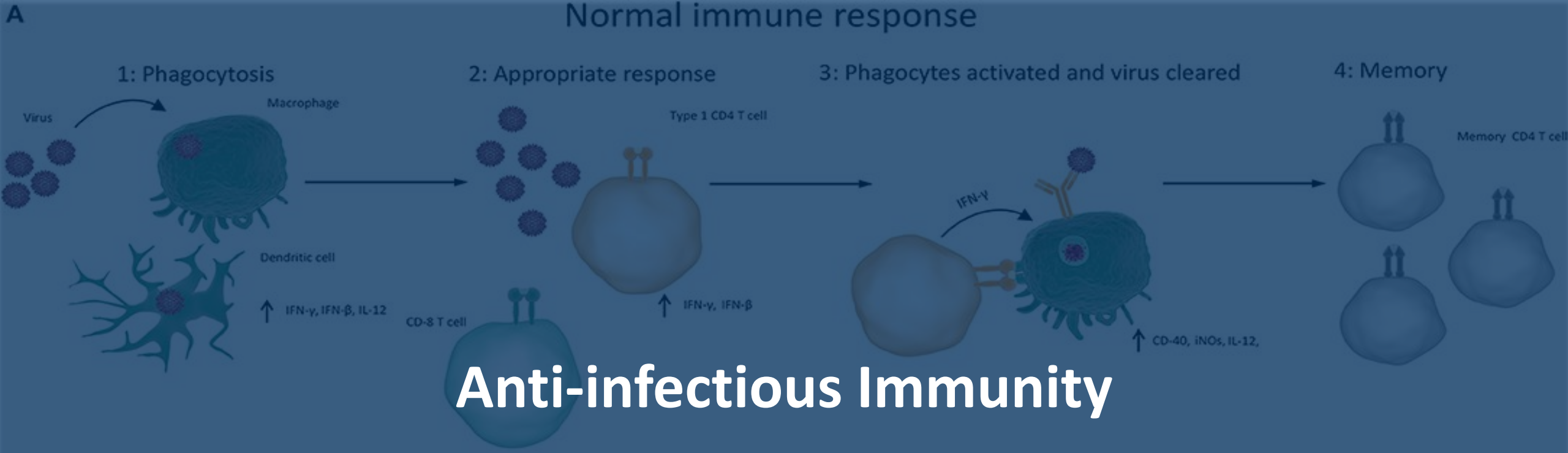
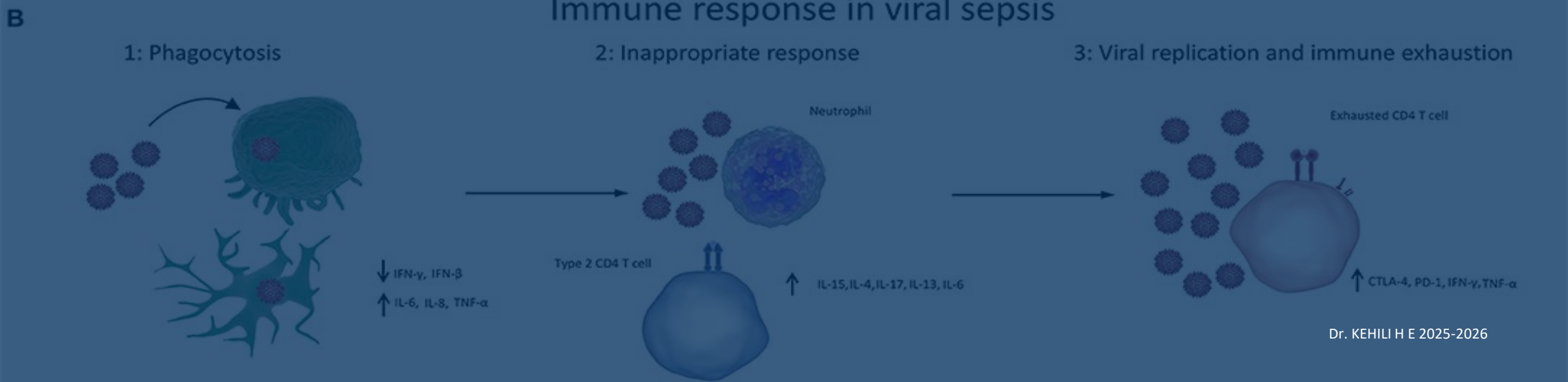
Anti-infectious Immunity

Mechanisms of Host Defense Against Bacterial and Viral Pathogens





Bacterial Pathogens: Overview

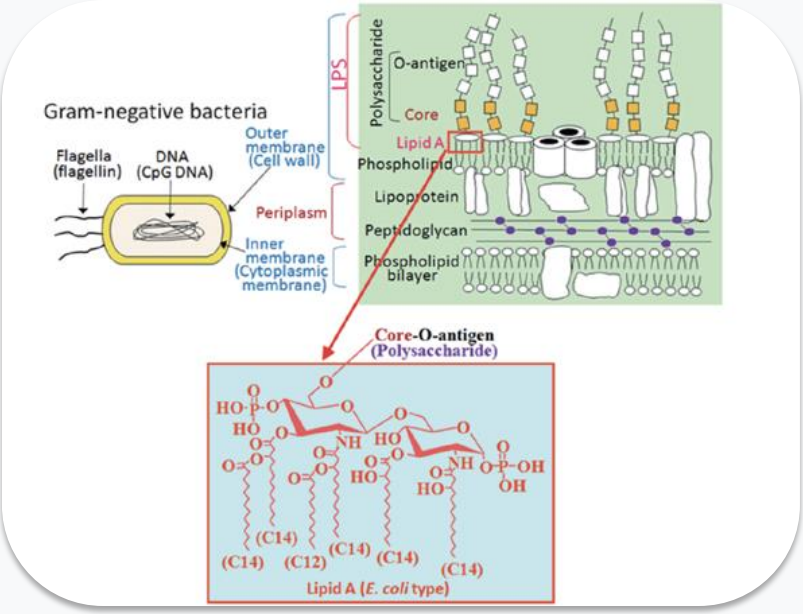
What Are Bacteria?

Microscopic **single-celled organisms**

Prokaryotic cells lacking membrane-bound organelles

Found in virtually every environment on Earth

10 times more bacterial cells than human cells in our body



Classification Methods

Shape: Cocci (spherical), Bacilli (rod-shaped), Spirochetes (helical)

Oxygen requirement: Aerobes (need oxygen), Anaerobes (cannot survive with oxygen), Facultative (can live with or without oxygen)

Gram staining: Gram-positive (thick peptidoglycan layer), Gram-negative (thin peptidoglycan layer with outer membrane)

Relevance to Human Health

Most bacteria are **harmless or beneficial** (microbiome)

Pathogenic bacteria cause infections by producing toxins or damaging tissues

Antibiotic resistance is a growing global health concern

Types of Bacteria Relevant to Human Infections

Streptococcus

Causes **strep throat**, pneumonia, meningitis, necrotizing fasciitis

Staphylococcus

Causes **skin infections**, pneumonia, sepsis, Methicillin-Resistant *Staphylococcus aureus* (MRSA)

Escherichia coli

Causes Urinary Tract Infections (**UTIs**), food poisoning, traveler's diarrhea

Salmonella

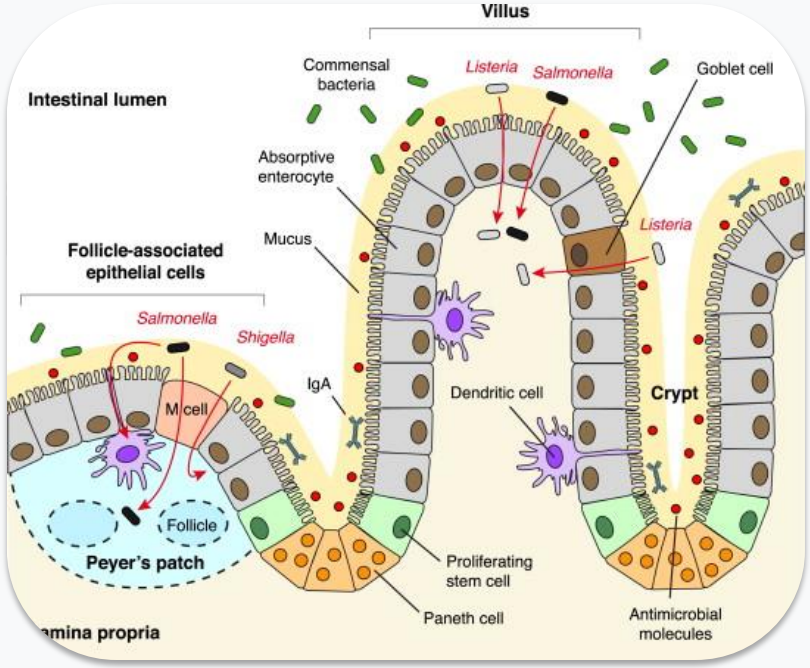
Causes **food poisoning**, typhoid fever, gastroenteritis

Chlamydia trachomatis

Causes Sexually Transmitted Infections (**STIs**), eye infections, pneumonia in newborns

Bordetella pertussis

Causes **whooping cough**, severe respiratory infections



Modes of Bacterial Infection and Colonization

Adhesion to Host Cells

Adhesins bind to host cell receptors

Pili, fimbriae, and surface proteins facilitate attachment

Specific interactions determine tissue tropism

Overcoming Host Barriers

Production of **enzymes** to degrade mucus

Resistance to antimicrobial peptides

Flagella-based motility through mucus layers

→ Crossing Host Barriers

Transcellular migration through epithelial cells

Paracellular migration between cells

Exploitation of M cells in Peyer's patches

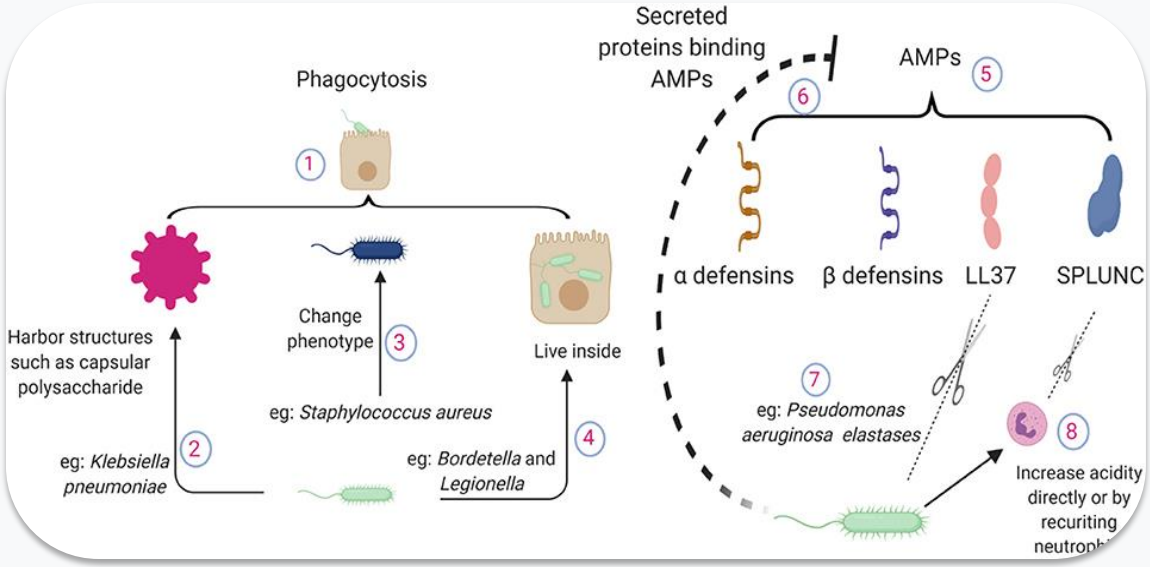
Manipulation of tight junctions

Establishing Infection

Biofilm formation for persistent colonization

Triggering inflammation to outcompete commensals

Intracellular survival within host cells



Bacterial Evasion Mechanisms

Cell Wall Modification

LPS acylation (E. coli, S. enterica)
D-alanylation of teichoic acids (S. aureus)
Changes surface charge to repel antimicrobial peptides

Capsule Production

Physical barrier against immune factors
N. meningitidis capsule synthesis regulation
Protection against complement and antimicrobial peptides

Antigenic Variation

Neisseria gonorrhoeae pilin variation
Borrelia burgdorferi VlsE antigenic variation
Avoids antibody recognition

Molecular Mimicry

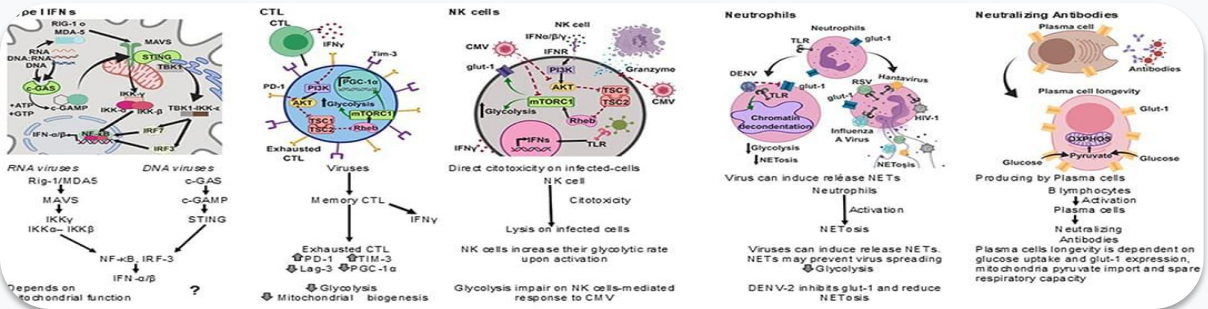
Polysaccharide similarity to host molecules
E. coli and **N. meningitidis** capsule mimicry
Avoids detection by immune system

Effector Proteins

Staphylococcal protein A (S. aureus)
Binds antibodies and B-cell receptors
Inhibits adaptive immune response

Intracellular Survival

Mycobacterium tuberculosis in alveolar macrophages
Protein Tyrosine Phosphatase A (**PtpA)** inhibits phagosomal acidification
Creates comfortable niche for persistence



Viral Pathogens: Overview

What Are Viruses?

Submicroscopic infectious agents requiring host cells for replication

Composed of genetic material (DNA or RNA) enclosed in a protein coat (capsid)

100-1,000 times smaller than human cells

Parasitic nature - need host to reproduce

Viral Classification

Genetic material: DNA viruses (e.g., Herpesviridae, Adenoviridae) vs. RNA viruses (e.g., Coronaviridae, Retroviridae)

Structure: Enveloped viruses (e.g., HIV, SARS-CoV-2) vs. Non-enveloped ("naked") viruses (e.g., Poliovirus)

Morphology: Helical, Icosahedral, Complex, or Poxvirus shapes

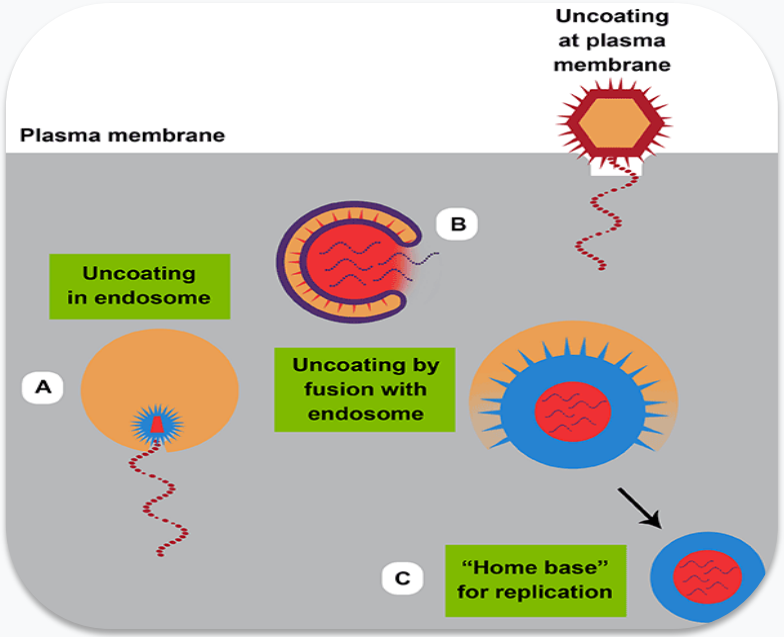
Relevance to Human Health

Viruses cause **diverse diseases** from mild colds to severe pandemics

High mutation rates enable rapid evolution and immune evasion

Some viruses can integrate into host genome (retroviruses)

Viral infections can trigger immune-mediated pathology



Types of Viruses Relevant to Human Infections

Influenza Viruses

Causes **seasonal flu**, avian flu, H1N1

Human Herpesviruses

Causes **oral/genital herpes**, chickenpox, shingles

Coronaviruses

Causes **COVID-19**, common colds, SARS, MERS

Human Papillomaviruses

Causes **warts**, cervical and other cancers

Enteroviruses

Causes **polio**, hand-foot-mouth disease

Flaviviruses

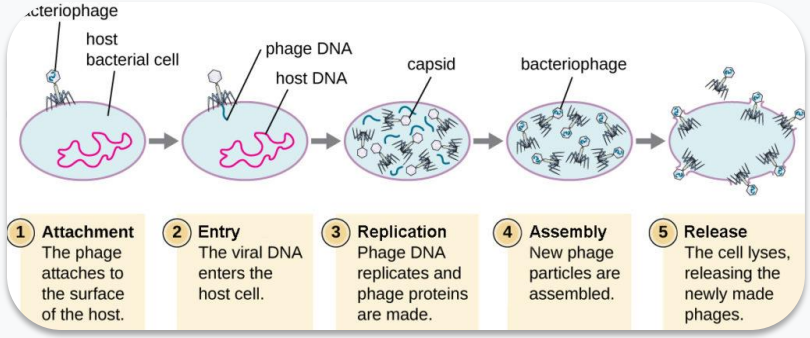
Causes **Zika**, Dengue, West Nile, Yellow fever

Hepatitis Viruses

Causes **liver inflammation**, cirrhosis, cancer

Retroviruses

Causes **AIDS** (HIV), integrates into host DNA



Modes of Viral Infection and Replication

1 **Attachment**

Viral **surface proteins** bind to specific receptors on host cell membrane

2 **Entry**

Fusion with cell membrane or **endocytosis** to deliver genetic material

3 **Uncoating**

Removal of capsid to **release viral genome** into host cell

4 **Replication**

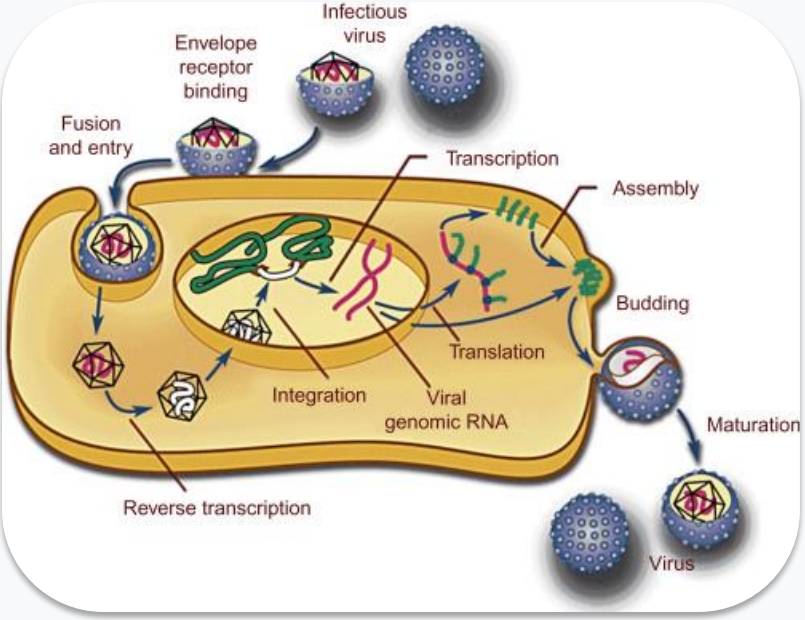
Viral genome replication and synthesis of viral proteins using host machinery

5 **Assembly**

New viral particles **assembled** from synthesized components

6 **Release**

Lysis of host cell or **budding** through cell membrane



Viral Evasion Strategies

Antigenic Variation

Influenza viruses undergo antigenic drift and shift
HIV high mutation rate in envelope proteins
Avoids recognition by neutralizing antibodies

Latency

Herpesviruses establish lifelong latent infections
HIV integrates into host genome as provirus
Reactivation leads to recurrent disease

MHC Inhibition

CMV US6 protein blocks TAP transporter
HIV Nef downregulates MHC-I expression
Prevents antigen presentation to T cells

Interferon Interference

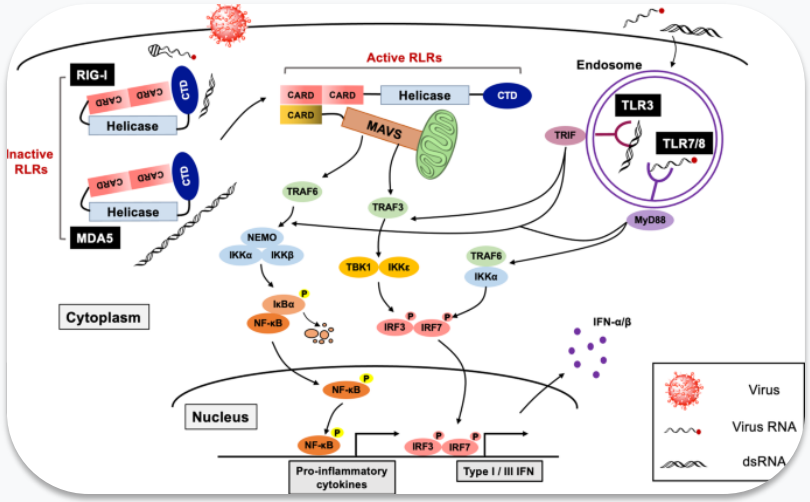
SARS-CoV-2 proteins inhibit IFN signaling
Ebola VP35 blocks RIG-I signaling pathway
Suppresses antiviral state in neighboring cells

Molecular Mimicry

Poxviruses encode cytokine receptors
CMV produces IL-10 homolog
Manipulates host immune signaling

APOBEC3 Counteraction

HIV Vif protein targets Apolipoprotein B mRNA Editing Catalytic Polypeptide-like 3 (APOBEC3) for degradation
Prevents hypermutation of viral genome
Maintains viral genetic integrity



Innate Anti-infectious Immunity: Overview

Key Characteristics

Nonspecific - recognizes common pathogen patterns

Rapid response - activated immediately upon infection

No memory - responds similarly to repeated exposures

Evolutionarily ancient - found in all multicellular organisms

Primary Defense Components

Physical barriers - skin, mucous membranes, cilia

Chemical barriers - antimicrobial peptides, enzymes, pH

Cellular components - phagocytes, NK cells, dendritic cells

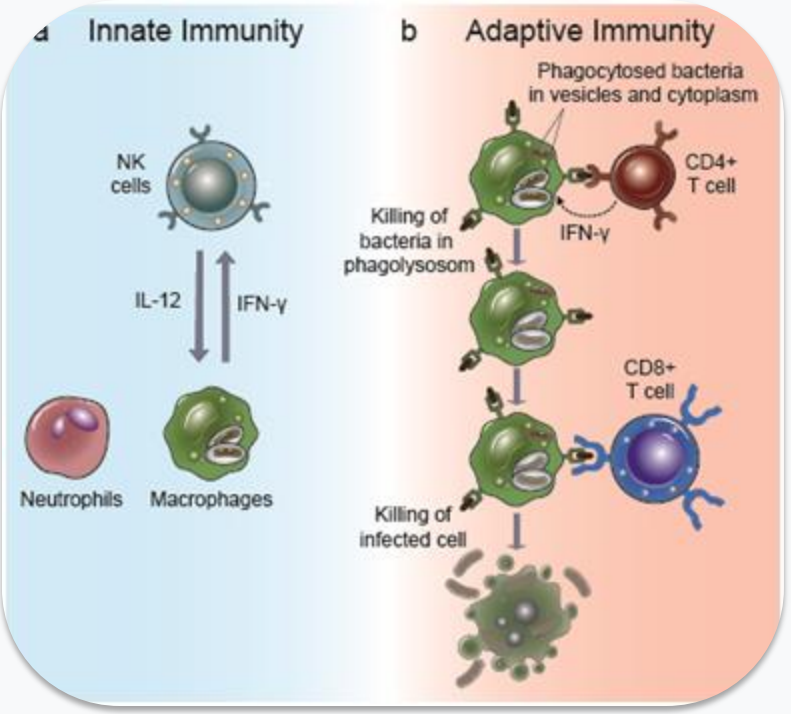
Soluble factors - complement, cytokines, interferons

Bridge to Adaptive Immunity

Dendritic cells present antigens to T cells

Cytokine production shapes adaptive response

Inflammation recruits immune cells to infection sites



Physical Barriers and Defense Mechanisms

Skin

Mechanical barrier against pathogens
Acidic pH inhibits bacterial growth
Antimicrobial peptides (defensins)
Normal microbiota prevents colonization

Mucous Membranes

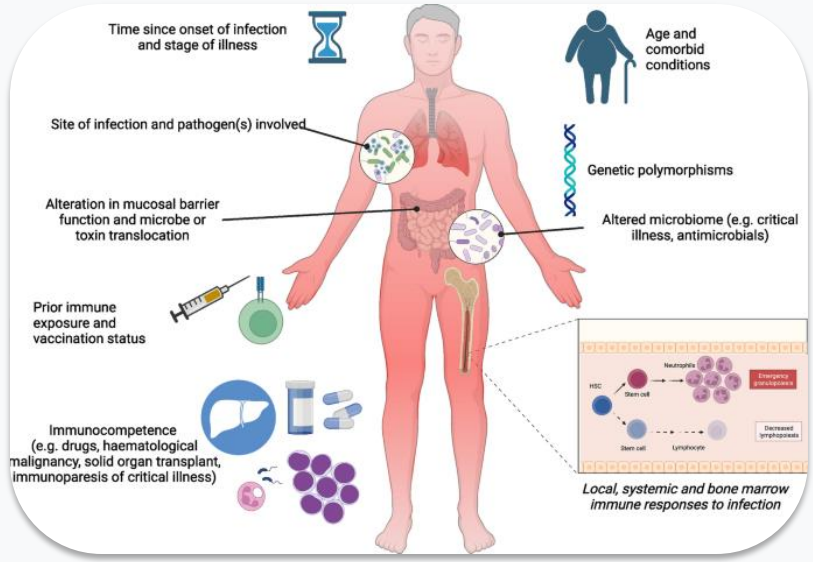
Traps pathogens in sticky secretions
Ciliary movement clears trapped microbes
Contains IgA antibodies
Mucus turnover prevents pathogen attachment

Chemical Barriers

Gastric acid kills ingested microbes
Lysozyme in tears and saliva
Sebum with antimicrobial fatty acids
Low pH in vaginal secretions

Antimicrobial Peptides

Defensins disrupt bacterial membranes
Cathelicidins have broad-spectrum activity
Histatins in oral cavity
Psoriasin against E. coli on skin



Cellular Components of Innate Immunity

Phagocytes

Macrophages: Engulf pathogens, present antigens
Neutrophils: First responders, release toxic granules
Monocytes: Circulating precursors to macrophages

Natural Killer Cells

Target infected cells with reduced MHC-I
Release perforin and granzymes to kill targets
Critical defense against viruses and tumor cells

Dendritic Cells

Bridge innate and adaptive immunity
Capture antigens and present to T cells
Migrate to lymph nodes to initiate adaptive response

Mast Cells

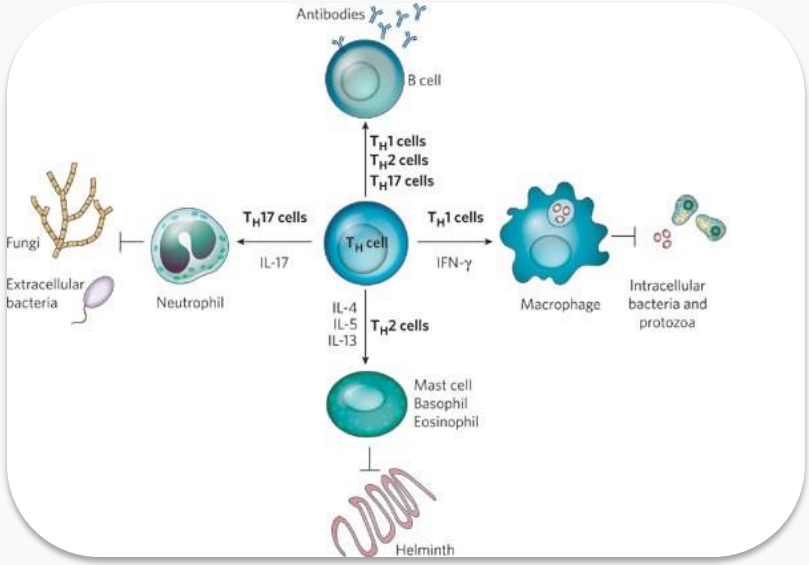
Release histamine during inflammation
Recruit immune cells to infection sites
Key role in allergic responses and defense against parasites

Eosinophils

Target multicellular parasites
Release toxic proteins and free radicals
Also involved in allergic reactions

Basophils

Release histamine like mast cells
Key players in allergic responses
Also attack multicellular parasites



Complement System and Soluble Factors

Complement Activation Pathways

→Classical

Triggered by **antibody-antigen complexes** binding to C1q

→Lectin

Activated by **mannose-binding lectin** recognizing microbial sugars

→Alternative

Directly activated by **microbial surfaces** without antibodies

Key Functions

Opsonization

C3b coats pathogens, **enhancing phagocytosis** by macrophages and neutrophils

Chemotaxis

C3a and C5a **recruit immune cells** to infection sites

Cell Lysis

Membrane Attack Complex (MAC) **creates pores** in bacterial membranes

Agglutination

Antibodies and complement **cluster pathogens** for easier clearance

Other Soluble Factors

Interferons

Type I (α, β): Antiviral defense
Type II (γ): Activates macrophages
Type III (λ): Mucosal immunity

Cytokines

IL-1, IL-6, TNF-α: Pro-inflammatory
IL-10, TGF-β: Anti-inflammatory
Chemokines: Cell recruitment

Adaptive Anti-infectious Immunity: Overview

Key Characteristics

Specificity - recognizes unique molecular patterns

Memory - faster, stronger response to repeat infections

Self-tolerance - distinguishes self from non-self

Slower onset - requires time for lymphocyte activation

Cellular Mediators

B lymphocytes - produce antibodies (humoral immunity)

T lymphocytes - cellular immunity (helper and cytotoxic)

Antigen-presenting cells - activate T cells

Memory cells - provide long-term protection

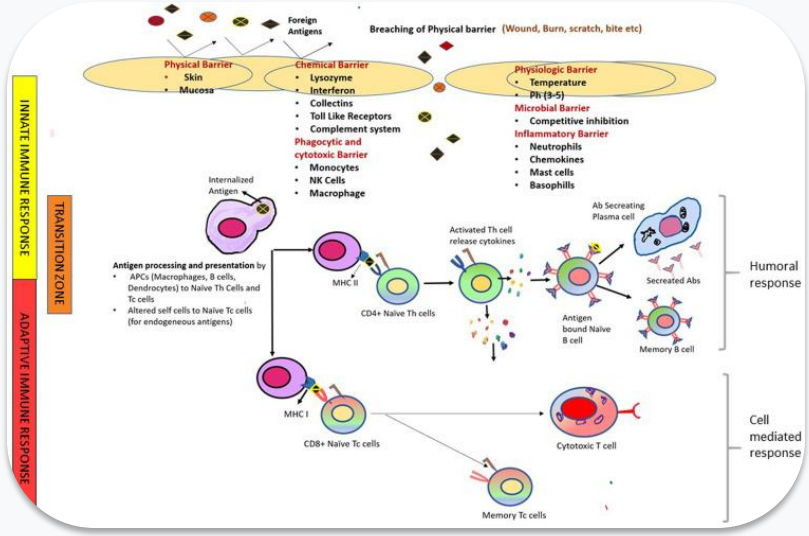
Interaction with Innate Immunity

Innate immunity provides initial defense and signals

Dendritic cells bridge innate and adaptive responses

Cytokines from innate cells shape adaptive response

Antibodies enhance innate effector functions



Antibody Responses to Bacterial and Viral Infections

B Cell Activation

Antigen recognition by B cell receptors
Helper T cell support for full activation
Differentiation into plasma cells

Antibody Classes

IgG: Most abundant, systemic immunity
IgM: First responder, pentameric structure
IgA: Mucosal protection
IgE: Parasite defense, allergies

Neutralization

Blocks viral entry into host cells
Inactivates bacterial toxins
Prevents adhesion to host surfaces

Opsonization

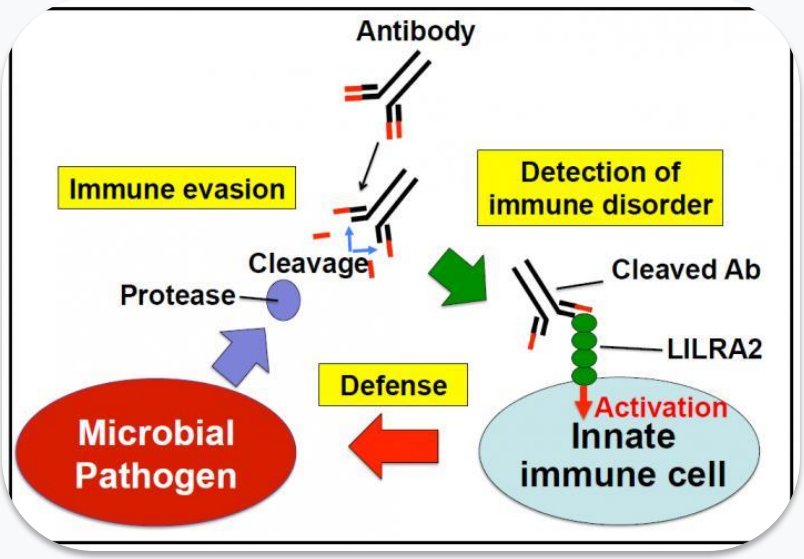
Coats pathogens for phagocytosis
Fc receptors on phagocytes bind antibodies
Enhances clearance of bacteria and viruses

Agglutination

Cross-links pathogens into clumps
Prevents spread through tissues
Facilitates clearance by phagocytes

Complement Activation

Classical pathway activation
Formation of MAC for bacterial lysis
Enhances inflammation and recruitment



T Cell Responses to Bacterial and Viral Infections

T Cell Activation

Antigen presentation by MHC molecules
Co-stimulatory signals from APCs
Cytokine environment determines differentiation

T Cell Subsets

Helper T cells (CD4+): Coordinate immunity
Cytotoxic T cells (CD8+): Kill infected cells
Regulatory T cells: Suppress immune responses

Helper T Cell Functions

Th1 cells: Activate macrophages
Th2 cells: Support B cell antibody production
Th17 cells: Recruit neutrophils

Cytotoxic T Cell Functions

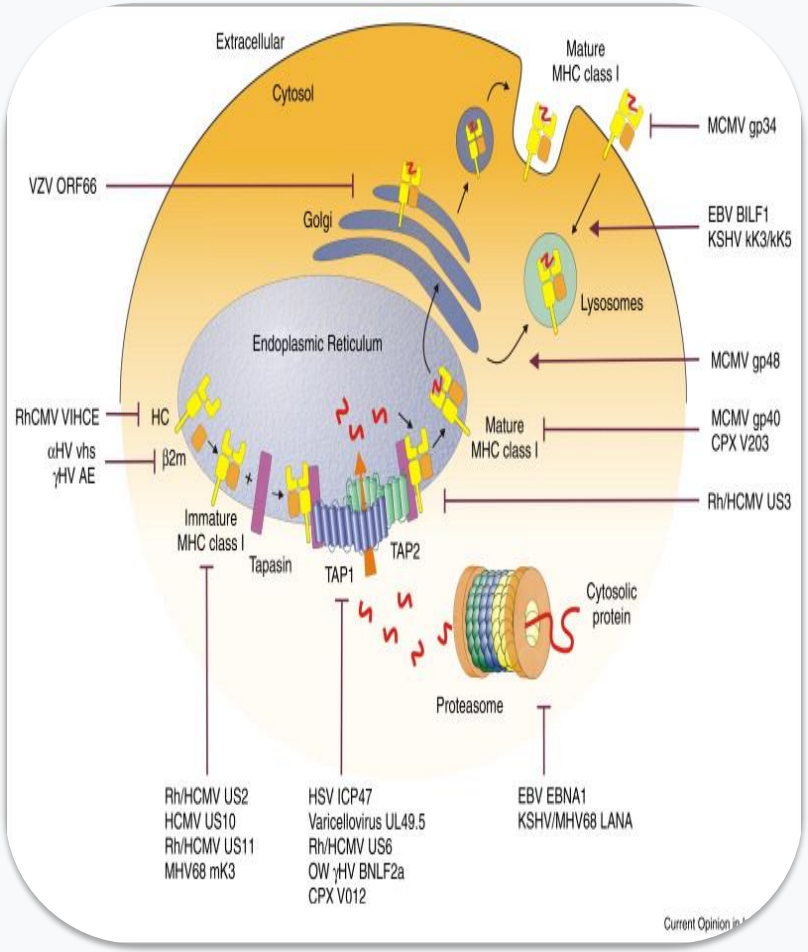
Perforin creates pores in target cells
Granzymes trigger apoptosis
FasL-Fas interaction induces cell death

Response to Viral Infections

CD8+ T cells recognize viral peptides on MHC-I
Eliminate infected cells before viral replication
CD4+ T cells support antiviral antibody production

Response to Bacterial Infections

Th1 cells activate macrophages for intracellular bacteria
Th17 cells recruit neutrophils for extracellular bacteria
Th2 cells support antibody production against toxins



Immune Memory and Long-Term Protection

Memory B Cells

Long-lived antigen-experienced B cells
Rapid differentiation into plasma cells
Higher affinity antibodies upon re-exposure

Memory T Cells

Central memory cells in lymphoid tissues
Effector memory cells in peripheral tissues
Resident memory cells in barrier tissues

Duration of Memory

Measles: Lifelong immunity
Influenza: Seasonal, strain-specific
COVID-19: Emerging data suggests months to years

Vaccination

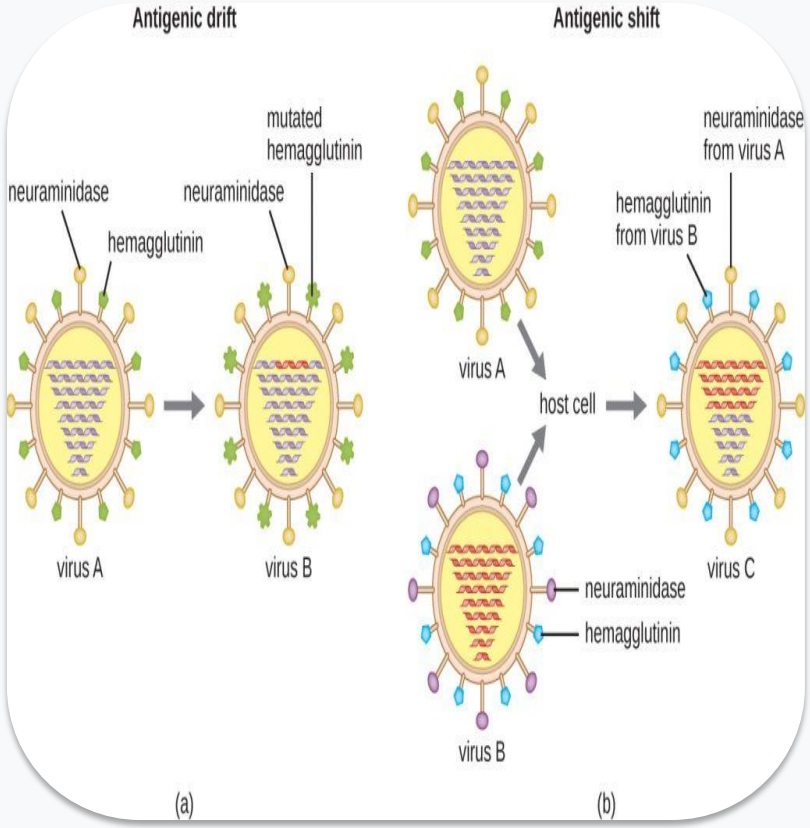
Mimics natural infection without disease
Generates memory cells for future protection
Booster doses enhance and prolong immunity

Viral Immunity Examples

Varicella-zoster: Lifelong immunity
Hepatitis B: 20+ years with vaccination
SARS-CoV-2: Hybrid immunity (infection + vaccine)

Bacterial Immunity Examples

Tetanus: Requires boosters every 10 years
Diphtheria: Similar to tetanus
Natural infection often provides limited protection



Clinical Implications and Therapeutic Approaches

Immunodeficiency Disorders

Primary immunodeficiencies: Genetic defects
Secondary immunodeficiencies: HIV, chemotherapy
Complement deficiencies: Increased infection risk

Vaccine Development

Live attenuated: Measles, mumps, rubella
Inactivated: Polio, hepatitis A
Subunit: Hepatitis B, HPV
mRNA: COVID-19

Immunotherapies

Monoclonal antibodies: RSV, COVID-19
Immune globulins: Passive immunity
Cytokine therapy: IFN-α for hepatitis C

Emerging Approaches

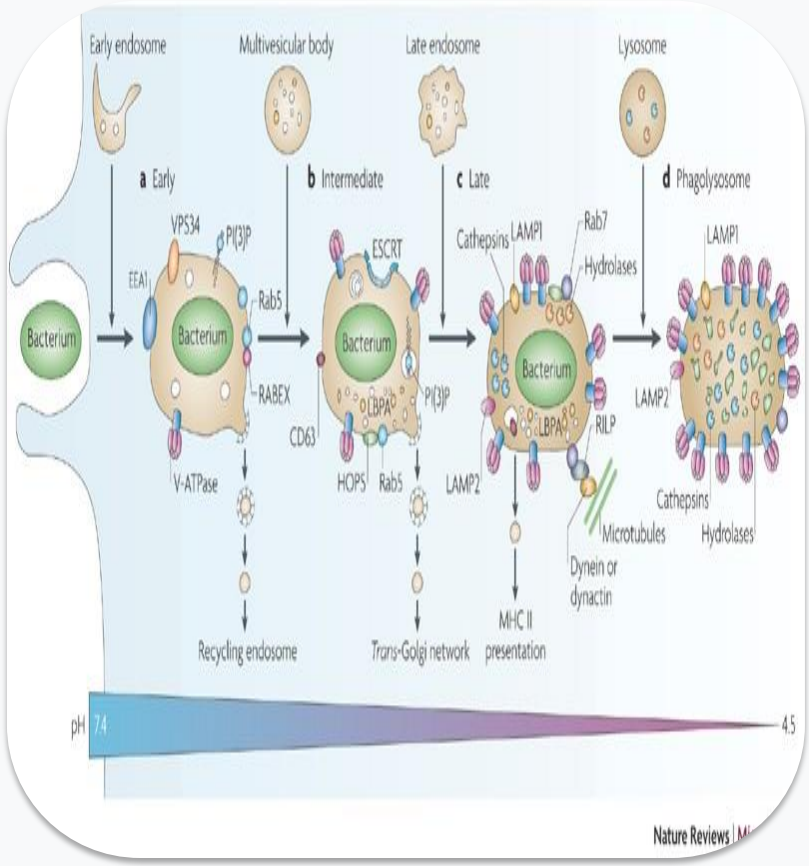
Broad-spectrum antivirals: Targeting host factors
Bacteriophage therapy: Antibiotic alternative
CRISPR-based antimicrobials: Precision targeting

Viral Infection Therapies

Entry inhibitors: HIV CCR5 antagonists
Polymerase inhibitors: Acyclovir, remdesivir
Protease inhibitors: HIV, HCV, SARS-CoV-2

Bacterial Infection Therapies

Antibiotics: Targeting bacterial processes
Anti-virulence agents: Disarm pathogens
Immune modulators: Enhance host defenses



Key Takeaways and Future Directions

Key Takeaways

Bacterial pathogens use cell wall modification, capsules, and effector proteins to evade immunity

Viral pathogens employ antigenic variation, latency, and MHC inhibition strategies

Innate immunity provides rapid, nonspecific defense through barriers, phagocytes, and complement

Adaptive immunity offers specific, long-lasting protection via antibodies and T cells

Clinical Applications

Vaccines harness immune memory for long-term protection

Immunotherapies enhance or supplement natural immune responses

Diagnostic tools detect specific immune responses to pathogens

Targeted treatments based on pathogen evasion mechanisms

Future Directions

Broad-spectrum antivirals targeting host factors

Personalized vaccines based on individual immune profiles

Microbiome modulation to enhance resistance

Novel delivery systems for immunotherapies

CRISPR-based antimicrobials for precision targeting