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Section 08

SPATIAL METABOLOMICS REVEALS THE ROLE OF PENICILLIC ACID IN CHEESE RIND MICROBIOME DISRUPTION BY A SPOILAGE FUNGUS

Carlismari Oliveira Grundmann[1*], Christopher Tomo[2], Julia Hershelman[2], Benjamin Wolfe[2], Laura Sanchez[1]

cgrundma@ucsc.edu

1- Department of Chemistry and Biochemistry - University of California Santa Cruz, UCSC, 1156 High Street, Santa Cruz, CA, USA. 2- Department of Biology, Tufts University, 200 College Avenue, Medford, MA, USA.

Microbial interactions in cheese rinds influence community structure, fermentation, and the development of sensory properties such as flavor, aroma, and texture[1,2]. However, the chemical mechanisms mediating these interactions in cheeses and other fermented foods remain poorly understood. Here, we investigated how the spoilage mold *Aspergillus westerdijkiae* chemically inhibits beneficial cheese-rind bacteria using microbial community assays, transcriptomics, MALDI-MSI, LC-MS/MS, and genome mining. In cheese rind community and co-culture experiments, *A. westerdijkiae* strongly inhibited bacterial growth, with pronounced effects on *Staphylococcus equorum* and *Brachybacterium alimentarium*. In co-culture with *S. equorum*, transcriptomic profiling revealed broad changes, including upregulation of a putative *bceAB* gene associated with resistance to antimicrobial compounds. The integration of MALDI-MSI, fungal genome mining, and LC-MS/MS revealed spatially localized production of bioactive metabolites at the fungal–bacterial interface, such as notoamides and circumdatins. Additionally, the mycotoxins penicillic acid and ochratoxin B showed broader spatial diffusion compared to the other metabolites, suggesting their primary role in community disruption. The presence of these mycotoxins was confirmed by LC-MS/MS comparison with commercial standards, with penicillic acid concentrations increasing 2.5-fold in co-culture with *B. alimentarium* compared to monoculture. In contrast, interactions with *S. equorum* did not show the same increase but triggered production of distinct metabolites, such as notoamides, underscoring a partner-specific metabolic response. To validate ecological function, purified penicillic acid was tested in cheese curd agar bioassays. After 10 days of exposure, increasing concentrations (10, 100, 1000 µM) produced progressively stronger inhibition of *B. alimentarium*, with only minor effects on *S. equorum* at these concentrations. These results show that *A. westerdijkiae* deploys a context-dependent arsenal of mycotoxins and indole alkaloids, with responses varying by bacterial partner, suggesting species-specific chemical strategies. Together, our findings show that fungal chemical mechanisms disrupt cheese-rind communities by inhibiting beneficial bacteria, leading to likely negative sensory outcomes with implications for microbial ecology and food safety.

References

1. Wolfe, B.E. et al. (2014) *Cell* 158: 422–433.
2. Melkonian, C. et al. (2023) *Nat. Commun.* 14: 8348.

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