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LETTER

Emerging Allergens: How Proallergenic Activity Disrupts Epithelial Barriers [Letter]

Ying Wei, Zhenggao Xie

Department of Opthalmology, Nanjing Drum Tower Hospital, Affiliated Hospital of Medical School, Nanjing University, Nanjing, People's Republic of China

Correspondence: Zhenggao Xie, Email zgxie87@163.com

Dear editor

We read with great interest the recent article titled "The Potential Proallergenic Activity of Transschelia pruni-spinosae and Phragmidium rubi-idaei: In Vitro Studies".[1] The study provides compelling evidence that these two rust fungi, commonly infecting plum and raspberry plants, exhibit proinflammatory and barrier-disrupting effects on human respiratory epithelial cells, suggesting their potential role as emerging fungal allergens. The study uses both morphological and molecular identification methods, along with comprehensive in vitro assays, strengthening the validity of their findings. However, we would like to offer several recommendations to further enhance the impact and translational value of this research.

First, the study utilized crude fungal extracts, which, while practical, contain a complex mixture of proteins, polysaccharides, and metabolites. Standardizing these extracts to identify specific allergenic components—such as proteases or chitinases—would greatly clarify the mechanisms underlying the observed proinflammatory effects. For instance, prior research has shown that fungal proteases from Aspergillus and Alternaria can directly disrupt epithelial tight junctions and induce cytokine production.[2,3] Isolating and characterizing the bioactive fractions of T. pruni-spinosae and P. rubi-idaei extracts would facilitate the development of specific diagnostic tools and therapeutic targets.

Second, the authors reported that T. pruni-spinosae extract at 200 μg/mL induced IL-1β production up to 28.7 ± 2.2 pg/mL in BEAS-2B cells and 20.5 ± 1.1 pg/mL in A549 cells, while P. rubi-idaei at 25 μg/mL stimulated GM-CSF release. These values, though statistically significant, are relatively modest compared to those induced by well-established allergens like Alternaria alternata, which can elicit IL-6 and IL-8 levels exceeding 100 pg/mL in similar models.[3] Future studies should include positive controls using known allergenic fungi to provide a comparative framework for interpreting the potency of these newly identified allergens.

Third, the flow cytometry data revealed that P. rubi-idaei extract at 400 μg/mL increased necrosis in A549 cells from 4.7 ± 0.5% to 23.9 ± 1.1%, and T. pruni-spinosae induced ROS production in 11.1 ± 1.0% of A549 cells. While these changes are significant, their biological relevance in the context of chronic allergen exposure remains unclear. Longitudinal or repeated-exposure models could help determine whether subcytotoxic concentrations-such as 12.5 μg/mL or 25 μg/mL-cause cumulative barrier damage or sustained cytokine release, as seen in asthma pathogenesis.[4]

Fourth, the study highlighted a reduction in E-cadherin and occludin fluorescence in epithelial cells treated with fungal extracts, suggesting barrier disruption. However, the mechanisms behind this effect were not fully elucidated. Given that reactive oxygen species (ROS) and metalloproteinases (MMPs) were only mildly elevated (eg, MMP-9 showed no significant change), other pathways-such as protease-activated receptor (PAR) activation or MAPK signaling-may be involved. Previous work has shown that fungal proteases can activate epithelial MAPK pathways, leading to junctional protein degradation.[5] Incorporating pathway-specific inhibitors could help identify key molecular drivers.

Finally, the authors rightly note that their in vitro findings require validation in in vivo models. Animal studies—particularly using murine models of allergic airway inflammation—would help confirm the sensitization potential of these fungi. For example, intranasal challenge with T. pruni-spinosae spores could assess IgE production, eosinophil infiltration, and airway

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hyperresponsiveness, as demonstrated with other fungal allergens.[6] Such models would also allow for dose-response studies closer to real-world exposure scenarios, especially in agricultural settings where spore concentrations can be high.

In conclusion, Sztandera-Tymoczek et al have made a valuable contribution to the field of allergology by identifying two new potential fungal allergens. Their work underscores the importance of expanding allergen screening beyond the commonly studied genera. We believe that addressing these recommendations will not only strengthen their conclusions but also accelerate the translation of these findings into clinical and environmental health applications.

Data Sharing Statement

Data sharing is not applicable to this communication as no datasets were generated or analysed for this communication.

Author Contributions

Ying Wei: Conceptualization, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing. Zhenggao Xie: Conceptualization, Investigation, Writing – review & editing.

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Disclosure

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