NATURE REVIEWS IMMUNOLOGY | REVIEW

The mycobiota: interactions between commensal fungi and the host immune system

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Abstract

Abstract • References • Author information

The body is host to a wide variety of microbial communities from which the immune system protects us and that are important for the normal development of the immune system and for the maintenance of healthy tissues and physiological processes. Investigators have mostly focused on the bacterial members of these communities, but fungi are increasingly being recognized to have a role in defining these communities and to interact with immune cells. In this Review, we discuss what is currently known about the makeup of fungal communities in the body and the features of the immune system that are particularly important for interacting with fungi at these sites.

Subject terms: Fungal infection ▪ Fungi ▪ Immunogenetics ▪ Microbiome ▪

At a glance

Figures

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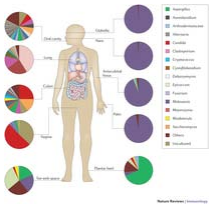

Figure 1: The human mycobiota.

Complex populations of fungi have been found associated with the skin and all mucosal surfaces of the healthy human body. The pie charts indicate the relative proportions of fungal genera that are reported to be associated with the respective sites in representative fungal deep-sequencing studies. The fungal populations that are found on mucosal surfaces tend to be more diverse than those on the skin. The healthy lung probably reflects mostly environmental fungi, which are not included in the key. 'Others' refers to sequences that represent <1% of the total recovered sequences at each site. 'Uncultured' are sequences identified in the National Center for Biotechnology Information (NCBI) GenBank database as fungal but of uncharacterized origin. Data for pie charts were derived from studies of the fungal genera that are present in the oral cavity[50], lungs[92], colon[16], vagina[79] and skin[70].

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defence against fungi. Fungi may also be recognized by soluble receptors, such as the mannose- binding lectin, which can direct complement activation for killing and the release of inflammatory mediators, as well as opsonize fungi for recognition by

additional membrane-bound receptors, such as complement receptors. The question mark indicates that the signalling pathways downstream of many of these receptors remain to be elucidated. BCL-10, B cell lymphoma 10; CARD9, caspase recruitment domain-containing protein 9; CLEC, C-type lectin domain family member; IL, interleukin; IRAKs, IL-1 receptor-associated kinases; MALT1, mucosa-associated lymphoid tissue lymphoma translocation protein 1; MARCO, macrophage receptor MINCLE, macrophage-inducible C-type lectin; MYD88, myeloid differentiation primary response protein 88; NLRP3, NOD-, LRR- and pyrin domain-containing 3; PGE2, prostaglandin E2; PTGES, prostaglandin E synthase; ROS, reactive oxygen species; SR-A, scavenger receptor type A; SREC, scavenger receptor expressed by endothelial cells; SYK, spleen tyrosine kinase; TNF, tumour necrosis factor; TRIF, TIR-domain-containing adaptor protein induced IFN-β.

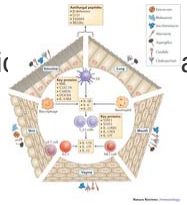

Figure 3: Mucosal immune responses involved in interacting with fungi at different body sites.

Different body sites are colonized by diverse groups of fungi and the communities are shaped by the characteristics of each environment. Epithelial cells at these surfaces produce antimicrobial peptides that directly modulate fungal survival. In response to fungi, cytokines and chemokines are also produced and these recruit immune cells to the site. Fungi may also be directly sensed by dendritic cells (DCs) and γδ T cells at epithelial surfaces. When epithelial barriers are breached, macrophages, DCs and neutrophils kill fungi and produce cytokines that promote adaptive immune responses. Innate lymphoid cells (ILCs) may also respond directly to fungi by producing cytokines. Genetic studies in humans have revealed key proteins that are particularly important for antifungal defence and that implicate a crucial role for the interleukin-17 (IL-17) pathway in this process. CARD9, caspase recruitment domain-containing protein 9; CLEC7A, C-type lectin domain family 7 member A; DOCK8, dedicator of cytokinesis protein 8; IL-12RB1, IL-12 receptor subunit β1; IL-17RA, IL-17 receptor A; MBL, mannose-binding lectin; NKT cell, natural killer T cell; REGIIIγ, regenerating islet-derived protein IIIγ; STAT, signal transducer and activator of transcription; TH_{17}, T helper 17.

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The authors declare no competing interests.

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