Type-17 immunity controls *Malassezia*-mediated skin infection

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1. Introduction

- Malassezia* is a dimorphic fungus (*Basidiomycota*) and represents the dominant eukaryotic part of the skin microbiota in warm-blooded vertebrates.
- Recent work suggests an association of *Malassezia* with chronic inflammatory skin diseases e. g. atopic dermatitis.
- Our current understanding about the role of *Malassezia* in skin pathologies is hampered by the lack of *in vivo* infection models.

Aim:

Employ a novel experimental model for *Malassezia*-mediated skin infection to explore the link between *Malassezia*-induced immune responses and chronic inflammatory skin diseases.

2. *Malassezia* induces skin pathology

Epicutaneous application of *Malassezia* onto tape-stripped ear skin of WT mice results in a robust colonization and a pronounced inflammatory host response, characterized by epidermal and dermal hyperplasia and recruitment of leukocytes to the site of infection.

3. Type-17 immunity controls *Malassezia* growth

Malassezia skin infection elicits a type-17 immune response in the infected tissue and skin-draining lymph node. Consistently, a functional IL-23/IL-17 immune axis is essential for preventing fungal overgrowth.

4. Atopic dermatitis shifts *Malassezia*-specific human T cells from a type-17 towards a type-2/type-17 profile

In vitro restimulation of human T cells from non-atopic individuals and AD patients with *Malassezia* spp.-pulsed monocytes, demonstrates a shift within fungus-specific memory T cells from primarily type-17 associated cytokine expression in control individuals towards a mixed type-2/17-profile in AD patients.

5. Conclusions & future perspectives

Conclusion:

- Host immunity to *Malassezia* is characterized by a prominent type 17 response in mice and humans.
- Under atopic conditions (barrier disruption), *Malassezia* greatly enhances skin inflammation.
- Malassezia*-specific human T cells from AD patients show increased proliferation and polarization towards a mixed type-17/2 immune phenotype.

Outlook:

- Combining the *Malassezia* infection model with AD mouse models will help to determine the role of this fungus in contributing to chronic inflammatory diseases such as AD.