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# Ways of microbial escape from the immune system: A brief overview

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**Abstract**

Viruses, bacteria and other microbes always try to disable our body system. Our immune system has a complex structure that continuously tries to defend our body against "foreign enemies". Microbes that infect other organisms encounter host immune responses and must overcome or evade innate and adaptive immune responses to successfully establish infection, providing fascinating insights into attack and escape. Many pathogens appear to have developed parallel pathways for escape, and several principles of escape are shared not only among members of the same genus but even among different organisms such as bacteria, viruses, fungi, and parasites. In this article, according to the recent findings, the unique escape strategies of microorganisms will be analyzed in more detail. Part of our immune system is responsible for clearing pathogens, either killing the pathogen directly or marking it for destruction by other immune cells. Therefore, it is possible to develop a new targeted therapy when the mechanism of microorganisms is fully understood. This review describes the mechanisms of interaction between the pathogen and its host in the context of infection.

**Keywords:** immune system, immune response, infection, innate immunity, adaptive immunity, phagocytosis

## 1. Introduction

Today, infectious diseases are one of the main causes of death worldwide and a great challenge for biomedical sciences (1). The main function of the immune system of humans and other animals is to protect against infection (2). This complex and coordinated system includes a set of cells, tissues and organs (3). Most of the diseases caused by the infection of bacteria, viruses, parasites and fungi can be classified into two categories of intracellular and extracellular pathogens according to the immunopathological point of view (4). In the face of infection, the innate immune system creates the host's first line of defense and thus plays an important role in early detection and then creating an inflammatory response to the invading pathogen (5). Antigen-presenting cells (APCs), which are equipped with receptors for microbial patterns, often provide the first response against a variety of pathogens (6). Professional phagocytes are recruited to the site of infection, where they form the host cell's first line of defense, tasked with engulfing and destroying pathogens. Therefore, bacteria must resist the bactericidal activity of professional phagocytes, including macrophages, to fight the host's immune system (7). Among other mechanisms of innate immunity against bacteria are complement activation and inflammatory response, and genetic modification of surface antigens is the main process used by bacteria to evade humoral immunity (8, 9). The adaptive immune system is responsible for eliminating pathogens in the final stage of infection and is also responsible for creating immunological memory (5). Bacteria and other pathogens can change chemical pathways in the body and secrete different virulence proteins, called effectors, to limit the host's defense mechanisms by disrupting host cell signaling pathways (8). Innate immunity against viruses is inhibition of infection and killing of infected cells by natural killer cells (NK cells), remaining viruses escape immune control by blockade of antigen presentation, cytokine escape, escape from NK cell activities, escape from apoptosis and antigenic changes (10). One of the general characteristics of proteins that help microorganisms to modulate immunity and actively evade host defenses is their structural and thus functional similarity to host proteins that they effectively mimic. In general, microorganisms create different mechanisms to block the cellular, humoral or systemic immune response (11). As a result, the immune escape of microorganisms from the host's immune system is a complex process that is created by a set of diverse interactions and strategies. Understanding the factors

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involved in this process can help us identify and develop ways to improve and strengthen the host's immune system against microorganisms. This study and research can ultimately help to improve the methods of prevention, diagnosis and treatment of infectious diseases and lead to the improvement of the health of the society and increase the immunity of our body. In the present study, we investigated the various escape routes of opportunistic pathogens from the host's immune system, in order to better understand how infectious diseases develop.

## 2. A common mechanism for bacterial escape

A common mechanism for bacterial escape from the immune system is their encapsulation, which is carried out by a number of extracellular bacteria that circulate systematically, for example, the capsule of *Streptococcus pneumonia (S. pneumonia)* remains far from access to antibodies and complementary substances and does not have the ability to be opsonized and phagocytized (12). A number of bacteria have the ability to repair and regenerate their cell membranes after the immune system attacks them. By manipulating APCs, these bacteria prevent their migration to the lymph nodes. As a result, cell-related antigens are not presented to cluster of differentiation (CD) 8+ T cells by major histocompatibility complex (MHC) and cell response is not activated (13). Some phagocytosed bacteria such as *Mycobacterium tuberculosis (M. tuberculosis)*, *Listeria monocytogenes (L. monocytogenes)*, *Shigella flexneri (S. flexneri)*, *Francisella tularensis (F. tularensis)* can enter from inside escape the phagosome and enter the cytoplasm. These bacteria prevent the maturation of the primary phagosome. Primary phagosomes initially lack the ability to kill bacteria, and if they merge with lysosomes, they mature and find the ability to produce acid and then kill bacteria. The primary phagosome is formed after the bacteria are engulfed by macrophages. The combination of endocytic vesicles with the early phagosome, as well as the separation of secretory vesicles from it, leads to the formation of the late phagosome. Some bacteria prevent acidification inside the phagosome by preventing the fusion of lysosomes with the phagosome. Then, using some enzymes and secretory systems, they lead to the lysis of the phagosome membrane and finally enter the host's cytoplasm (14). *Listeria* can hydrolyze the phagosome membrane by enzymes listeriolysin and phospholipase and escape to the cytoplasm (15). *Staphylococcus aureus (S. aureus)* is not an intracellular pathogen by nature, but to escape the host's immune system, it has acquired the ability to enter the host's cells. Another escape mechanism of *S. aureus* inside the phagosome is the production of ammonia, which deacidifies and neutralizes the acidic environment inside the phagolysosome (16).

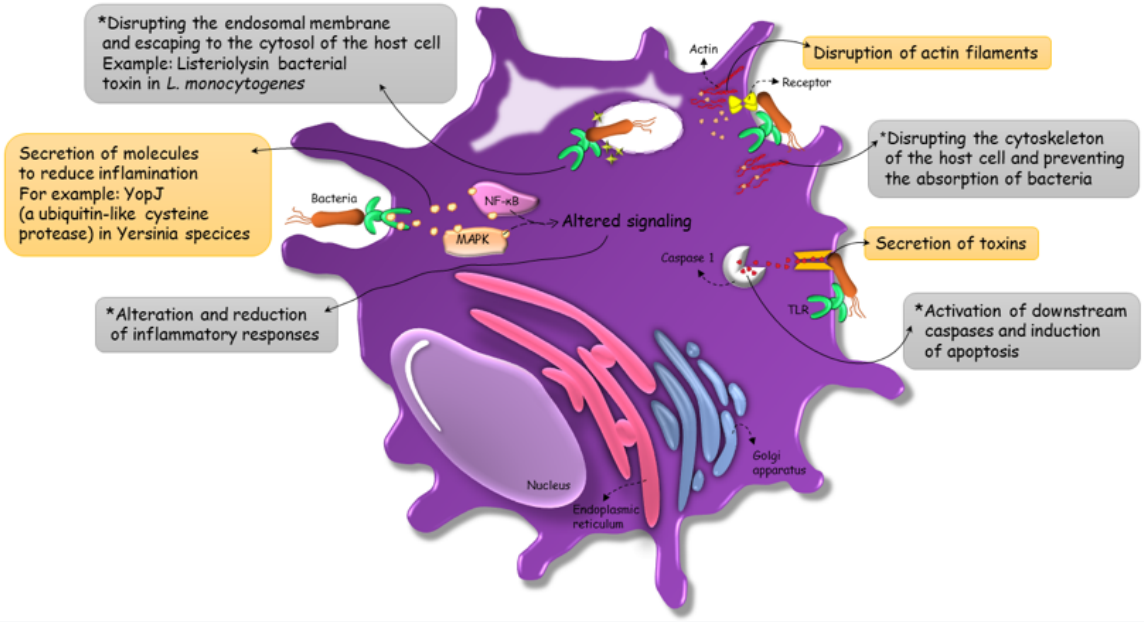


**Fig. 1.** Some bacterial escape routes from macrophage phagocytosis

NF-κB (Nuclear factor kappa-light-chain-enhancer of activated B cells), MAPK (A mitogen-activated protein kinase), TLR (Toll-like receptor)

In some cases, when *S. aureus* falls into the trap of immune phagocytic cells, reactive oxygen species (ROS) and reactive nitrogen species (RNS) mediators are released inside the phagolysosome. Bacteria neutralize their effect by producing and secreting protective enzymes such as catalase, superoxide dismutase (SOD) and peroxiredoxin (Prx). A number of bacteria can avoid being recognized by pattern recognition receptors (PRR) by making antigenic changes in the surface of flagellum, lipid A and peptidoglycan (17). *Yersinia* species target signaling pathways such as mitogen-activated protein kinase (MAPK) and nuclear factor kappa B (NF-κB). *Yersinia pestis (Y. pestis)* produces interleukin (IL) 10 by inhibiting Toll-like receptor (TLR) 2/6 signaling. IL-10 is a type of inhibitory cytokine that inhibits the immune response of the host (18, 19). *Salmonella* have a two-component sensor (PhoP, PhoQ). With these sensors, they can regulate their virulence genes (20). Salmonellas create structural changes in the lipid part of their membrane with the mechanisms of deacylation,

palmitylation and addition of amino arabinose. As a result, they create a negatively charged surface of the cell membrane due to the effect of positively charged cationic peptides (21, 22). They also reduce defensin and cathelicidin. Autophagy is one of the body's cell defense mechanisms where cytoplasmic compounds and whatever are inside the cell is broken down and destroyed by lysosomes (23). Autophagy is one of the defense mechanisms of body cells in which cytoplasmic compounds and everything inside the cell are broken down and destroyed by lysosomes. Microorganisms inside the cell are also destroyed by this mechanism, but some intracellular bacteria prevent the autophagy of the host cell by producing proteins in an irreversible way, so autophagy does not take place in the infected cell (24). Some microorganisms escape from the immune system by causing genetic changes and creating antigenic diversity. For example, *Neisseria* species (gonorrhea and meningitidis) have one of the most complete changes, and for this reason it has not been possible to design a vaccine (25) (Fig. 1).

### 2.1. Escape of extracellular and intracellular bacteria

In Table 1, the virulence of extracellular bacteria is related to some mechanisms that resist innate immunity. Bacteria with capsules rich in polysaccharides resist phagocytosis and, as a result, are more virulent than similar species without capsules (26). In contrast to intracellular bacteria, several strategies have been developed to resist removal by phagocytes. These strategies include:

•Inhibition of phagolysosome incorporation or escaping into the cytosol and thus hiding from the germicidal mechanisms of lysosomes.

•Direct inactivation or clearance of germicidal substances such as ROS. The outcome of infection with these organisms often depends on the interaction between the antimicrobial mechanisms of macrophages stimulated by T cells and the resistance of the microbe to killing. Resistance to phagocyte-mediated removal is also the reason why such bacteria tend to cause chronic infections that may last for years, often recur after complete treatment, and are difficult to eradicate (27-29).

**Table 1.** Comparison of immune evasion mechanisms of extracellular and intracellular bacteria with example

| Extracellular bacteria | | Intracellular bacteria | |
|---|---|---|---|
| **Example** | **Escape Mechanism** | **Example** | **Escape Mechanism** |
| *Neisseria gonorrhoeae* | Antigenic change | *Mycobacterium tuberculosis* | Inhibition of phagolysosome formation |
| *Escherichia coli* | | | |
| *Salmonella typhimurium* | | *Legionella pneumophila* | |
| Many bacteria | Inhibition of complement | | |
| *Pneumococcus* | Activation | *Listeria monocytogenes* | Deactivation of reactive oxygen and nitrogen species |
| *Neisseria meningitidis* | | *Chlamydia trachomatis* | Distruption of the phagosome membrane and escape to the cytoplasm |
| Catalase positive bacteria (Many bacteria) | Purification of reactive oxygen species | | |

## 3. A common mechanism for fungi escape

C-type lectin receptor (CLR), which is a part of the PRR family, plays a major and outstanding role in the identification of fungi (30). According to a general classification, fungi evade the immune system in three ways:

a) Hiding: Chitin and beta-glucan (β-glucan) are components of the cell wall of fungi and are classified as pathogen-associated molecular pattern molecules (PAMPs), molecular patterns associated with pathogens and can be recognized by Dectin-1. Dectins are part of PRR, A number of fungi can hide from dectin-1 by changing the structure of these membrane molecules and cannot be phagocytosed (31). *Candida albicans (C. albicans)* can cover the beta-glucan surface by o-mannan and secrete them (32). *Aspergillus fumigatus (A. fumigatus)*, *Cryptococcus neoformans (C. neoformans)*, *C. albicans* and *Histoplasma capsulatum (H. capsulatum)* have the ability to produce biofilm. Dimorphic fungi such as *H. capsulatum* and *Paracoccidioides* can change from the β-glucan form to the α-glucan form and are therefore undetectable. Biofilms are microbial communities and are two billion years old. Biofilms adhere to surfaces and form a nearly impenetrable mass, thereby keeping fungi out of the reach of the host's immune system (33).

b) Control: Despite all this stealth, most of the time, a healthy immune system will eventually identify pathogens and initiate an appropriate response, at this time, it is the microorganism's turn to fight and control the immune response. *C. albicans* can express regulatory proteins on its surface to control the complement system (34). Complement regulatory proteins include C4b binding protein (C4BP) and factor H. *C. albicans* by expressing a ligand called phosphoglycerate mutase (PGM) 1 that interacts with complement regulatory proteins, inhibits complement regulatory activity and inhibits the immune response .In addition, This fungus can produce and secrete aspartic protease enzymes .Which are completed by the destruction of C3b, C4b and C5 elements (35, 36).

c) Attack: The last way to survive is to secrete toxins. At this stage, the goal of microorganisms is not to escape the immune system, but only to survive. These enzymatic mechanisms include SOD, catalases, glutathione peroxidases (GPX), and non-enzymatic types such as fungal melanin, mannitol, and trehalose, which are toxins against immune system elements (37). The table below shows the escape

mechanism of fungi, which is different from that of bacteria. Some common fungal examples are listed in Table 2.

**Table 2.** Escape mechanisms of fungi from the immune system

| Example | Escape mechanism |
|---|---|
| *Cryptococcus neoformans* | Production of polysaccharide capsule to prevent phagocytosis and weaken opsonin effects of complement and antibody. |
| *Candida albicans* | Hiding glucan under mannan outer coat to avoid detection by Dectins |
| *Histoplasma capsulatum* | Preventing the formation of phagolysosomes and changing the natural path of maturation of phagosomes |
| *Dermatophytes (Trichophyton, Microsporum, Epidermophyton)* | Suppression of the host T-mediated response |

Cytokine and chemokine responses of phagocytes to fungal stimuli are highly dependent (38). *In vitro*, it seems that TRL2 is the most important TLR for signaling responses to fungi (39). Some fungi are able to enter cells by using phagocyte receptors. This facilitates intracellular parasitism and inhibits mechanisms that are activated in response to opsonins, mannans, and beta-glucans (40-42). *H. capsulatum* entry into macrophages and neutrophils is mediated by the interaction between heat shock proteins 60 (HSP60) on the fungal cell surface and CD18 on the phagocytic cell surface. In contrast, although dendritic cells (DCs) express CD18, they instead utilize very late antigen-5 (VLA-5) to phagocytose *H. capsulatum*. *Blastomyces dermatitidis (B. dermatitidis)* uses a cell wall protein blastomyces adhesin-1 (BAD-1) to access macrophages via complement receptor 3 (CR3) and initiate an anti-inflammatory program that induces pathogen survival (43). *C. albicans* begins to express the yeast flavohemoglobin1 (YHB1) gene when exposed to nitric oxide (NO) produced by macrophages. The product of this gene is a flavoprotein that copes with the stress caused by RNS (44). Cytochrome C peroxidases reduce the effects of RNS against the fungus and force the host to produce less RNS (45). When some fungi enter the phagolysosome, by changing their metabolic patterns, they produce substances that are toxic to macrophages and induce them to undergo apoptosis (46). The immune response against fungi, which are mainly extracellular, is the responsibility of neutrophils, which are the first line of defense of innate immunity. A number of fungi damage the DNA of neutrophils by producing DNase enzymes and escape from them (47). Some fungi interact with their receptor on the surface of leukocytes by expressing a ligand called pH-regulated antigen 1 (Pra1) and prevent leukocytes from sticking to the surface of fungi (48). Typically, *Pneumocystis jirovecii (P. jirovecii)* takes over the human lung and adapts to live. In immunocompromised individuals, it can develop into a deadly pathogen and cause pneumonia in the correct circumstances. *P. jirovecii* frequently evades the host's immune system's destruction by switching to the major surface glycoprotein (MSG) antigen (49, 50). In contrast to other pathogenic fungi, *P. jirovecii* lacks chitin and glucan in some cell cycle stages, which may inhibit the host's innate and acquired immune responses (51) (Fig. 2).

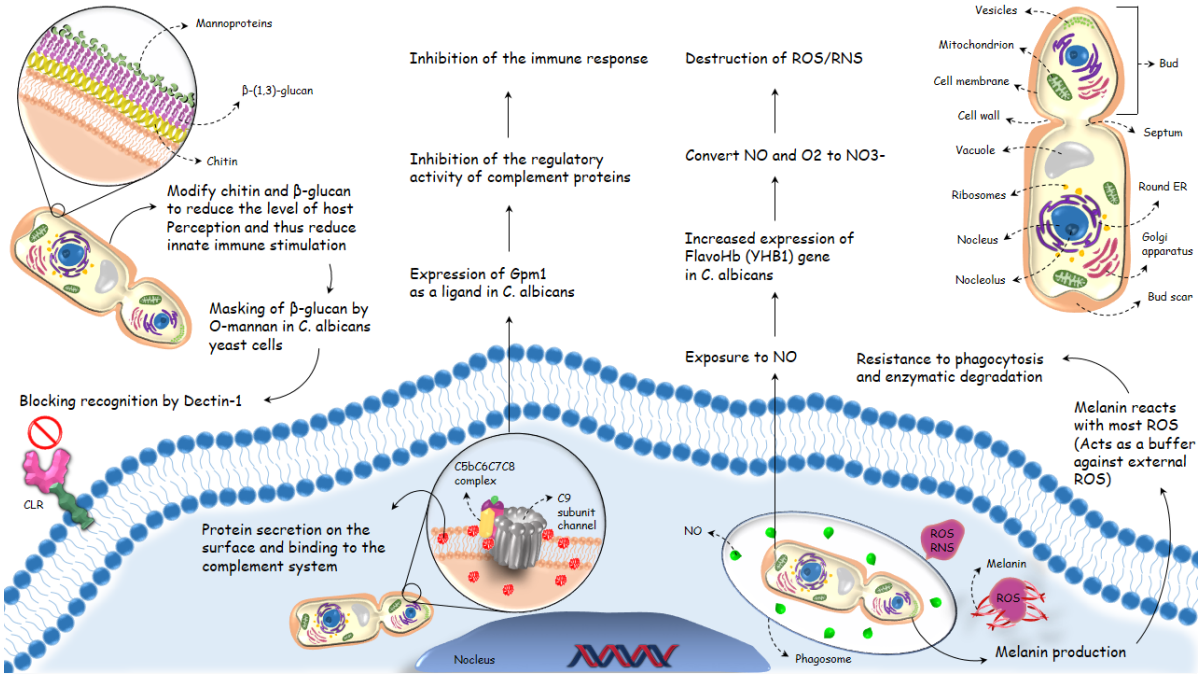


**Fig. 2.** A summary of anti-immune mechanisms of fungi
CLR (C-type lectin receptors), ROS (Reactive oxygen species), RNS (Reactive nitrogen species), PGM (phosphoglycerate mutase), ER (Endoplasmic reticulum), YHB1 (Yeast flavohemoglobin1), NO (Nitric oxide).

## 4. A common mechanism for virus to escape

Viruses are all obligate intracellular parasites and have various strategies to escape from the elements of the immune system (52), such as molecular mimicry of host cell surface receptors, complement inhibitors and leukocyte activity regulators. One of the important mechanisms that exists in viruses, bacteria and a number of parasites is mutation in genomic nucleotides, which leads to antigenic changes. This practice is known as antigenic variation, which misleads acquired immunity. In fact, it is a kind of bypass of humoral and cellular immunity. The most common antigenic changes in viruses are changes in surface glycoproteins (53). Mutations in RNA viruses are more than in DNA viruses. Among the types of mutations, we can mention the point mutation, which is more common in viruses. The reason is that the frequency of RNA replicase mutations is higher than that of DNA polymerase. Due to the fact that influenza viruses have several hosts of different species, they can perform genome rearrangement in the cells of these hosts and become recombinant which is different from their early ancestors (54). A number of viruses, such as Epstein-Barr virus (EBV) and Herpes simplex virus (HSV), can remain alive inside the host's target cells for years and even until the end of a person's life and start multiplying if optimal conditions are created (55). Some viruses can avoid the attack of the immune system by mimicking the proteins and receptors of the host cells. Given that NK cells have activated receptors, some viruses can bind to the inhibitory receptors of NK cells by producing specific bonds and preventing their activation (56). Viruses, like some bacteria and fungi, have protective mechanisms to counter the antimicrobial action of NO and free oxygen radicals of active macrophages. After entering the host cell, some viruses cause the expression of complement membrane regulating molecules such as decay-accelerating factor (DAF) and major capsid proteins (MCP) on the surface of the membrane of the infected host cell. By affecting macrophages, some viruses prevent the expression of endosomal TLRs or prevent the transmission of TLRs, interferon regulatory factor 3 (IRF3), NF-κB messages in the downstream areas (56-58). When HSVs enter the target cell, they inhibit apoptosis by inhibiting caspase 3, and as a result, they start multiplying easily inside the infected cell. There is a surface glycoprotein called C1 in HSV that binds to the C3b component and inhibits it (59). Some large DNA viruses can mimic cytokine molecules to bind to specific receptors on the target cell. This increase in the number of cytokines increases the replication of the virus and the immune response is inconsistent in this case. In some cases, when antiviral cytokines are produced, viruses block the receptors of those cytokines so that the antiviral immune response does not take place (60). RNA viruses that are located in the cytoplasm of host cells are recognized by cytoplasmic receptors such as retinoic acid-inducible gene I (RIG-I) and melanoma differentiation-associated protein 5 (MDA5) PRRs and an appropriate immune response is given, but these viruses make nucleotide changes in their genome in order to escape from this immune response. As a result, cytoplasmic receptors cannot recognize them (61) (Fig. 3).

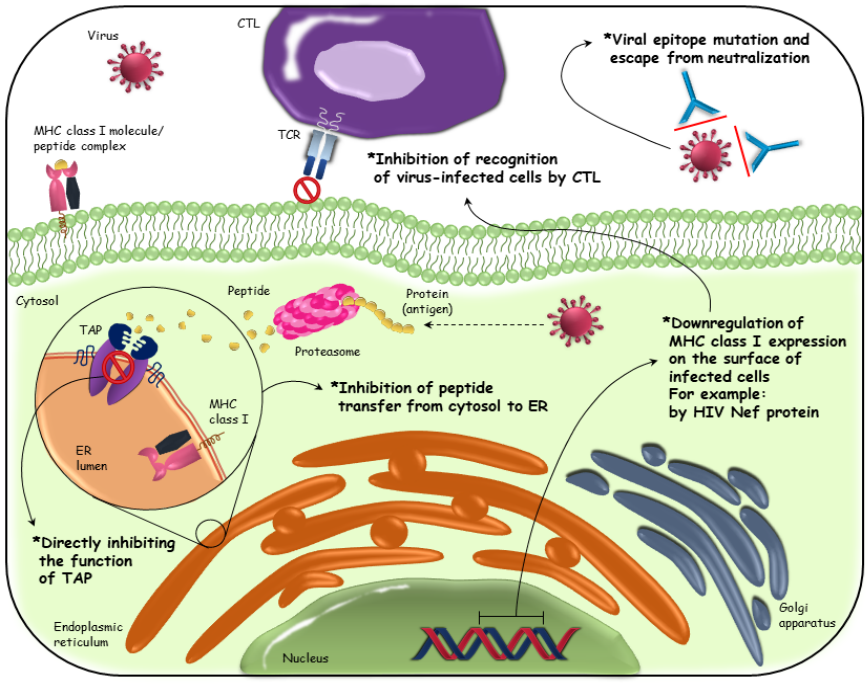


**Fig. 3.** An overview of some escape routes of viral pathogens from the immune system
CTL (Cytotoxic T lymphocyte), TCR (T-cell receptor), MHC (Major histocompatibility complex), TAP (Transporter associated with antigen processing), ER (Endoplasmic reticulum)

Human cytomegalovirus (HCMV), human immunodeficiency virus (HIV) and human T-lymphotropic virus type1 (HTLV-1) when releasing virus particles from inside the host cell, cause the production of complement system regulators such as DAF, CD59, MCP (62). These proteins prevent the activity of complement. The family of HSV are able to prevent the expression of cytokines interferon type I (IFN-I) and IFN-II, tumor necrosis factor (TNF) and interleukin-1 (IL-1) (63). There are viruses that, upon entering the host cell, force it to use less MHC molecules to escape from microorganisms NKs and cytotoxic T lymphocytes (CTLs) that evade the immune system, enter certain tissues or cells, and may remain in the host for months or years and this host acts as a healthy vector of chronic and latent infection (64) (Table 3).

**Table 3.** Escape mechanisms of viruses from the immune system

| Examples | Virus family | Genome type | Escape Mechanism |
|---|---|---|---|
| HCMV | *Herpesviridae* | DNA | • Downregulation of host MHC class I expression<br>• Inhibition of NK cell activation<br>• Modulation of cytokine and chemokine signaling<br>• Inhibition of apoptosis<br>• Latency and reactivation |
| EBV | *Herpesviridae* | DNA | • Downregulation of MHC class I expression<br>• Inhibition of antigen processing<br>• Modulation of cytokine signaling<br>• Induction of immune cell transformation<br>• Evasion of NK cell recognition |
| Vaccinia virus (VACV or VV) | *Poxviridae* | DNA | • Inhibition of apoptosis<br>• Suppression of inflammatory responses<br>• Disruption of chemokine gradients<br>• Interference with complement activation<br>• Modulation of antigen presentation |
| HPV | *Papillomaviridae* | DNA | • Suppression of innate immune responses<br>• Inhibition of antigen presentation<br>• Modulation of apoptosis<br>• Suppression of T cell function<br>• Induction of immune tolerance |
| Influenza viruses | *Orthomyxoviridae* | RNA | • Antigenic variation<br>• Inhibition of innate immune responses<br>• Evasion of adaptive immune responses<br>• Exploitation of immune privilege<br>• Induction of immune exhaustion |
| HIV | *Retroviridae* | RNA | • Rapid genetic variation<br>• Targeting and destroying CD4+ T cells<br>• Inhibition of antigen presentation<br>• Induction of immune exhaustion<br>• Suppression of innate immune responses<br>• Establishment of latent reservoirs |
| Coronaviruses (CoVs) | *Coronaviridae* | RNA | • Inhibition of IFN response<br>• Disruption of antigen presentation<br>• Induction of immune exhaustion<br>• Evasion of antibody neutralization<br>• Exploitation of immune privilege<br>• Subversion of macrophage and dendritic cell function |
| Ebola virus (EBOV) | *Filoviridae* | RNA | • Impairment of the innate immune response<br>• Disruption of antigen presentation<br>• Induction of immune exhaustion<br>• Evasion of antibody neutralization<br>• Suppression of inflammatory responses<br>• Induction of apoptosis in immune cells |
| Marburg virus disease | *Filoviridae* | RNA | • Suppression of the IFN response<br>• Disruption of antigen presentation<br>• Induction of immune exhaustion<br>• Evasion of antibody neutralization<br>• Suppression of inflammatory responses<br>• Induction of apoptosis in immune cells |

## 5. A common mechanism for parasite escape

Many parasites, particularly those that are diploid and have a life cycle involving a vertebrate host, have developed the ability to change their surface antigens as an immune evasion mechanism. This is a common strategy employed by various parasitic organisms to avoid recognition and elimination by the host's immune system (65). Mutations usually occur in regions that are targeted by antibodies and T cells. Protozoa are unicellular eukaryotic microorganisms belonging to the Protista family. The body wall is covered by a cell membrane. Its cytoplasm consists of ectoplasm and the endoplasm of the nucleus is usually single, but it may be two or more. Reproduction can be asexual such as binary fission, schizogony, endodygony or sexual. Most worms require more than 1 intermediate host to complete their life cycle. Worms, unlike protozoa, do not multiply in the human body, which leads to multiple infections (66). Protozoa hide from the immune system by producing resistant cysts. Some worms enter the intestinal tract and are out of reach. When the specific antibody recognizes *Entamoeba histolytica (E. histolytica)*'s antigenic coating and binds to it, the *Entamoeba trophozoites* (*E. trophozoites*) sheds the antigen in response to this action. In fact, a kind of skinning is done (67). Since the functional immune response against parasites is the responsibility of macrophages, here too will we observe the production of ROS and RNS. Some parasites prevent the production of cytokines or change the expression pattern of cytokines. For example, they switch from the IFN-γ form to the IL-10-producing form (68). In the *Leishmania* parasite, promastigote forms that are phagocytosed by neutrophils produce the lipophosphoglycan (LPG) molecule, which inhibits phagosome maturation. *Leishmania donovani (L. donovani)* prevents respiratory bursts by producing tartrate-resistant acid phosphatase (TRAP or TRAPase) (69). In the malaria parasite, sporozoites and merozoites are antigenically different. There is a latent state in all types of malaria. After the successful and complete treatment of malaria in the affected person, a form called hypnozoites remains. These forms are non-replicable and metabolically inactive. These forms can remain in the liver cells of the affected person for a long time, and during this time no humoral or cellular reaction is created against these hidden elements. In some situations, these insects become active and cause disease. To escape from Kupffer cells, liver merozoites enter vesicles called merosomes. In this case, the phagocytes located in the liver tissue can no longer respond to them (70, 71). About parasites that produce larvae. For example, schistosomes, larvalization renders the complement system and CTLs unable to recognize them. The larvalization of some parasites, such as schistosomes, leads to their non-recognition by MHCs and CTLs, and ultimately their escape from the host's immune system (72).

**Table 4.** Parasite escape mechanisms from the immune system

| Classification | Examples | Escape mechanism |
|---|---|---|
| Protozoa | *Trypanosoma* | Antigenic change |
| | *Plasmodium* | |
| | *Entamoeba* | Antigen production and shedding |
| Metazoa | *Schistosomes* | Acquired resistance to complement |
| | *Filaria* (after lymphatic blockage) | Inhibition of host immune responses |
| | *Toxoplasma gondii* | |

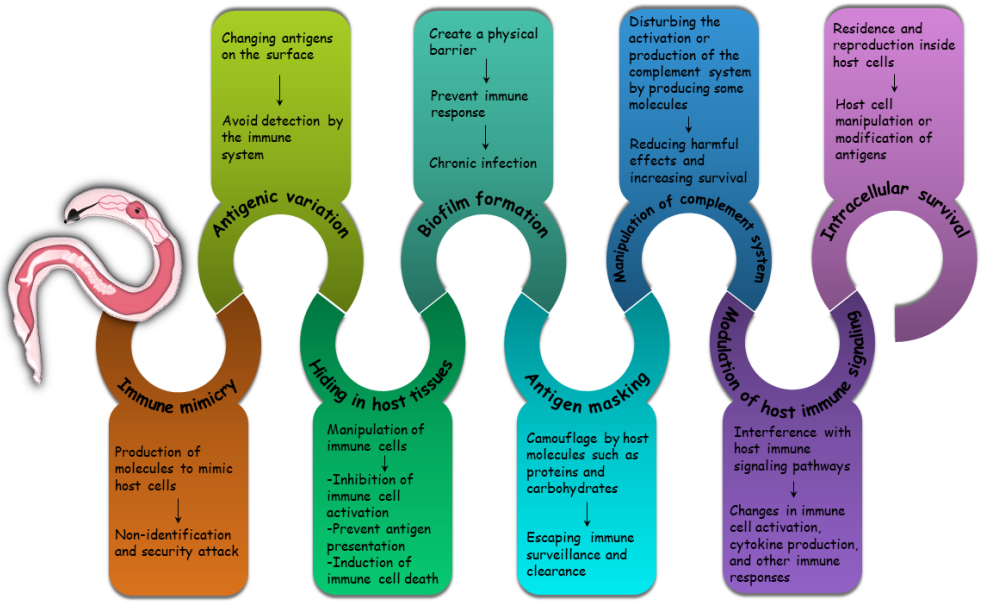


**Fig. 4.** A summary of immune evasion methods by pathogenic parasite

Table 4 shows the mechanisms of escape from the immune system. Parasites inhibit the host's immune responses through several mechanisms. These organisms reduce their immunogenicity and escape from the immune system by inhibiting the host's immune responses, antigen displacement, and acquired resistance to covalents, inhibiting the host's response to antigens. Some parasites, such as *Leishmania* and *Filariasis*, stimulate the development of regulatory T cells (Treg), which suppresses immune responses against the parasite and ultimately provides the continuation of the presence of the parasite (73). *Leishmania major* specifically inhibits the production of IL-12 by host macrophages, as a result, the production of IFN-ɣ by NK cells is inhibited and the differentiation and function of T helper type 1 (Th1) cells are also inhibited (74). In addition, it has been shown that *Leishmania major* actively induces Treg cells to produce IL-10, which suppresses the clearance of infection (75) (Fig. 4).

Technological advances in the last decade have facilitated studies on the mechanisms of interaction between the pathogen and its host in the context of infection. Each person's microbiota prevents the emergence and proliferation of pathogenic microorganisms as a strong and reliable mechanism. The immune system and the human physiological system, in general, are able to prevent the entry of microbial elements into the body, and in case of entry, they can give appropriate immune responses that cause their immediate removal, that is, in the shortest time, with the greatest response and the least damage to themselves. Microorganisms that enter certain tissues or cells and escape from the immune system may remain in the host for months or years, and the host acts as a healthy vector, and chronic infection remains latent. Part of our immune system is responsible for clearing pathogens, either killing the pathogen directly or marking it for destruction by other immune cells. The essay highlights the need of comprehending the immune system evasion methods by bacteria in order to design efficacious preventive and therapeutic approaches. By learning more about these escape techniques, scientists can pinpoint possible areas for intervention, such as creating vaccinations that specifically target conserved microbial components or creating medications that interfere with the ways in which bacteria evade the immune system. In conclusion, the paper emphasizes the variety and complexity of methods that microbes might evade the immune system. In addition to advancing our knowledge of host-pathogen interactions, more study in this area will make it easier to create cutting-edge strategies for fighting infectious diseases.

**Conflict of interest**

The authors declare that they have no competing interests.

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The data that support the findings of this study are available from the corresponding author upon reasonable request.

**Authors' contributions**

Concept: M.P., A.J.S, Design: M.P., Data Collection or Processing: A.J.S, Analysis or Interpretation: G.P., K.S., K.H.K., Literature Search: G.P., K.S., K.H.K., F.M., Writing: G.P., K.S., K.H.K., N.Y.

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