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Editorial

Effect of *Lacticaseibacillus casei* AMBR2 on Epithelial Barrier Function in Chronic Rhinosinusitis With Nasal Polyps

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▸ See the article "*Lacticaseibacillus casei* AMBR2 Restores Airway Epithelial Integrity in Chronic Rhinosinusitis With Nasal Polyps" in volume 13 on page 560.

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Chronic rhinosinusitis (CRS) is a group of disorders characterized by inflammation of the sinonasal mucosa that persists for at least 12 weeks.[1] CRS is generally subdivided into 2 phenotypes: CRS with nasal polyps (CRSwNP) and CRS without nasal polyps (CRSsNP). A defective epithelial barrier is found in patients with CRSwNP along with a decreased expression of tight junction proteins, such as occludin-1 and zonula occludens-1 (ZO-1).[2,3] Additionally, epithelial dysfunction and epithelial-to-mesenchymal transition are commonly detected in severe CRS patients.[4-6]

In the current issue, Martens *et al.*[7] aimed to investigate the effect of *Lacticaseibacillus casei* AMBR2 (*L. casei* AMBR2) on nasal epithelial barrier function of human primary nasal epithelial cells (pNECs) in CRSwNP patients. They also reported that the anterior nares and nasopharynx of CRSsNP and CRSwNP patients had significantly low relative abundance of lactobacilli compared to controls.[8] The authors hypothesized that impaired barrier integrity in CRSwNP could be restored by *L. casei* AMBR2. The pNECs cultured under air-liquid interface from 7 controls and 14 CRSwNP patients were stimulated for 6 hours with 10^7 CFU/mL *L. casei* AMBR2. It was found that the mRNA expression levels of claudin-1 and claudin-4 as well as protein levels of occludin and ZO-1 were significantly increased in pNECs from CRSwNP patients. Blocking TLR2 signaling restored reorganization in pNECs from CRSwNP patients. Especially, IL-4-driven epithelial barrier dysfunction was restored after treatment with *L. casei* AMBR2, which was confirmed by rearranging the expression of tight junctions in a TLR2 signaling-dependent manner.

The upper airway is highly colonized by diverse microbiomes. The dysbiosis of nasal microbiome and biofilm has been suggested to contribute to the pathogenesis of CRS.[9] Besides identifying the nasal microbiome in CRS patients, recent studies have investigated the associations between host and the microbiome. A study showed that *Moraxella* was negatively correlated with up-regulated proteins in CRS, such as Ras-related proteins that

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play a role in basement membrane development.[10] Kim *et al.*[11] revealed a strong association between nasal microbiome in nasal secretion and secreted proteome from nasal epithelium according to disease status. However, we are not aware about mechanisms of interaction between host and the nasal microbiome in CRS. The underlying mechanisms could provide an insight to discover potential therapeutic approaches. Thus, further studies are needed to confirm what molecules secreted from lactobacilli, such as metabolites and proteins, could interact with the nasal epithelium in CRS patients.

Based on the previous and present results, the microbiome could contribute to the pathogenesis of CRS by interacting with host systems. The association between host and microbiome may be a key to unlock therapeutic strategies. Therefore, further efforts should focus on their association.

REFERENCES

1. Fokkens WJ, Lund VJ, Mullol J, Bachert C, Alobid I, Baroody F, et al. EPOS 2012: European position paper on rhinosinusitis and nasal polyps 2012. A summary for otorhinolaryngologists. Rhinology 2012;50:1-12.
PUBMED | CROSSREF
2. Soyka MB, Wawrzyniak P, Eiwegger T, Holzmann D, Treis A, Wanke K, et al. Defective epithelial barrier in chronic rhinosinusitis: the regulation of tight junctions by IFN-γ and IL-4. J Allergy Clin Immunol 2012;130:1087-1096.e10.
PUBMED | CROSSREF
3. Khalmuratova R, Park JW, Shin HW. Immune cell responses and mucosal barrier disruptions in chronic rhinosinusitis. Immune Netw 2017;17:60-7.
PUBMED | CROSSREF
4. Shin HW, Cho K, Kim DW, Han DH, Khalmuratova R, Kim SW, et al. Hypoxia-inducible factor 1 mediates nasal polypogenesis by inducing epithelial-to-mesenchymal transition. Am J Respir Crit Care Med 2012;185:944-54.
PUBMED | CROSSREF
5. Lee M, Kim DW, Yoon H, So D, Khalmuratova R, Rhee CS, et al. Sirtuin 1 attenuates nasal polypogenesis by suppressing epithelial-to-mesenchymal transition. J Allergy Clin Immunol 2016;137:87-98.e7.
PUBMED | CROSSREF
6. Konnecke M, Burmeister M, Pries R, Boscke R, Bruchhage KL, Ungefroren H, et al. Epithelial-mesenchymal transition in chronic rhinosinusitis: differences revealed between epithelial cells from nasal polyps and inferior turbinates. Arch Immunol Ther Exp (Warsz) 2017;65:157-73.
PUBMED | CROSSREF
7. Martens K, De Boeck I, Jokicevic K, Kiekens F, Farré R, Vanderveken OM, et al. *Lacticaseibacillus casei* AMBR2 restores airway epithelial integrity in chronic rhinosinusitis with nasal polyps. Allergy Asthma Immunol Res 2021;13:560-75.
CROSSREF
8. De Boeck I, van den Broek MF, Allonsius CN, Spacova I, Wittouck S, Martens K, et al. Lactobacilli have a niche in the human nose. Cell Rep 2020;31:107674.
PUBMED | CROSSREF
9. Lee K, Pletcher SD, Lynch SV, Goldberg AN, Cope EK. Heterogeneity of microbiota dysbiosis in chronic rhinosinusitis: potential clinical implications and microbial community mechanisms contributing to sinonasal inflammation. Front Cell Infect Microbiol 2018;8:168.
PUBMED | CROSSREF
10. Biswas K, Wagner Mackenzie B, Waldvogel-Thurlow S, Middleditch M, Jullig M, Zoing M, et al. Differentially regulated host proteins associated with chronic rhinosinusitis are correlated with the sinonasal microbiome. Front Cell Infect Microbiol 2017;7:504.
PUBMED | CROSSREF
11. Kim YS, Han D, Mo JH, Kim YM, Kim DW, Choi HG, et al. Antibiotic-dependent relationships between the nasal microbiome and secreted proteome in nasal polyps. Allergy Asthma Immunol Res 2021;13:589-608.
CROSSREF