Review
บทความปริทัศน์

Transmission of HIV-1 Via Oral Route: Why is it difficult?

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Abstract

Transmission of human immunodeficiency virus type 1 (HIV-1) via oral route is considered to be uncommon. Several factors at mucosal surfaces and in saliva may play roles in local defense against the viral infection of target cells. The objective of this article was to review local innate immunity that contributes to the oral resistance against HIV-1. Oral epithelial cells play significant roles in local innate immunity. They provide physical barrier and also produce antimicrobial peptides that possess anti-HIV-1 activity. This article described mechanisms of HIV-1 transmission, role of epithelial cells and antiviral mechanisms in the oral cavity including human beta-defensins (hBDs) in HIV-1 transmission at mucosal surfaces.

Key words: antimicrobial peptides; beta-defensins; oral HIV-1 transmission; oral innate immunity; saliva

Introduction

Mucosal surfaces are predominant sites of human immunodeficiency virus type 1 (HIV-1) transmission. Epithelial cells lining the oral cavity get exposed to the virus through breast-feeding and oral–genital sexual contact. However, oral mucosa appears to be naturally resistant to infection with HIV-1.[1] The mechanisms contributing to the protective effect in the oral cavity are incompletely understood. It has been postulated that the innate immune response is a key defense against HIV-1, especially at mucosal surfaces.[2]

The oral epithelium, which is organized into stratified squamous structure, provides a physical barrier as the first line of innate immune defense against penetration of the virus.[2] Antimicrobial peptides produced by oral epithelial cells, including human beta defensins (hBDs) and other salivary proteins such as thrombospondin, albumins, lysozyme, and lactoferrin have been shown to possess anti-HIV-1 activity at physiologic concentrations.[3-6] However, it is not clear to what degree locally produced innate immune factors contribute to HIV-1 resistance of the oral mucosa.

This article described possible mechanisms of HIV-1 transmission, roles of epithelial cells in HIV-1 transmission, antiviral mechanisms in the oral cavity with special focus on antiviral activities of hBDs.

Mechanisms of HIV-1 transmission

Although mucosal surfaces are the primary sites of HIV-1 entry, the mechanisms of HIV-1 transmission across epithelial surfaces are not clearly understood. It was demonstrated that to initiate HIV-1 infection, fusion of the virus membrane and a target cell membrane is required. The virus envelope glycoprotein 120 (gp120) and gp 41 sequentially interacts with two cell surface receptors; CD4 is the primary receptor, and the beta-chemokine receptors CCR5 or CXCR4 serve as secondary receptors.[7-8]

Transmission of HIV-1 strains *in vivo* generally uses CCR5 (R5-tropic), which predominate during the acute and asymptomatic phases of infection.[9] When chronic infection is established, viruses preferentially using CXCR4 (X4-tropic) emerge in approximately 50% of infected individuals.[9-10] In addition to CCR5 and CXCR4, several other receptors including glycosphingolipid galactosyl ceramide (GalCer) can mediate the entry of some HIV-1 isolates.[11]

Interaction of X4- and R5- tropic viruses with their specific receptors is necessary to establish productive HIV-1 infection in target cells as shown in Figure 1. Thus, agents that target CCR5 or CXCR4 can block HIV-1 entry and prevent infection

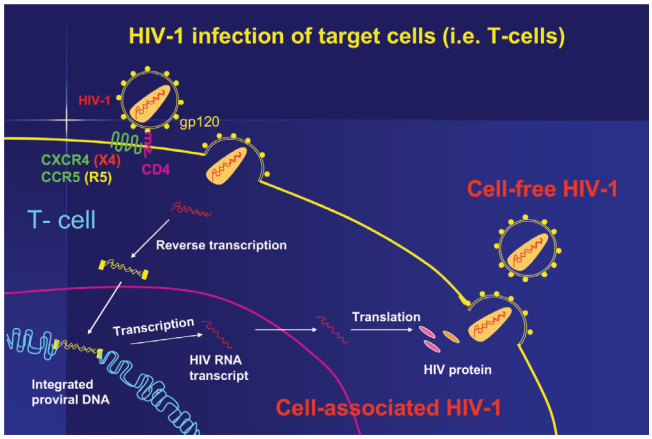

Fig. 1 *HIV-1 infection of target cells.*
The first step is the attachment of the virus to receptors on the cell surface. The HIV-1 RNA genome then enters the cytoplasm. The viral RNA genome is reverse- transcribed into viral DNA before entering the nucleus and being integrated with the host-cell genome to serve as a template for viral transcription. Transcription of the proviral DNA template creates viral mRNA species encoding the viral proteins. The cycle is completed by the release of infectious retroviral particles from the cell.

in vivo and *in vitro*. These include Regulated on Activation, Normal T Expressed and Secreted (RANTES), Macrophage Inflammatory Protein (MIP)-1α and MIP-1β, the natural chemokine ligands for CCR5; and Stromal Cell-Derived Factor-1 (SDF-1), the natural ligand for CXCR4.[12,13] Modulation of CXCR4 and CCR5 expression after HIV-1 infection is one of the results of such interaction, which may affect the course of the infection.

Immune cells expressing CD4 receptor, and CCR5 or CXCR4 co-receptors are the target cells for HIV-1 and primary reservoirs of the virus. These include monocytes/macrophages, lymphocytes, and dendritic cells (DCs). $CD4^+$ T cells are the main source of HIV-1 replication and dissemination. Most infectious HIV-1 occurs in infected leukocytes and a smaller fraction as cell-free HIV-1 in blood and secretion.[14] Both cell-free and cell-associated HIV-1 particles can be sexually transmitted.

DCs play an important role in HIV-1 transmission at mucosal surfaces and in HIV-1 pathogenesis. They express relatively low levels of CD4 receptor, and CCR5 and CXCR4 co-receptors.[15] Thus, compared with $CD4^+$ T cells, HIV-1 replication in DCs is generally less productive[16,17] with about 10-100 fold lower frequency of HIV-1 infected DCs *in vivo*.[18] DCs are located in the oral and vaginal mucosae and the lymphoid tissues. Thus, it has been proposed that during the sexual transmission of HIV-1, DCs including Langerhans cells (LCs) in epithelial and mucosal tissues, and immature myeloid DCs in the submucosa are among the first cells that encounter the virus.[19-21] However, a recent study by Hladik and co-workers[22] demonstrated that both LCs and $CD4^+$ T cells residing in the vaginal epithelium are simultaneously infected by HIV-1. C-type lectins, a family of transmembrane proteins that function as cell-adhesion molecules, and other HIV-1 attachment factors that are expressed by immature DCs capture HIV-1, and migrate to lymphoid tissues that are enriched in $CD4^+$ T cells.[15]

Roles of epithelial cells in HIV-1 transmission

As part of innate immunity, epithelial cells lining mucosal surfaces form important barriers against invasion of various microorganisms.[23,24] To maintain these critical barriers, epithelial tissues undergo constant renewal and repair, and the cells undergo a program of terminal differentiation.[25] Since the majority of HIV-1 infections occur as a result of the viral passage across the mucosal membrane, the virus must gain

access through the epithelial surfaces before going on to initiate a systemic infection.

Although HIV-1 infection through heterosexual intercourse accounts for the majority of infections worldwide, the mechanisms of viral transmission across the epithelium of the reproductive tract is poorly understood. Previous animal studies revealed that rhesus macaques became infected by simian immunodeficiency virus (SIV) placed on the apparently intact cervix, vagina, or penile urethra.[26,27] Thus, the virus is capable of crossing the "*intact*" epithelial barrier by undefined mechanisms. In general, epithelial organization dictates the mechanisms of viral entry and translocation. Viruses have evolved several pathways to initiate entry through epithelial barriers. They may enter and infect epithelial cells by accessing the cell cytosol using one of two mechanisms; direct entry at the epithelial plasma membrane, or entry through the epithelial endocytotic pathway.[28]

Different potential mechanisms for HIV-1 transmission across mucosal epithelium have been proposed as shown in Figure 2. A study by Moore et al[29] revealed that oral epithelial cells can be infected by cell-free R5-, but not cell-free X4-tropic viruses, and release infectious virions that can infect $CD4^+$ T cells. In contrast, it has been shown that HIV-1 can cross

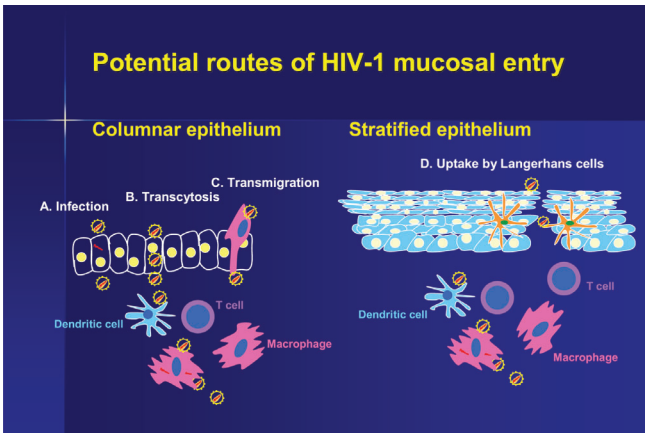

Fig. 2 *Potential mechanisms for HIV-1 transmission across mucosal epithelium A, Direct infection of epithelial cells. B, Transcytosis through epithelial cells and/or specialized microfold (M) cells. C, Epithelial transmigration of infected donor cells. D, Uptake by intra-epithelial Langerhans cells during physical breaches. Successful transfer of virus across epithelial barriers would result in HIV-1 uptake by migratory dendritic cells and subsequent dissemination to draining lymph nodes and/or localized mucosal HIV-1 infection.*

simple epithelial cells of small intestine by rapid transcytosis without infection.[11,30,31] Bomsel et al[30,31] used a monostratified epithelial cell line barrier as an *in vitro* model to study HIV-1 infection and found that peripheral blood mononuclear cells (PBMCs) infected with HIV-1 primary isolates ($HIV\text{-}1^+$ PBMCs) adhered to the apical surface of the epithelial cells, and massive polarized budding of HIV-1 was induced by contact between HIV-1 infected PBMCs and epithelial cells. The newly formed virus is rapidly transcytosed to the basolateral pole of the cell, and released to infect mononuclear cells in lamina propria.

Transcytosis of HIV-1 across CD4-negative epithelial cells requires two molecules; gp120 and GalCer.[11] GalCer is markedly enriched at the apical surface of epithelial cells.[11] It has been demonstrated that in transcytosis, the transmembrane gp41 subunit of the viral envelope binds to the epithelial GalCer.[11] This is supported by further evidence that disrupting the raft organization of the GalCer-containing microdomains at the apical surface inhibited HIV-1 transcytosis.[32]

A study by Meng et al[11] revealed that primary intestinal epithelial cells express GalCer and CCR5, but not CXCR4. Thus, the cells transfer R5-tropic, but not X4-tropic viruses to $CCR5^+$ indicator cells, which can efficiently replicate and amplify the virus. The transfer was not inhibited by the fusion blocker T-20 (a novel antiretroviral agent that inhibits the fusion of human HIV-1 with target cell membranes), but was substantially reduced by colchicine and low temperature (4°C), suggesting endocytotic uptake and microtubule-dependent transcytosis of HIV-1. The findings of this study that $CCR5^+$ intestinal epithelial cells select and transfer exclusively R5-tropic viruses indicates a mechanism for the selective transmission of R5 HIV-1 in the upper gastrointestinal tract.

Despite a growing number of reports, the issue whether oral epithelial cells are infected by HIV-1 is still debatable.[33] A study in human gingival tissue revealed that GalCer and CXCR4 are detected in healthy gingiva, but only in the deeper layers that are close to the basal layer[33]. A study by Quinones-Mateu et al[5] found that oral epithelial cells were not infected by HIV-1. In contrast, a study by Moore et al[29] demonstrated that oral epithelial cells could be infected with a R5-tropic strain but not an X4-tropic strain. Recently, a study by Giacamen et al[34] reported that CCR5, which is not usually expressed in oral epithelial cells, was up-regulated by lipopolysaccharide (LPS) of *Porphylomonas gingivalis*

(*P. gingivalis*). Thus, coinfection with *P. gingivalis* could promote selective R5-tropic HIV-1 infection of oral epithelial cells by inducing CCR5 expression. Further *in vitro* studies with a physiologically relevant model of oral mucosa are needed to determine epithelial cells and HIV-1 interaction.

Antiviral mechanisms in the oral cavity

Oro-genital transmission has a very low *per*-contact risk of acquiring HIV-1 infection. It has been estimated that only 4/10,000 contacts result in infection.[35-37] Vertical HIV-1 transmission from mother to infant during breastfeeding also has a low incidence, which accounts for one third of all transmission events.[38] The low estimated rate of HIV-1 oral transmission may be associated with the protective role of the mucosa and salivary constituents in the oral cavity. The presence of unique anti-HIV-1 molecules in saliva, as well as higher concentrations of common antimicrobial and antiretroviral factors, may account for the fact that infectious virus is rarely present in saliva.[39] However, HIV-1 oral transmission may occur when large volumes of potential viral inoculum overwhelm the natural protective mechanisms.

The mechanisms of action of salivary viral inhibitors include acidic proline-rich proteins (PRPs), thrombospondin, albumins, lactoferrin, mucins, and salivary agglutinins that may block cell binding and fusion through interactions with gp 120. Defensins appear to inhibit HIV-1 infection at a step prior to reverse-transcription, whereas cystatins may interfere with proteolytic viral processing in the late stages of the viral life cycle.[40] Lactoperoxidase and lysozyme have also been shown to have activity against HIV-1.[39] Several of these salivary viral inhibitors are summarized in Table 1. In addition,

Table 1 *Mechanism of HIV inhibition by salivary components*

Component	Proposed mechanism	Reference
Defensins	β-defensins 2,3 inhibit HIV-1 replication, especially of X4 viruses	Quiñones-Mateu et al.[5]
	α-defensins inhibit HIV replication at a step that precedes reverse-transcription	Tanabe et al.[80]
	α- and β-defensins bind to gp120 and CD4	Wang et al.[81]
SLPI	Inhibits HIV infection at a stage prior to reverse-transcription	McNeely et al.[3]
	Binds to annexin II that may facilitate viral entry through its association with phosphatidylserine	Ma et al.[82]
Mucins and salivary agglutinins	Interact with gp 120 and aggregate viral particles	Nagashunmugam et al.[83]
Lactoperoxidase and lysozyme	General antimicrobial actions/ demonstrated HIV inhibition	Shugars & Wahl[38]
Lactoferrin	Binds to the V3 domain of gp120 Inhibits HIV infection/viral replication	Swart et al.[84] Puddu et al.[85]

non-specific mechanisms, such as lysis of infected cells by the hypotonicity of saliva may also play a role.[39] Among these salivary factors, hBDs are the endogenous antiretroviral agents that have received considerable attention.

What are hBDs?

HBDs are small, cationic antimicrobial peptides encoded by multiple genes located in a cluster on chromosome 8p23.[41] In humans, expression of 4 members of the hBDs family has been characterized.[42] HBD1 is constitutively expressed by epithelial cells and found in the interstitial spaces between the cells. In contrast, hBD2-4 are inducible and produced by epithelial cells in response to LPS and proinflammatory cytokines such as interleukin-1 (IL-1), and tumor necrosis factor alpha (TNFα).[43] HBD1 may play a role in preventing commensal bacteria from becoming opportunistic pathogens, whereas hBD2, hBD3 and hBD4 may be more effective against pathogens.[44,45]

HBDs are characterized by six cysteine residues in specific locations. They have disulfide bonds between cysteine 1-5, 2-4, and 3-6 and consist of a triple-stranded β-sheet with a distinctive "defensin" fold. Structures of hBDs contribute to their functions.[46] For example, disulfide bonds are not required for the antibacterial functions of hBD3, whereas it is important to its chemotactic function.[47]

HBDs are expressed mainly by epithelial cells in different sites of the body.[23,44] However, they are not exclusively epithelial-cell-associated, as the expression of hBD1 and hBD2 has also been detected in monocytes, macrophages, and monocyte-derived DCs.[48] Various tissue distributions and cell sources of hBDs are shown in Table 2.[46]

Table 2 *Distribution and source of β-defensins*

β-defensins	Cell source	Synthesis and regulation
hBD1	Epithelial cells*, monocytes, macrophages, monocyte-derived dendritic cells	Constitutive or inducible in response to interferon-γ, lipopolysaccharide, and peptidoglycan
hBD2 and hBD3	Epithelial cells*, monocytes, macrophages, monocyte-derived dendritic cells	Inducible in response to viruses, bacteria, lipopolysaccharide, peptidoglycan, lipoproteins, cytokines IL-1β, TNF, and growth factors
hBD4	Epithelial cells* (especially of testis and gastric antrum), neutrophils	Inducible in response to bacteria such as *Pseudomonas aeruginosa*, and *Streptococcus pneumoniae*

*Main cellular source. hBD, human β-defensin; HD, human α-defensin; IL-1β, interleukin-1β; TNF, tumor-necrosis factor

The antimicrobial activity of hBDs is due to the cationic charge and amphipathic structure with polar and hydrophobic surfaces. They are thought to function against the microorganisms by forming pores and disrupting the membrane integrity.[42] In addition to their potent microbicidal action against microorganisms, hBDs have also been described to display chemotactic activity towards immature DCs and T-cells by binding to CC-chemokine receptor 6 (CCR6).[49] HBDs have important signaling potential, exhibiting cross-talk between the innate and acquired immune responses, as well as inducing the production of cytokines by epithelial cells.[50]

Several studies described the presence of hBDs in the human oral cavity.[51-58] Expression of hBD1 and hBD2 mRNA were observed in suprabasal stratified epithelium, whereas the peptides were detected in upper epithelial layers. Of interest, they both were not detected in the junctional epithelium (JE). A notable difference between oral and most other epithelia is the expression of hBD2 and hBD3. These hBDs in most tissues, including skin, trachea, and gut epithelium are expressed only in the presence of infection or inflammation.[59] However, hBD2 and hBD3 are detected in normal uninflamed gingival tissue.[55,58] It has been postulated that this baseline level of hBD2 and hBD3 could be due to the exposure of

the tissue to specific commensal bacteria that are constantly present in the oral cavity.[44] This may enhance expression of hBD2 in subsequent responses to other potentially pathogenic organisms. A previous study demonstrated that *Fusobacterium nucleatum,* an ubiquitous gram-negative organism of the human oral cavity, stimulates hBD2 expression in normal human oral epithelial cells.[57] A study by Lu et al[60] demonstrated that hBD1 and hBD2 are not only expressed in the granular and spinous regions of normal gingival epithelia, but also in the basal cell layers. This may indicate the immunomodulatory activity of hBDs to attract immature DCs, monocytes, and T-cells,[47,49] and maturation of iDCs.[61] Thus, hBDs are involved in 'cross-talk' with cells of the adaptive immune system.

Roles of hBDs in HIV-1 oral transmission

A dual role of hBDs in antiviral activity has been proposed; direct interaction with viral envelope, and indirect effects by interacting with potential target cells.[46] The mechanisms of direct inactivation of the virion by hBDs are not well understood. The activities may include disruption of viral membrane or interacting with viral glycoproteins such as HIV-1 gp120. HBDs may also act on target cells by interfering with signaling pathways required for the viral replication.[46]

Some hBDs show chemotactic activity for T-cells, monocytes, and immature DCs. They also induce cytokine production by monocytes and epithelial cells.[62] Thus, in addition to acting as direct effectors, hBDs may control viral replication by modulating the immune system.[46] It has been demonstrated that the chemotactic activity of hBDs for memory T-cells and immature DCs is mediated by CCR6, the receptor for CC-chemokine ligand 20 (CCL20 or MIP-3α).[49,63]

All classes of hBDs have been shown to suppress HIV-1 replication and possess anti-HIV-1 activity.[5,64-69] Different mechanisms of anti-HIV-1 activity by hBDs have been proposed as shown in Figure 3. A study by Sun et al[67] revealed that hBD2 and hBD3 inhibit both X4- and R5-tropic HIV-1 in a dose-dependent manner, and the inhibition occurs at an early stage of reverse transcription. The study also demonstrated that hBD2 directly inactivated HIV-1, and exerted its antiviral activity without affecting cellular proliferation.[67] Besides a direct inactivation of the virus, hBD2 also inhibits HIV-1 replication in the intracellular environment. HBD2 antimicrobial peptides are constitutively expressed in oral epithelia, forming a barrier layer across the epithelium in healthy subjects. In contrast, levels of the expression are

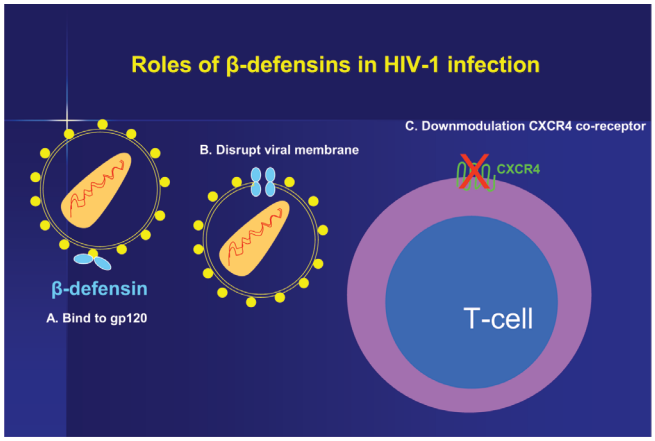

Fig. 3 *Mechanisms of anti-HIV-1 activity by β-defensins*
A, β-defensins inactivate enveloped virus particles by interacting with viral glycoproteins such as gp120. B, β-defensins can also disrupt viral envelopes by pore formation. C, β-defensins act on host target cells by downmodulating CXCR4 co-receptor.

dramatically diminished in HIV-1 infected subjects.[67] This may contribute to the increased incidence of oral lesions associated with HIV-1 infection among those subjects.

A previous study by Quiñones-Mateu et al[5] revealed that in normal human oral epithelial cells, HIV-1 was found to induce expression of hBD2 and hBD3 mRNA 4- to 78-fold above baseline. However, a recent study by Nittayananta et al[70] reported that HIV-1 failed to induce mucosal innate immune factors including hBDs in differentiated oral epithelium. The failure of HIV-1 to induce innate immune factors in the epithelium was not due to a lack of tissue penetration, as fluorescence-tagged HIV-1 virions were detected several layers deep from the apical surface.[70] HIV-1 failed to infect oral epithelial cells, even after 5 days of exposure.[5] In addition, recombinant hBD2 and hBD3 showed concentration-dependent inhibition of HIV-1 replication. The inhibition was greater against X4-tropic than against the R5-tropic HIV-1 isolates. Recombinant hBD2 and hBD3 have been shown to possess anti-HIV-1 activity by blocking infection via direct interaction with virions as well as down-modulation of CXCR4 co-receptors on immunocompetent cells.[5] In contrast, vaginal, ectocervical, and endocervical cells do not appear to up-regulate hBD2 and hBD3 in response to HIV-1.[71] Thus, it has been postulated that hBDs may act in concert with other HIV-1 inducible epithelial cell-derived substances to inhibit HIV-1 infection at oral mucosal sites.[71] Since hBDs are highly expressed in the oral epithelium,[55,58,72] they are candidates as components of innate resistance to oral HIV-1 infection.

Discussion

Oral mucosa appears to be naturally resistant to HIV-1 transmission. The mechanisms contributing to the protective effect against HIV-1 transmission at mucosal surfaces are incompletely understood. The rarity of HIV-1 transmission by the oral route may suggest either that infective viral particles are absent or low[73], or that viral inhibitory factors are present and effective.[74] HIV-1 transmission via oral route may also be influenced by the time of exposure to the virus before swallowing, the surface area of the mucosal tissues relative to the infectious dose of the oral inoculum, and the infectivity of the presented form of HIV-1 in saliva, breast milk, or semen. In addition, antimicrobial peptides produced by oral epithelial cells may serve as key effector molecules that work in concert to protect the oral mucosa against HIV-1 infection.[4,5]

It has been demonstrated that oral epithelial cells play a crucial role in innate host defense.[24,42] This role may be generated by the constant presence of variety of commensal and pathogenic bacteria in the oral cavity.[44] Oral epithelial cells respond to those microbes by secreting chemokines and cytokines to attract immune cells. They also constitutively and inducibly produce antimicrobial peptides and proteins as part of the innate immune system. However, it is not clear to what degree the local innate immune factors contribute to HIV-1 resistance of the oral mucosa. These antimicrobial peptides have also been found in the vagina and in semen, and yet these compartments are quite susceptible to infection.[75]

Differences in genetic susceptibilities and selective factors at mucosal sites may play significant roles during transmission by any route of HIV-1 infection. The selective factors include host factors such as innate immune response, density of target cells and/or their co-receptors at the site of infection, number of transmitted virions, and the structure of transmitted viral species.[71] Environmental differences including pH, target cells, and mucosal composition at the site of exposure may also affect the efficiency of transmission of the infecting isolates.[76,77] Although HIV-1 RNA, proviral DNA, and infected cells are present in salivary secretions of infected individuals,[78] relatively low infectious HIV-1 can be detected.[73] Since the innate immune response is a key defense against HIV-1, further studies on the oral innate defense against the virus may shed light on new strategies to reduce transmission at genital and anorectal sites, where most infections occur *in vivo*.

Epithelial organization and mucosal integrity may dictate the mechanisms of viral entry and translocation. In addition to the requisite availability of susceptible cells, HIV-1 infection may be dependent upon mucosal integrity. There are potential target cells that may be present in oral epithelium *in vivo*, and HIV-1 may cross epithelial barriers when microtrauma is present and where innate immune cells, including PMNs and LCs are recruited to the site of tissue damage. Mucosal trauma such as erosion or ulceration caused by other oral co-infections may disrupt the epithelial barrier and provide HIV-1 with direct access to the mucosal microcirculation. The immunosuppression caused by fungal, viral, parasitic, and bacterial pathogens may contribute to HIV-1 replication *in vivo*.[79] Keratinization and inflammation of oral epithelia may also lead to differences in tissue susceptibility to HIV-1 infection.

HIV-1 transmission via oral route is rare and this phenomenon *in vivo* could be more complex than previously thought. HIV-1 infection via oral route is unlikely, perhaps due to effective physical barrier of oral mucosa, as well as several factors in saliva, cytokines, and the production of antimicrobial peptides including hBDs by oral epithelial cells that are constitutively expressed, and ready to protect oral mucosa from the infection.[44] Given the differences in structures among these molecules or others to be discovered, their mechanisms of action are expected to differ, and each may function independently or synergistically.

Studies of mucosal infection by HIV-1 have been mainly performed in intestinal and vaginal tissues, which structurally differ from the oral mucosa. HIV-1 transmission and the earliest stage of HIV-1 infection cannot be investigated systematically in humans. *In vivo* studies in animals are not fully representative of all aspects of the infection. Likewise, a single monolayer fails to represent HIV-1 infection across the complex stratified squamous epithelium *in vivo*. Thus, further studies by using a multilayered organotypic tissue model of the human buccal epithelium should be performed. Future studies on the roles of hBDs in HIV-1 infection, and the interplay between HIV-1 and oral epithelial tissue may shed light on the properties of the oral mucosa that potentially contributes to its relative resistance to the virus. Understanding the mechanisms of oral resistance to HIV-1 transmission may lead to the discovery of novel strategies to prevent transmission at other more vulnerable mucosal surfaces.

Conclusions

Mucosal surfaces are the major route of HIV-1 transmission. The interplay between HIV-1 and epithelial cells represents a critical aspect in understanding mucosal transmission of the virus. The epithelium of the oral mucosa is organized into a stratified squamous structure to serve as a physical barrier. Epithelial cells lining the oral cavity cover subepithelial tissues, which contain viral-susceptible host cells including $CD4^+$ T lymphocytes, monocytes/macrophages, and DCs. Oral epithelia are among the sites of first exposure to both cell-free and cell-associated HIV-1 particles through breastfeeding and oral–genital contact. However, oral mucosa is considered to be naturally resistant to HIV-1 transmission, unlike genital and anorectal tissues. Multiple factors at mucosal surfaces and in saliva may collectively contribute to viral resistance in the oral cavity.

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บทความปริทัศน์

การติดเชื้อเอชไอวี-1 ผ่านทางช่องปาก: เพราะเหตุใดจึงเป็นไปได้ยาก?

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บทคัดย่อ

การติดเชื้อเอชไอวี-1 ผ่านทางช่องปากมีโอกาสเกิดขึ้นได้น้อยมาก ปัจจัยต่าง ๆ ที่ผิวเยื่อเมือกและในน้ำลายมีบทบาทสำคัญต่อการยับยั้งการติดเชื้อเอชไอวี-1 ผ่านเซลล์เยื่อบุผิวไปสู่เซลล์เป้าหมาย บทความนี้มีวัตถุประสงค์เพื่อกล่าวถึงภูมิคุ้มกันเฉพาะที่ในช่องปากซึ่งมีผลต่อการยับยั้งการติดเชื้อเอชไอวี-1 เซลล์เยื่อบุผิวช่องปากมีบทบาทสำคัญในระบบภูมิคุ้มกันเฉพาะที่ โดยทำหน้าที่ในการปกป้องทางกายภาพและสร้างสารต้านจุลชีพที่มีคุณสมบัติยับยั้งเชื้อเอชไอวี-1 บทความนี้บรรยายเกี่ยวกับกลไกการส่งผ่านเชื้อเอชไอวี-1 บทบาทของเซลล์เยื่อบุผิว และกลไกในการยับยั้งการติดเชื้อเอชไอวี-1 ในช่องปาก โดยเฉพาะอย่างยิ่ง บทบาทของสารต้านจุลชีพเบต้า-ดีเฟ็นซินในการยับยั้งการติดเชื้อเอชไอวี-1 ที่ผิวเยื่อเมือก