



Reply to Million et al.: Lactobacilli and listeriosis

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Research on gut microbiota and its influence on normal physiological processes and various diseases, including inflammatory bowel diseases, obesity, or infectious diseases, is rapidly expanding. However, we are not aware of previous studies deciphering the molecular effects of a particular microbe on the infection by a given enteropathogen. The goal of our study was to take advantage of a relevant animal model for a human pathogen, the E16P humanized mouse line, and of powerful tools; that is, *Listeria*-specific tiling arrays that we have developed to undertake a comprehensive analysis of both the host and the pathogen transcriptional profiles in germ-free mice preinoculated with either a *Lactobacillus casei* or a *Lactobacillus paracasei* strain (1).

Having worked on *Listeria* for decades, we are aware of the ability of some bacterial species to inhibit *Listeria* growth and did cite the report describing a bacteriocin-producing *Lactobacillus salivarius* strain inhibiting *Listeria* growth in vivo (2). We are also aware of the use of bacterial derivatives, such as nisin as food protectants.

Million et al. (3) claim that the interpretation of our results is incorrect or could have been simpler according to the Occam's razor principle, and that we "suggest that changes in the expression of IFN-stimulated genes and of mi-RNA, together with the *L. monocytogenes* metabolism redirection by *Lactobacillus* strains, may explain the modulation of the infection." What Million et al. should have noticed is that we did not claim to have discovered any mechanism and did not rule out any explanation. What our study shows—and this is the strength of our study—is that there is a significant and specific effect of each *Lactobacillus* strain on the host response to *Listeria*, as we expected. However, before our study, we did not know which genes would be affected, or how and to what level. Only a precise and well-designed protocol, such as the one we used, could provide the results that we have reported. These data cannot be explained by a simple mechanism.

Strikingly, we showed that there is a decrease of interferon-stimulated gene transcription after inoculation of lactobacilli and also a down-regulation of IFN- γ production. We would have proposed a mechanism if IFN- γ production had increased after preinoculation with the lactobacilli; this was not the case. However, we do not agree with Million et al. that the simplest explanation for the effect of lactobacilli is because of a direct antibacterial effect. There is—and we have so shown—an antibacterial in vitro effect of the lactobacilli mainly attributable to acid production, yet we have no indication that the addition of a single bacterial species would significantly change the pH in the intestinal lumen of conventional mice to exert this effect. Regarding Million et al.'s questionable in silico analysis, all our attempts to experimentally detect a bacteriocin activity in the two strains led to negative results. This result is not a proof but an indication that the observed lactobacilli effect may not be as simple as proposed by Million et al.

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The authors declare no conflict of interest.

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