



A fungal scent from the cheese

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1 *Highlight on Cosetta et al doi: 10.1111/1462-2920.15223*

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3 **A fungal scent from the cheese**

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12 Running title: Fungal volatile affected bacterial growth

13 Keywords: bacteria-fungi interaction; cheese rind; microbiome; community assembly; volatiles

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16 **Summary**

17 Assembly of microbial communities is shaped by various physical and chemical factors deriving
18 from their environment, including other microbes inhabiting the certain niche. In addition to direct
19 cell-cell contacts, primary and secondary metabolites impact the growth of microbial community
20 members. Metabolites might act as growth-promoting (e.g. cross-feeding), growth-inhibiting (e.g.
21 antimicrobials), or signaling molecules. In multi-species microbial assemblies, secreted metabolites
22 might influence specific members of the community, altering species abundances and therefore
23 the functioning of these microcosms. In the current issue, Cosetta and colleagues describe a
24 unique volatile metabolite-mediated cross-kingdom interaction that shapes the cheese rind
25 community assembly. The study paves the way of our understanding how fungus-produced
26 volatile compounds promote the growth of a certain bacterial genus, a principal connection
27 between community members of the cheese rind.

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30 **Main text**

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32 Since the first formulation of the microbiological tenet '*Everything is everywhere, but, the*
33 *environment selects*' by Baas Becking motivated by Martinus Beijerinck's work (Beijerinck, 1913;
34 Baas-Becking, 1934; De Wit and Bouvier, 2006), microbial ecologists have been researching the
35 factors determining microbial community assemblies. Complex association of diverse microbes in a
36 certain niche is driven by numerous influences from the environment, physical, chemical and
37 biological factors including temperature, humidity, nutrient availability, and various metabolites
38 from other organisms. Microbes can inhibit the growth of each other by producing specific or
39 general antimicrobial compounds, they can gain by acquiring beneficial metabolites secreted by
40 surrounding companions, in specific cases resulting in complex cross-feeding networks (D'Souza *et*
41 *al.*, 2018). In addition, the secreted primary- and secondary-metabolites could convey signaling
42 function that affect development of other microbes (Pishchany and Kolter, 2020). To gain deeper
43 understanding how the 'environment selects', simplified microbial systems are inspected ranging
44 from two or very few members to complex communities.

45 Cheese rind provides a relatively simple, tractable system that repetitively assembles into defined
46 composition of communities dominated by key genera, therefore allows examining microbial
47 succession (Wolfe *et al.*, 2014). The cheese diversity, including smell and taste, around the world is
48 in principle defined by the microorganisms accompanying the fermentation process that that is
49 thought to be invested and used since for 10.000 years. Originating from both natural
50 'contaminating' and inoculated microorganisms, the cheese rind community is dominated by few
51 prokaryotic phyla (*Firmicutes*, *Actinobacteria*, *Proteobacteria* and *Bacteriodes*) and eukaryotes
52 (yeast and molds) that forms a dense, biofilm-like layer around the cheese. The composition of such

53 rind cheese community is dynamic during the fermentation process and defined by abiotic and
54 biotic factors. This exceptional experimental system offers a platform to study interaction among
55 fungi and bacteria. The intricate interplay between these two kingdoms of life has been recently
56 exploited to understand the influence of diverse metabolites in microbial community dynamics.
57 What determines the abundances of microbial genera during cheese rind maturation? How do
58 specific metabolites impact the growth of microbes during the cheese ripening?
59 Cosetta and colleagues (2020) answer these questions and reveal how volatile organic compounds
60 (VOCs) produced by widespread cheese rind fungi specifically stimulate the growth of specific
61 cheese rind bacteria (Fig. 1). Exploiting a novel 'microtiter-plate sandwich' system, in which volatile
62 producers and responders are physically separated in the wells of the bottom and top plates,
63 respectively, but having common airspace, the influence of VOCs produced by five different cheese
64 rind derived fungi was inspected on the growth of bacterial isolates inoculated on cheese curd agar.
65 Intriguingly, the growth of various *Vibrio* species was generally promoted by the VOCs produced by
66 cheese rind fungi, including *Debaryomyces*, *Penicillium*, and *Galactomyces* isolates, but not when
67 bacteria and fungi were co-cultured. The promotion of *Vibrio* growth was also observed when a
68 synthetic bacterial community, representing a typical rind bacteria composition, was exposed to the
69 VOCs of the fungi. Characterization of the transcriptional profile of *Vibrio* population revealed that
70 VOCs promote the expression of genes involved in glyoxylate shunt, which allows bacteria to utilize
71 acetate and other fatty acids as carbon source. Indeed, esters and fatty acids, like acetic acid, are
72 widely detected in ripening cheeses, contributing to the sweet, fruity perception of surface-ripened
73 cheeses (Urbach, 1997). In line with this general observation, acetate-containing fatty acids could
74 be detected using gas chromatography/mass spectrometry in the headspace of cheese rind fungi
75 (Cosetta *et al.*, 2020). Finally, acetic acid, as well as heptyl acetate and methyl isobutyrate

76 specifically increased *Vibrio* growth and shifted the abundance of *Vibrio* within the synthetic
77 microbial community.

78 The work of Cosetta and colleagues provides a valuable insight on VOC-mediated microbial
79 interaction. Moreover, it reveals how growth promotion of specific genus shifts the composition of
80 a synthetic microbial consortium and pinpoints the direct stimulation of growth by acetate-
81 containing VOCs through metabolism in the glyoxylate shunt. VOCs have diverse impact on microbial
82 growth and development, acting as nutrients, environmental modulators or signal molecules (Tyc
83 *et al.*, 2017). Acetate-containing VOCs has been detected in numerous microbial systems (Ryu *et al.*,
84 2020), and while acetate acts a metabolic signal inside bacterial cells (Wolfe, 2005), among microbial
85 cells, it can also act as signaling compound, altering development and differentiation, for example
86 stimulating biofilm formation (Chen *et al.*, 2015). While the broad impact of this small volatile
87 molecule has been previously suggested, Cosetta and colleagues have uniquely demonstrated the
88 impact of microbial community composition.

89 The creation of synthetic microbial communities provides a tractable system to dissect the influence
90 of various VOCs or generally of secondary metabolites to reveal the true nature of these compounds
91 in nature. The activity of secondary metabolites has been traditionally explored in pairwise
92 interactions and only recently, the influence of these specialized metabolites examined on microbial
93 communities (Kiesewalter *et al.*, 2020). Once thought to act as fierce antimicrobial compounds, the
94 real ecological impact of secondary metabolites within complex microbial communities still to be
95 explored. The scent of the cheese is not only appreciated by its consumers, but also by the microbial
96 community during the anciently acquired food fermentation process.

97 **Acknowledgements**

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101 **Competing Interests**

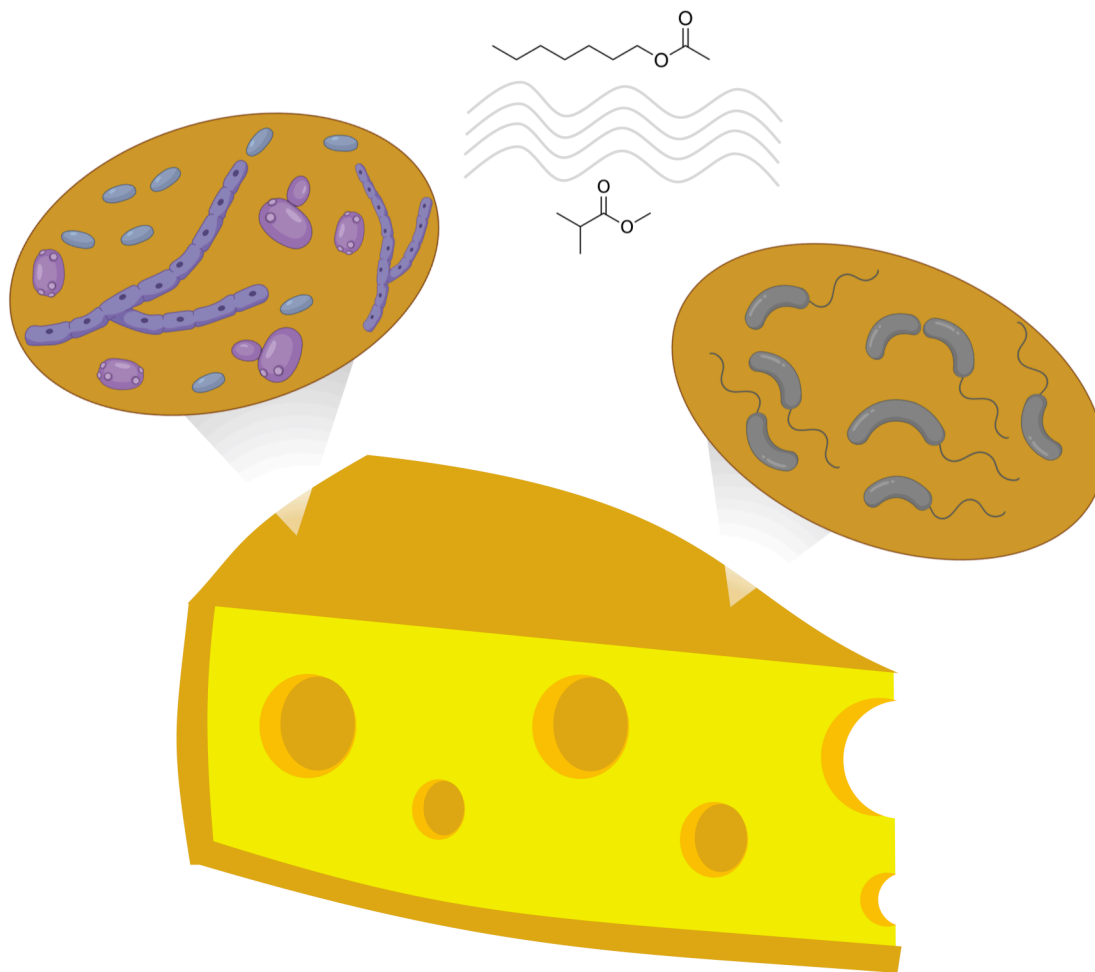
102 The author has no competing interests to declare.

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130 tractable systems for in situ and in vitro studies of microbial diversity. *Cell* **158**: 422–433.
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135 Fig. 1 VOCs (heptyl acetate and methyl isobutyrate) mediated interaction between fungi (left inlet)

136 and bacteria (*Vibrio*, right inlet). Inlets were prepared on BioRender.com