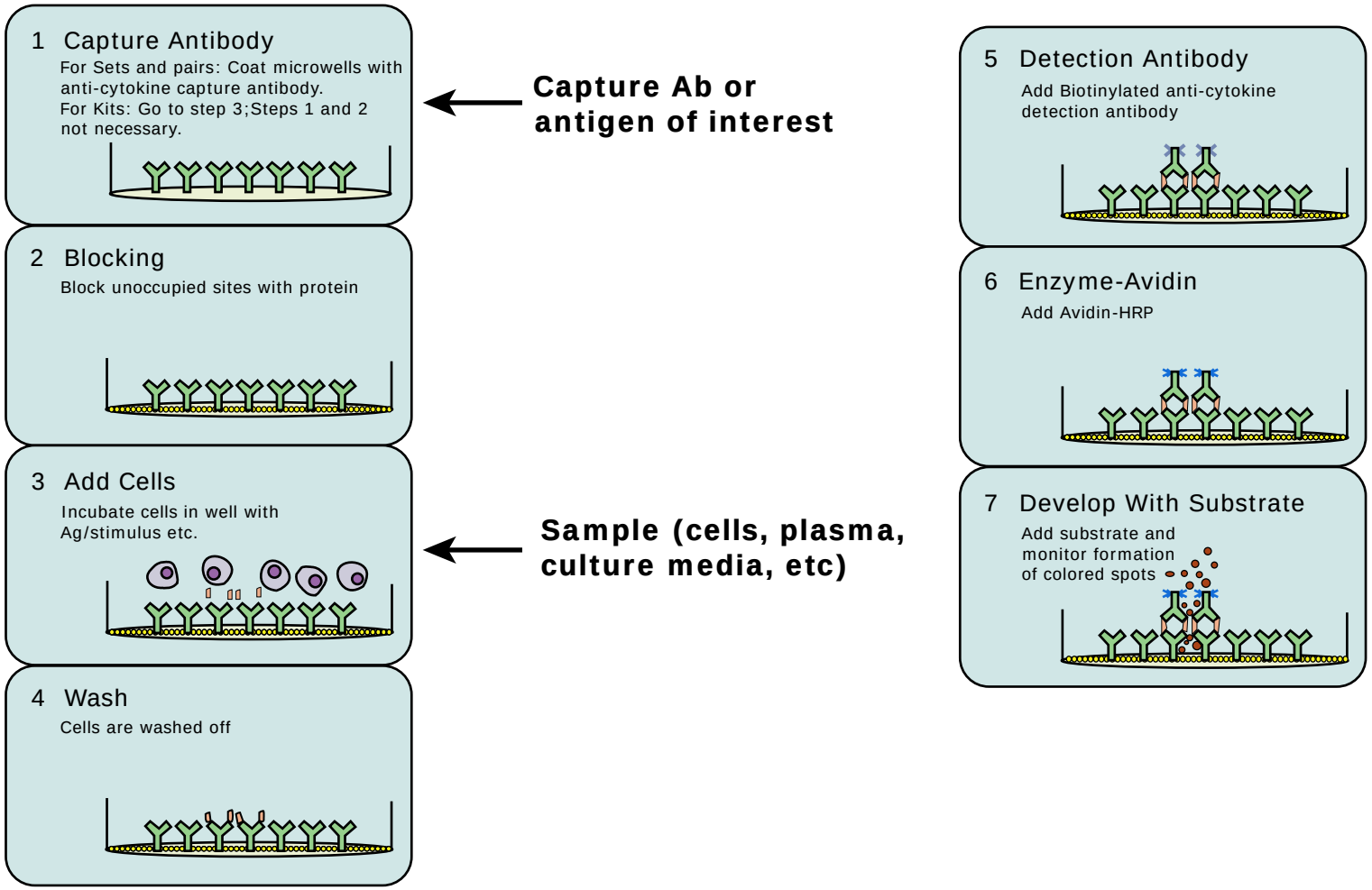
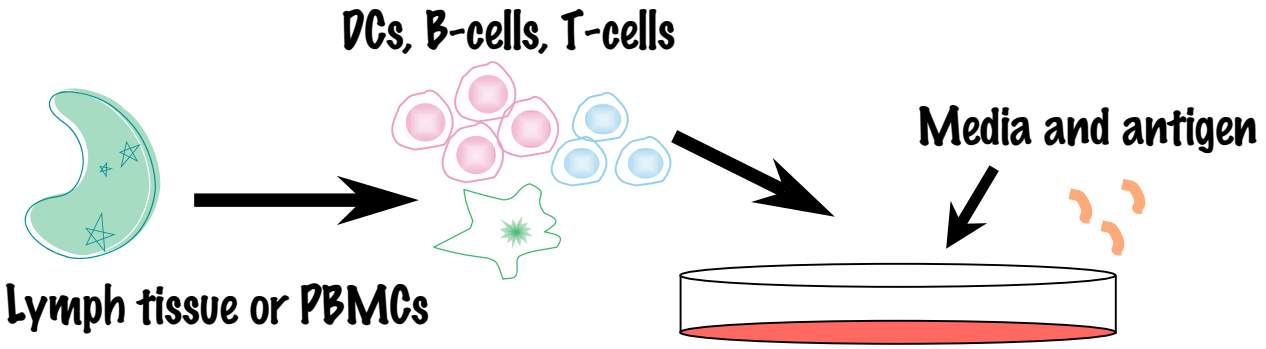


Figure by MIT OCW.

Lymphocyte Proliferation Assay

Measures cell-mediated immune response to antigen of interest



- ✓Pulse culture with ^{3}H Thymidine
- ✓Harvest cells at various time points
- ✓Measure incorportion in scintillation counter