

Immune Evasion Strategies of Pathogens

Overview of how pathogens evade host immune defenses, with examples from bacteria, viruses, fungi, and parasites

Introduction: The Need for Immune Evasion

- Pathogens evolve strategies to survive immune attack.
- Evasion allows persistence, dissemination, and transmission.
- Targets include innate and adaptive immune mechanisms.

1. Inhibition of Toll-Like Receptor (TLR) Signaling

- TLRs detect microbial PAMPs and trigger inflammation.
- Some pathogens inhibit TLR signaling to suppress cytokine release.
- Example: Vaccinia virus protein A46 binds adaptor proteins (MyD88, TRIF), blocking downstream NF- κ B activation.

2. Complement Inhibition

- Complement causes opsonization, inflammation, and pathogen lysis.
- Pathogens express complement inhibitory proteins or recruit host regulators.
- Examples:
 - *Neisseria meningitidis*: binds Factor H to prevent C3b deposition.
 - *Staphylococcus aureus*: secretes SCIN to block C3 convertase formation.

3. Antigenic Variation

- Continuous change in surface antigens prevents immune recognition.
- Examples:
 - Influenza virus: antigenic drift/shift in HA and NA.
 - Trypanosoma brucei: switches variant surface glycoproteins (VSGs).
 - Neisseria gonorrhoeae: variation in pilin genes.
- Effect: Escapes antibody and T-cell recognition.

4. Antibody Degradation or Binding Interference

- Pathogens degrade or neutralize antibodies to block opsonization.
- Examples:
 - Streptococcus pyogenes: secretes IdeS protease to cleave IgG.
 - Staphylococcus aureus: Protein A binds Fc portion of IgG, preventing phagocytosis.

5. Hiding Inside Host Cells

- Intracellular localization shields pathogens from antibodies and complement.
- Examples:
 - Mycobacterium tuberculosis: blocks phagosome-lysosome fusion.
 - Listeria monocytogenes: escapes into cytoplasm using listeriolysin O.
 - Salmonella: remodels vacuole to prevent degradation.

6. Evasion of Phagocytosis

- Capsules or surface molecules prevent engulfment by phagocytes.
- Examples:
 - *Streptococcus pneumoniae*: capsule inhibits complement binding.
 - *Yersinia pestis*: type III secretion system injects YopH to disrupt actin cytoskeleton.

7. Persistence and Latency

- Some pathogens enter dormant or low- replication states.
- Examples:
 - Herpes simplex virus: latent infection in neurons.
 - Mycobacterium tuberculosis: persists within granulomas.
 - Epstein–Barr virus: latent in B cells, expresses limited antigens.

8. Direct Killing or Suppression of Immune Cells

- Pathogens produce toxins or effectors that kill immune cells.
- Examples:
 - HIV: infects and depletes CD4+ T cells.
 - *Shigella flexneri*: induces macrophage apoptosis via IpaB.
 - EBV: produces viral IL-10 (vIL-10) to suppress Th1 responses.

9. Modulation of Cytokine Networks

- Some microbes mimic or inhibit cytokines to manipulate immune responses.
- Examples:
 - Poxviruses: secrete soluble TNF and IFN receptor homologs.
 - EBV: produces viral IL-10 to inhibit inflammation.
- Result: Impaired immune activation and delayed clearance.

10. Summary Table of Evasion Strategies

Mechanism	Example Pathogen	Key Molecule	Effect
TLR inhibition	Vaccinia virus	A46	Suppresses cytokine signaling
Complement inhibition	N. meningitidis	Factor H binding	Avoids opsonization
Antigenic variation	Influenza virus	HA/NA drift	Escapes antibodies
Ig cleavage	S. pyogenes	IdeS	Neutralizes IgG
Intracellular hiding	M. tuberculosis	Phagosome block	Evades humoral immunity
Phagocytosis evasion	S. pneumoniae	Capsule	Prevents engulfment
Latency	HSV	Latent genome	Persistent infection
Immune cell killing	HIV	gp120	CD4+ T cell depletion

Key Takeaways

- Pathogens use diverse and overlapping evasion mechanisms.
- These include inhibition of innate sensors, antigenic change, and immune cell killing.
- Understanding these processes informs vaccine and drug design.