

Mechanisms by which smoking worsens periodontitis discovered

Researchers identify altered expression of genes that worsens periodontitis among smokers, and a new target molecule for therapies

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Researchers identify altered expression of genes that worsens periodontitis among smokers, and a new target molecule for therapies

Smoking tobacco is known to worsen symptoms of periodontitis and reduce responsiveness to treatment. Using high-resolution spatial transcriptomics, researchers identified differences between smokers and non-smokers in the expression of genes that weaken gum epithelial integrity and cause

bone damage through inflammation. They also identified CXCL12 secreted by endothelial cells in gums as a crucial mediator of immune-cell recruitment that drives excessive inflammation. CXCL12 is a possible target for new therapies against periodontitis aggravated by smoking.

Healthy gums, or periodontal tissue, are a key to good oral health. Gums provide crucial nutritional, immunological and mechanical support to the teeth and jaws. Unfortunately, millions of people suffer from severe chronic inflammation of the gums, a condition called periodontitis. Periodontitis occurs when the immune system responds abnormally to microbes entering the gum tissue. Over time, periodontitis causes gums to recede, bones surrounding the mouth to weaken, and may even lead to the loss of teeth.

Previous research has shown that tobacco smokers are not only more likely to develop periodontitis, but the disease also progresses faster, shows more severe symptoms, and



Smoking is known to worsen symptoms of periodontitis. This study unravels the molecular mechanisms that worsen periodontitis after exposure to tobacco smoke.

responds poorly to treatment compared with non-smokers. These differences have been linked to smoking-related alterations in:

- the gum's epithelial barrier,
- fibroblast function and epithelial–fibroblast communication, and
- immune and inflammatory responses within periodontal tissue.

Yet, the precise cellular mechanisms have remained unclear due to limitations in available research technologies.

A team of researchers from Sun Yat-sen University, China, led by Professor Chuanjiang Zhao, have used high resolution Visium HD single-cell spatial transcriptomics to analyze the different molecular pathways activated in smokers and non-smokers with periodontitis. Their findings have been published in [Volume 17 of the International Journal of Oral Science](#) on August 01, 2025.

“Understanding the complex cellular interactions that contribute to disease progression in smoking-associated periodontitis is important,” remarked Prof. Zhao regarding the importance of this study. He added, “By employing the Visium HD platform, we aimed to map the spatial distribution of different cell types within healthy and diseased periodontal tissues and identify smoking-induced changes in gene expression patterns across various cell populations.”

To explore how smoking affects epithelial cells, the team first examined cells exposed to bacterial lipopolysaccharide (LPS) alone versus LPS plus nicotine. The combination triggered larger changes in genes related to epithelial structure, barrier integrity, communication, and inflammation—suggesting that smoking weakens the epithelial barrier and heightens inflammatory susceptibility.

The researchers then compared gene expression across multiple cell types in tissue samples from healthy gums (HG), non-smokers with periodontitis (P), and smokers with periodontitis (SP).

Describing differences in fibroblasts, cells that maintain gum structure and integrity, Prof. Zhao says, “Our results revealed that individuals in the smoking group, as opposed to healthy controls, presented upregulated expression of genes linked to ageing, intrinsic apoptotic signalling, and mitotic processes.” SP fibroblasts also showed elevated expression of genes associated with inflammation and immune cell recruitment, helping explain the more pronounced tissue damage in smokers.

Spatial transcriptomic analysis further revealed that endothelial cells and macrophages were positioned in close proximity only in smoking-associated periodontitis, enabling stronger inflammatory interactions. SP tissues also contained a higher proportion of pro-inflammatory macrophages, which played a central role in driving periodontal destruction.

Interestingly, this recruitment and activation of macrophages seemed to depend on one

molecule –C-X-C motif chemokine 12 or CXCL12. In the presence of CXCL12 secreted by endothelial cells, macrophages turned pro-inflammatory. Suppressing CXCL12 secretion made the macrophages anti-inflammatory. As further confirmation of these findings, the team found that CXCL12 suppression reduced inflammation and bone damage in mice with periodontitis aggravated by nicotine.

“Targeting CXCL12 shows promise in mitigating inflammation and bone resorption in individuals with smoking-induced periodontitis,” says Prof. Zhao, describing a potential new therapeutic approach. He concludes, “Future research should investigate local delivery systems, like nanoparticles or liposomes, to reduce systemic side effects and improve treatment precision.”

Reference

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About Sun Yat-sen University, China

Founded in 1924, Sun Yat-sen University (SYSU) is one of China’s largest and most prestigious universities. The university’s nearly 34,000 undergraduate and 36,000 postgraduate students pursue degrees in over 250 majors and disciplines across humanities, social sciences, natural sciences, medical sciences, and engineering. SYSU has five campuses across the cities of Guangzhou, Shenzhen and Zhuhai, which house 330 labs and research institutes. 10 hospitals are affiliated with the university, including the Hospital of Stomatology. For 2026, Times Higher Education places SYSU in the top 250 universities globally and in the top 20 within China.

Website: <https://www.sysu.edu.cn/>

About Professor Chuanjiang Zhao from Sun Yat-sen University

Professor Chuanjiang Zhao is a faculty member and Doctoral Adviser at the Guanghua School of Stomatology, Sun Yat-sen University. He completed his PhD in 2003 from Sichuan University. His research focuses on the causes of and treatments for periodontitis. Prof. Zhao has authored over 20 SCI-indexed publications as first or corresponding author. He also serves as a member of several national and provincial committees in periodontics and stomatology, and contributes to the editorial boards of academic journals in these fields. In addition to his academic work, he plays an active role in advancing periodontal diagnosis and treatment standards in China.

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