



Oral Microbiota Dysbiosis: Significance in Co-Existence of Rheumatoid Arthritis and Oral Lichen Planus

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Abstract

The oral-cavity and GI tract contains a complex and diverse micro-biome composition community that is important for both health and disease. Major oral infections like Oral Lichen Planus and caries diseases, which are aggravated by oral microbiota dysbiosis, are heavily influenced by it. Similar to the oral microbiota more than 100 trillion bacteria, or the largest variety of microorganisms, reside in the gastrointestinal (GI) system (1,500 distinct species). Chronic systemic diseases can either be caused by or made worse by oral as well as gastrointestinal tract microbial dysbiosis. The oral and gut micro-flora axis is a novel target in the detection, monitoring, and treatment of systemic diseases. According to latest report, the oral and gastrointestinal microbiomes have a significant influence on musculoskeletal health such as rheumatoid arthritis (RA) disease. The genus Haemophilus is a cylindrical, gram negative, facultative-anaerobic microorganism naturally occurring in the oral cavity that needs the coenzymes (V-factor), such as nicotinamide adenine dinucleotide (NAD), hemin, and/or other porphyrins (X-factor). Dysbiosis in the many species of this genus causes a variety of chronic systemic illnesses. The role of oral-gut microbial contact in disease hasn't received enough attention, though. We will emphasize the significance of oral gut micro-flora interaction and its consequences in the etiology of rheumatoid arthritis (RA) and Oral Lichen Planus (OLP) in this article. A thorough knowledge of the involvement of the oral-gut microbiome axis in disease pathogenesis would assist in accurate diagnosis, prognosis, and successful therapy.

Keywords: *oral–gut micro flora; dysbiosis; rheumatoid arthritis (RA); Oral Lichen Planus (OLP); Haemophilus; Chronic systemic diseases; LPS.*

Introduction

There are at least 10 times more microorganisms on and in the human body than there are human cells. Since bacteria "laid" in the interior mucosae (like reproductive organs, respiratory-tract, and gastrointestinal-tract) as well as externally in the body (such as skin and hair), humans are more prokaryotic than eukaryotic. Even among healthy people, the microbial community is extremely diversified. The pattern of microbial communities in each microorganism's environment varies from one individual to another (Albuquerque-Souza and Sahingur; Park et al.; Qin et al.). The human microbial biome is made up of a wide range of microorganisms, such as viruses, bacterium, archaea, protozoan, and fungi. The equilibrium between homeostatic health and pathology is governed by such a varied and multifarious population of microorganisms, which also plays a role in the etiopathogenesis of dysbiotic infection and offers the host significant functional and immunologic advantages during eubiosis (Iebba et al., 2016). The two main microbial habitats, the oral passage and the gut, are important in diseases linked to the micro flora. The oral and gut barrier keeps both microbiome profiles separate, irrespective of the fact that the intestine and oral region are one continuous area linked by the gastrointestinal (GI) tract. Notably, pathological situations in the GI tract have shown characteristic oral-resident species (Khor et al., 2021). These microorganisms provide their host with important physiological benefits including immunologic homeostasis and pathogen invasion tolerance (Table 1). Dysregulation of the microbial communities in the mouth and gut is a precursor to many oral and systemic illnesses, including as cancer, autoimmune disorders, and inflammatory diseases. Inherent barrier failure, immunological dysfunction, pro-inflammatory signaling pathways, and biochemical imitation can all contribute to this dysregulation (Belkaid & Hand, 2014; Sadrekarimi et al., 2022). Instead of using an integrated approach, the majority of studies on the dental and intestinal micro biomes has been done in isolation and has focused on individual systems. Recent investigations have demonstrated the role of the microbiota composition in inter-organ networks. It has been observed that fecal-oral transmission and intestinal colonization of oral microbiota regularly take place and influence pathological events in the human. (Charoensappakit et al., 2022; Park et al., 2021).

In the majority of investigations on the microflora of different areas of the human oral cavity, Haemophilus and other facultative Gram-negative rods have gotten special attention. This bacterial group is sometimes regarded as a minor component of the oral bacteria ecology (Kovalenko, 2021). The genera Haemophilus has a variety of pathogens that cause a range of illnesses but share a similar morphological structure and a required blood-derived nutrients for growth, which gives the genus its name (Musher, 2011).

Organ surface	Genera	Reference
Tooth Surfaces	<i>Actinomyces, Fusobacterium, and Veillonella,</i>	(Caselli et al., 2020)
Soft Tissue Surfaces	<i>Veillonella , Prevotella, Streptococcus, Haemophilus, Porphyromonas , Leptotrichia, Neisseria and Actinomyces,</i>	(Ren et al., 2017; Zhang et al., 2021)
Saliva	<i>Veillonella Actinobacteria and Porphyromonas, Fusobacteria, Haemophilus, Neisseria, , Prevotella, Streptococcus, and Gemella</i>	(Murugesan et al., 2020)
Intestinal flora	<i>Bacteroides and Prevotella Actinobacteria, Proteobacteria</i>	(D'Argenio & Salvatore, 2015; Song et al., 2021)
Uro-genital tract	<i>Firmicutes, Bacteroidetes, Actinobacteria</i>	(D'Argenio & Salvatore, 2015)

Table 1: Normal microbiota in human oral-cavity and gut

Based on the antigenic nature of the envelope glycoproteins, the major pathogenic species, *Haemophilus influenzae*, is classified into enteric coated or typable strains, which there are seven subspecies (a, b, c, d, e and f plus e'). The most virulent agent in this group, type b *H influenzae*, frequently injures infants under 2 years old by invading their bloodstream and causing meningitis. Newborn, toddlers, and adult who have respiratory tract infections frequently get them from non-typable strains (Adderson, 2021; Baron et al., 1996). *H influenzae* is a common cause of meningococcal disease (meningitis), pyogenic pneumonia, and blood poisoning in kids, but it can also cause chronic inflammatory disease, erysipelas, infectious arthritis, and bone infection. According to estimates, it has a fatality rate of 5% and a 15–30 percentage chance of leading to neurological disability. The risk is highest during the second semester of life. (Olivieri et al., 2021).

For the purpose of removing pathogenic microbes as well as accepting symbiotic microorganisms, unique anti-inflammatory mechanisms have been established by the buccal cavity immune system (oral as well as mucosal tolerance). However, the mucosal inflammatory response also needs to provide localized responses against environmental risks (e.g., invading pathogenic microorganism) (Tlaskalová-Hogenová et al., 2004). Pathogenic microorganisms and their toxins, as well as poorly performing mucosal immune response systems, can alter intestinal mucosal homeostasis. On the other hand, a manifestation of pathologically elevated immune activity may cause a variety of inflammatory

diseases. Therefore, alterations in the processes governing mucosal immunity or abnormalities of mucosal barrier functionality might lead to a variety of chronic illnesses. This might encompass autoimmune disorders beginning on mucosal surfaces or progressing there during their entire course, as well as viral diseases, immunological disorders (allergies), and multi-organ dysfunction. (Ahluwalia et al., 2017; Bullard et al., 2022).

A persistent inflammatory condition of the oral mucosa known as oral lichen planus (OLP), it usually affects women during their 40s (Ismail et al., 2007). Six clinical subtypes of OLP have been identified: erosive plaque, papular, atrophic, reticular and bulbous. Erosional and reticular variants, which have white-lines and lesions, are the most prevalent (Lauritano et al., 2016). Speaking, swallowing, and eating can all be painful for persons with OLP. In contrast to reticular lesions, which are often asymptomatic, atrophic and erosional plaques are frequently agonizing. Despite the fact that a T cell-mediated immune response has been associated with the onset of OLP, the pathophysiology and etiology of OLP are still unknown (Jung & Jang, 2022).

Recent scientific studies have also emphasized how the gut microbiota affects various pathologic disorders that frequently affect far-off anatomical areas including the liver, brain, heart, and skeleton system. These studies have called attention to the gut micro-biota's immunomodulatory impact on these organs (Schroeder & Bäckhed, 2016). The involvement of bacteria in the health of bones and joints has been explained by a number of processes and variables. Many essential vitamins, including folate, pyridoxal 5-phosphate, vit-B12, vit-B7, thiamine (B1), vit-B5, vit-B3, phyloquinone, and tetrahydrofolate (THF), which are existent in the gastrointestinal microbiota and are essential for the health of the musculoskeletal system (Kamada et al., 2013). It has been noted that rheumatic arthritis, particularly Juvenile rheumatoid arthritis, rheumatoid arthritis (RA), dermatitis, and the associated pelvospondylitis ossificans, such as ankylosing spondylitis (AS) and Reiter's disease might affect the gut micro flora. It has been proposed that gut bacteria play a vital role in the etiopathogenesis of the aforementioned illnesses (Drago et al., 2019; Wu et al., 2010). The autoimmune disorder rheumatoid arthritis (RA) is a persistent, inflammatory infection that causes systemic complications and premature mortality. The primary features of rheumatoid arthritis include collagenous hyperplasia, rheumatoid factor (RF) as well as anti-citrullinated-protein-antibody (ACPA) secretion, articular cartilage-bone, as well as systemically symptoms such heart, lung, psychiatric, skin, and skeletal diseases. (Jang et al., 2022).

Targeting molecular biomarkers and inflammatory mediators has been proven to be an efficient strategy in the developing field of precision medicine for modifying host immune response. Although

links among the human immune system, microbiota, and systemic diseases are becoming increasingly clear, additional study and interdisciplinary cooperation will be needed to fully understand the complex interaction and potential future advancements in treatment methods. In this review, we have mainly focused on the role of oral microorganism, *Haemophilus*, interaction and its effects in the progression of rheumatoid arthritis (RA) and oral lichen planus (OLP). A comprehensive understanding of the involvement of *Haemophilus* species in the pathophysiology of both diseases would aid in accurate diagnosis/prognosis and efficient treatment.

Oral-Gut Microbiota: Cross-talk and Exclusion

The buccal cavity is one of the body's major reservoirs of microbes, and it has been the subject of extensive investigation for recent time. The mouth microbiota, a complex microbial population that habitat in the buccal cavity, is mostly made up of bacteria but also comprises viral, protozoa, fungus, archaea, bacteriophage, and extremely tiny bacteria from the candidate phylum radiation group (Verma et al., 2018). More than 500 distinct bacterial species make up the oral microbiota, which began to grow within the first few minutes of a newborn existence. The specific composition of micro flora varies from individual to individual depending on a number of variables including age, diet, and lifestyle decisions like smoking and physical exercise. (Thomas et al., 2021). In a healthy anatomical condition, these bacteria coexist with the human body in a symbiotic relationship (Table 2). There are two equilibrium state: the one between propagation of the various species and the host immunological defenses system, and another between the various species of microorganism itself. When this balance is disrupted by dysbiosis, one or more species of bacteria grow and, at least briefly, seize control of the immune system(Peng et al., 2022).

The intestinal microbiome plays a critical responsibility in preserving human health and contains over 10-100 trillion microbial cells, the majority of which are varied bacterial symbiotic organisms, colonized opportunist pathogen (COPs), and simple opportunist pathogen (SOPs) in a homeostatic ratio(Kulkarni et al., 2019). The beneficial bacteria and the latent opportunist pathobionts (COPs and SOPs) cohabit in the gut in a cooperative way as a "good gut" and regularly invade, colonize, and remain there without causing symptoms. Nonetheless, any disruption in the proportionate cohabitation of COPs or SOPs dwelling alongside the symbiotic organisms results in dysregulation, sometimes known as a "leaky gut," and when these opportunistic bacteria reach a certain threshold, they can cause serious severe, prolonged, or underlying human illnesses. Health condition, environmental variables, genetics, and even life styles can change the human gut microbiota patterns (Price et al., 2017; Singhvi

et al., 2020). According to the metagenomic research, the bacterial population that lives in the human gut controls metabolic processes such as amino acid synthesis and carbon metabolism (Zhu et al., 2010). Microbial-associated-molecular-patterns (MAMPs) and pathogen-associated-molecular-patterns (PAMPs) are conserved molecular motifs shown by microorganisms that may be identified by the host through pattern-recognition-receptors (PRRs), such as toll-like-receptors (TLRs) (Ding et al., 2022).

The Human-Microbiome-Project (HMP) and the Human-Oral-Microbiome-Database (HOMD) are two significant oral microbiome datasets that were emerged in previous decades. The goal of HMP is to describe the ecosystem of human microbial populations and to investigate various ways microbes can affect human health and illness. The mouth canal, nasal passages, vaginal, intestine, and epidermis are the five main areas of the human body where it maps the meta-genomics of micro-organisms (“The Integrative Human Microbiome Project,” 2019).

Core Oral Microbiota	Types of microbial population	Reference
Healthy individual	Firmicutes (<i>genus Granulicatella</i> and <i>Streptococcus</i>), <i>Treponema</i> , Actino-bacteria (<i>genus Corynebacterium Actinomyces</i> and <i>Rothia</i>) <i>Veillonella</i> Fuso-bacteria (<i>genus Fusobacterium</i>), Bacteroidetes (<i>genus Prevotella</i> , <i>Capnocytophaga</i> , <i>Prevotella</i> , and <i>Porphyromonas</i>), Proteo-bacteria (<i>genus Haemophilus</i> and <i>Neisseria</i>), <i>Porphyromonas</i> ,	(Zaura et al., 2015)
Microflora in female during menstrual cycle	<i>Campylobacter</i> , <i>Haemophilus</i> , <i>Oribacterium</i> , and <i>Prevotella</i> ,	(Bostanci et al., 2021)
Pregnant women	<i>Neisseria</i> , <i>Porphyromonas</i> , and <i>Treponema</i>	(Saadaoui et al., 2021)

Table 2: Oral microbiota in a healthy person under various situations

Physio-pathologic significance of oral microbiota in systemic inflammation

Emerging reports from the published research suggests a linkage between the presence of an imbalance in the oral flora and the development and/or worsening of several systemic illnesses(Lamont et al., 2018). These illnesses share a pathogenic pathway based on the presence of a low-grade systemic inflammatory state, which cannot be resolved or stabilized in the presence of oral microbiota dysbiosis. Additionally, other researchers suggested that microbes can induce dysbiosis in the oral microbiota, which can circulate throughout the body or release some of its components into the circulation, creating difficulties far from where they first began to proliferate (Kaur et al., 2021). The term "bacterial meta factors" refers to all bacterial components (such as lipopolysaccharide, flagellin, and teichoic acid) that are potential of pathogenicity or immune system activation throughout physiology and physiopathology (Hettne et al., 2007).

Bacteria or their parts, such as the endotoxin (lipopolysaccharide-LPS), found on the outer-membrane of Gram negative bacteria, are a constant resource of infection and inflammation that pass through the epithelial barrier, enter the circulation, and affect a number of different organs in the body. Dysbiosis of the oral microbiota is the primary cause of this bacterial translocation. The disruption of the salivary bacterial composition causes overabundance of gram negative as well as gram-positive bacteria or its disease causing factors. Pathogen-Associated-Molecular-Patterns (PAMPs), which are identified by Pattern-Recognition-Receptors (PRRs) of innate immunity cells, are used by oral microorganism or meta-factors to stimulate intrinsic immunological responses.

Vaiours surface molecules, such as teichoic acid (unique to gram positive bacteria) or lipopolysaccharide, serve as PAMPs (gram negative specific). Similarly, toll-Like Receptors are a class of receptors that are also included in Pattern-Recognition-Receptors (Zelkha et al., 2010). When oral microbiota dysbiosis causes systemic disorders, there are two main reasonable mechanisms (through bacterial translocation in the blood) that might be to blame for an increase in pro-inflammatory cytokines. The other is a sequence of protein kinase-catalyzed phosphorylation chain events required for the transmission of an inflammatory signal to the nucleus of a cell. Several pathways, including MAPK (Mitogen-Activated-Protein-Kinases), and JAK/STAT, IKKs (Inhibitor of Kappa-B-Kinases), are employed to activate the inflammasome such as Janus-Kinase (Signal Transducers and Activators of Transcription) (Thomas et al., 2021) .

Rheumatoid arthritis (RA) co-morbid with Oral lichen planus (OLP)

Oral lichen planus is a skin and mucous membrane inflammatory condition. It causes white lesions that resemble plaques or reticulated patterns (Cheng et al., 2016). It is a chronic inflammatory condition related to T-cell that affects more women than males, especially those who are over fifty. Although it's unclear if oral microbes affect OLP disease status, certain research have supported the link between OLP and oral microbes (Yu et al., 2020). In recent decades, considerable emphasis has been placed on the patho-physiology of OLP caused by microbial infection. For examples, one of the major causes of OLP is thought hepatitis C virus (HCV) infection (Deng et al., 2020). A research carried out by Li et al. in 2019 elaborated that oral bacterial composition alterations might impact the immunological responses of host and contribute to the progression of the OLO. Dyregulation of the salivary microbiome (i.e., lower salivary mycobiome bio-diversity and higher bacterial bio-diversity) contributes to OLP (Villa et al., 2021). Antimicrobial peptides such as histatins, defensins (both α and β), and precursor of cathelicidin hCAP-18 (identified to as LL-37) are considered to be involved in OLP. According to Davidopoulou et al. (2014), LL-37 can protect from dangerous microorganisms and hasten the healing of wounds, due to the fact that people with this condition were shown to have higher amounts of cathelicidin than the general population. There was a distinct correlation between the degree of the disease progration and the quantity of the peptide produced. (Davidopoulou et al., 2014). The pathogenetic processes of OLP production suggest an autoimmune response in which T cells infiltrate basal keratinocytes that have undergone antigen modification. In OLP, macrophages and a modest number of lymphocytes make up the inflammatory infiltrate. T-lymphocytes predominate over B- lymphocytes, and CD4+T-helper-lymphocytes are prevalent than CD8+ T (cytotoxic/suppressor) lymphocytes. Research also suggest that various auto-immune processes are the cause of the pathological condition known as autoimmunity disease (AID), and it could be multifactorial (Rodríguez-Núñez et al., 2001).

OLP frequently co-occurs with other pathological conditions, including various autoimmune disorders such diabetes mellitus (type 1), thyroid problems, and rheumatoid arthritis (De Porras-Carrique et al., 2022). Inflammation and swelling of the synovial membrane are hallmarks of the immune system mediated, chronic-inflammatory-disease known as rheumatoid arthritis. The major clinical symptoms of rheumatoid arthritis are extra-articular lesions and persistent, symmetric, polysynovial arthritis (Chung et al., 2015). In 2013, López-Jornet conducted research on the relationship between autoimmune disorder and oral lichen planus (OLP), comparing OLP patients with a control group. His findings revealed that the coexistence of RA and OLP may be responsible for the onset and development of lichen planus. However, it is challenging to determine the degree of relationship

between the two disorders because there are so few research that address this cohabitation (López-Jornet et al., 2014). The correlation between Oral lichen planus and other autoimmune conditions raises the potential that individuals with OLP may be developing an autoimmune condition that makes them more likely to engage in autoaggression against various targets. The research published in this area have found a link between rheumatoid arthritis (prevalence value = 2.40%) and OLP. However, the information that is now available is based on a few studies and patients, making abovementioned findings weak and lacking in support (De Porrás-Carrique et al., 2022).

Possible significance of Haemophilus species dysbiosis in RA and OLP comorbidity

Haemophilus is poorly differentiated coccobacilli bacteria in the Pasteurellaceae family. Haemophilus bacteria are multinucleated bacteria due to the vast diversity of forms they occasionally acquire, despite the fact that they are normally tiny coccobacilli (BORENSTEIN & SIMON, 1986). No matter the niche location in oral cavity, the healthy person carries the Haemophilus genus throughout all oral locations (Segata et al., 2012). Remarkably, pathological scenarios have resulted in the detection of typical oral-resident species throughout the GI tract (Del Castillo et al., 2019). Haemophilus bacteria have proteins known as auto-transporters, which are present onto the outer membrane and perform a number of significant functions such as adhesion, invasion, proteolytic activity, and cytotoxic activity. Respiratory tract illnesses in newborns, children, and adults are frequently caused on by Haemophilus influenzae (Baron et al., 1996; Spahich & St Geme III, 2011). Other Haemophilus species are less common pathogenic. Sometimes, pneumonia or bacterial endocarditis is carried on by Haemophilus parainfluenzae. Additionally, chancroid is caused by Haemophilus ducreyi. The bacteria Haemophilus aphrophilus, which occasionally results in bacterial endocarditis, are a natural component of oral flora. Both Haemophilus haemolyticus and Haemophilus aegyptius, which produce Brazilian purpuric fever and conjunctivitis, were formerly classified as nontypable H. influenzae strains based on their proteolysis ability or agglutinate red blood cells, respectively (Musher, 2011).

An article published on bacterial populations found within OLP lesions (2020) revealed that even though the relative abundance of Haemophilus parainfluenzae was substantially lower than it was on the surface of normal control. However, H. parainfluenzae was still the dominant species in the OLP intra-tissue community (Baek et al., 2020). Contrarily, there were considerably more Haemophilus, Cellulosimicrobium, Coryne-bacterium and Campylobacter in the healthy than in the OLP group. Few species, meanwhile, showed significantly differing abundance levels amongst the three groups. Prevotella melaninogenica exhibited considerably greater levels in reticular OLP compared to

Haemophilus parainfluenzae, and *Streptococcus parasanguinis*, which were less prevalent in erosive OLP (Wang et al., 2016).

A research article published in a scientific report journal accomplished that bacteria have a unique role in the progression of OLP by damaging epithelial barriers, internalizing into epithelial-cells and T-cells, and inducing T-cell mediated chemokines (Choi et al., 2016). In line with the study by Deng et al., the comparative density of gram negative bacteria, such as *Derxia*, *Haemophilus*, and *Pseudomonas*, reduced in the OLP patients, and the levels of TLR4, NF-B p65, IL-6, and TNF- were all enhanced, suggesting that the Lipopolysaccharide of *Haemophilus*, *Pseudomonas* as well as *Derxia* potentially adhere to the immunological cellular membranes surface receptor (TLR4) to conduct cellular responses. TLR4 activates the NF-B signaling route as well as other associated pathways such as the TNF- α - tumor-necrosis-factor-receptor-1 related signaling system and the JAK/STAT mediated signaling pathway, which is connected to IL-6; and the TGF signaling pathway, which can influence T lymphocyte cell immunity (Deng et al., 2020). This indicates that the alteration in the flora's ratio disturbed the delicate balance of the original flora, disrupting the physical barrier provided by the epithelium (Deng et al., 2020).

It's noteworthy that autoimmune disorders typically affect tissues other than those where the microbiome is anticipated to play a pathogenic function. Beginning in the twentieth century, when it was established that treating periodontal infections helped RA patients with their symptoms, dysbiosis in the oral microbiota provided significant hints for relevant causes of the disease (Sturridge, 1918). Lately, it has been abundantly evident that RA development is greatly influenced by dental health, particularly the oral flora (Diamanti et al., 2016; du Teil Espina et al., 2019). There are various results supported association of RA with *H. influenza* (Ike, 1998). Similarly other species such as *paraphrohaemolyticus*, *parainfluenzae* and also involved in pathogenesis of RA (Faintuch & Faintuch, 2019). We used the mBodyMap data source, a curated database, on human body microorganisms and their relationships to health and diseased conditions. The findings revealed an association between rheumatoid arthritis and various species of *Haemophilus*, such as *H. haemolyticus*, *H. influenza*, *H. parahaemolyticus*, *H. parainfluenzae*, *H. paraphrohaemolyticus*, and *H. sputorum* (Table 3) (Jin et al., 2022). Sabrina Weber also reported that *H. haemolyticus* have been seen in n immune-compromised patients with septic knee arthritis (Weber et al., 2020).

Name	relative_ abundance_avg	relative_ abundance_me d	relative_ abundance_std	relative_ abundance_su m
<i>Haemophilus haemolyticus</i>	0.11452	0.05326	0.1528	2.86292
<i>Haemophilus influenza</i>	0.25065	0.03523	0.51182	6.51695
<i>Haemophilus parahaemolyticus</i>	0.10894	0.02908	0.16015	2.2878
<i>Haemophilus parainfluenzae</i>	2.82519	1.86541	3.12644	76.28007
<i>Haemophilus paraphrohaemolyticus</i>	0.15793	0.0226	0.46067	3.79038
<i>Haemophilus sputorum</i>	0.0586	0.01733	0.10176	1.28911

Table 3: Association of Haemophilus species with Rheumatoid Arthritis (data procured from mBodyMap; <https://mbodymap.microbiome.cloud>)

According to a number of authors, it was hypothesized that Oral lichen planus and rheumatoid arthritis problems are related. Nevertheless, on the particular abnormal immunological pathways nothing is known. With this review, we theoretical hypothesized that OLP pathogenesis results in epithelial barrier cells being damaged and Haemophilus species bacterial lipopolysaccharide entangling to the immune cell membrane to start various signal transduction (Deng et al., 2020). The infection and inflammation that led to this attachment crossed the epithelial barrier, entered the bloodstream, and activated a number of signaling pathways including MAPK, IKKs, and JAK/STAT (Thomas et al., 2021). As a result, the Janus kinase/STAT pathways are activated, which is a crucial stage in the pathogenesis and progression of rheumatoid arthritis (Malemud, 2018) (Figure 1).

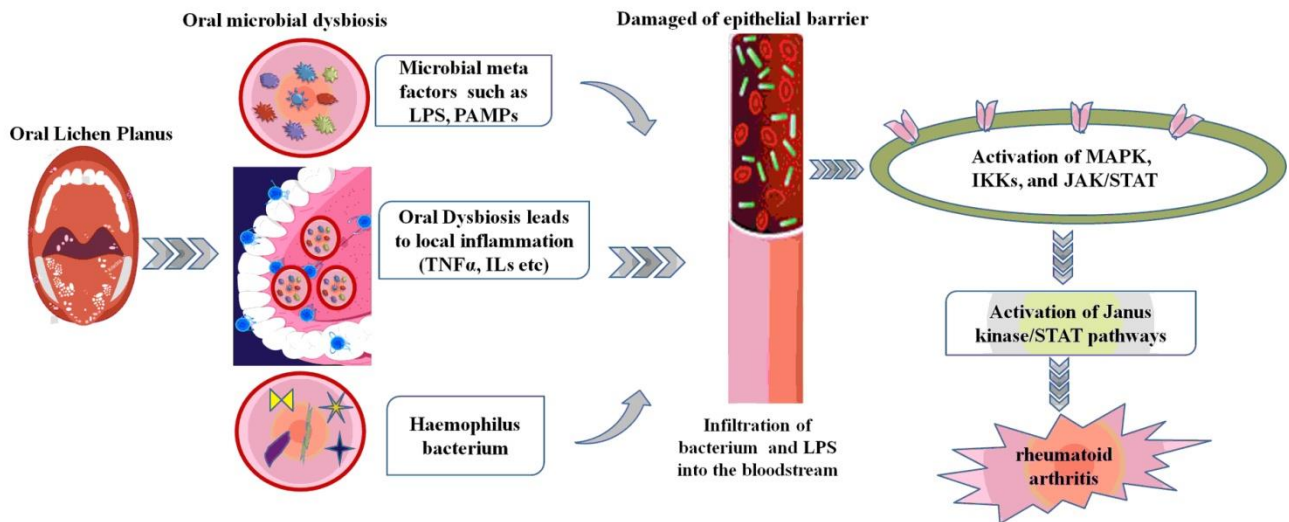


Figure 1: Potential role of Haemophilus species in the co-existence of Oral Lichen Planus and Rheumatoid arthritis

Conclusion

Microbes are a significant risk factor for both oral and systemic chronic diseases. Even if the function of microorganisms and the microbiota is still not fully understood, any alteration in dental health should be taken into consideration as a warning sign in the fight against the onset of systemic disorders. We have outlined the potential contribution of Haemophilus species in the coexistence of OLP and RA disease in this review. However, there is no direct connection among Haemophilus, RA, and OLP. It was abundantly obvious that microbial-host interactions might activate inflammatory and immunological responses in patients. This means that the oral microbiota can affect the body's metabolism, immunology, and central biological processes, resulting in dysbiosis, which is linked to a variety of human disorders, from OLP to RA. The potential link between OLP and RA caused by the dysbiosis of Haemophilus species requires more research with bigger sample numbers from various geographical locations.

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