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The regulation of host resistance to fungal infections by the microbiota

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An increased understanding of the importance of microbiota in shaping the host's immune and metabolic activities has rendered fungal interactions with their hosts more complex than previously appreciated. It is now clear that a three-way interaction between host, fungi and microbiota dictates the types of host-fungus relationship. Indeed, microbial dysbiosis predisposes to a variety of chronic fungal infections and diseases at local and distant sites. We have explored metagenomics for the purpose of deciphering the contribution of the microbiota to fungal commensalism and parasitism. By correlating changes in metabolite profiles with microbiota metagenomic composition, we have defined a functional node by which certain bacteria species contribute to host-fungal symbiosis and mucosal homeostasis in the gut. The trpyptophan metabolism pathway is exploited by commensal bacteria and the mammalian host to increase fitness in response to *Candida albicans* by inducing resistance and tolerance mechanisms of the antifungal immunity. Similarly to the gut, the lung microbiome also has a profound impact on lung immunity and resistance to pulmonary infection. We have explored in both human and mice airways the dynamics and diversity of prokaryotic population as a key alarm of upcoming *Aspergillus fumigatus* infection, a threatening infection in lung or hematopoietic transplanted patients. Using 16S rRNA sequencing, a substantial bacterial diversity was observed in intact or *Aspergillus*-infected mice. At the taxa level, the Firmicutes decreased significantly both in the lung and BAL upon infection while the Proteobacteria significantly increased. A similar bacterial diversity was observed in BAL samples from a cohort of patients undergoing allogeneic hematopoietic transplantation with and without positive *Aspergillus* diagnosis. These data suggest that the study of the human microbiota in the trans-omics era with a focus on metagenomics and metabonomics is providing novel insights into the microbial regulation of host immune resistance to fungi.

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