

Balaji, H., Heratizadeh, A., Wichmann, K., Niebuhr, M., Cramer, R., Scheynius, A., Werfel, T. (2011). *Malassezia sympodialis* thioredoxin-specific T cells are highly cross-reactive to human thioredoxin in atopic dermatitis. *J Allergy Clin Immunol*, 128: 92-99.e4.

Background: IgE-mediated cross-reactivity between fungal antigens and human proteins has been described in patients with atopic dermatitis (AD), but it remains to be elucidated whether there is also cross-reactivity at the T-cell level.

Objective: We sought to explore cross-reactivity at the T-cell level between the fungal thioredoxin (Mala s 13) of the skin colonizing yeast *Malassezia sympodialis* and its homologous human thioredoxin (hTrx).

Methods: T-cell lines (TCLs) were generated in the presence of rMala s 13 from the peripheral blood and from skin biopsy specimens of positive patch test reactions of patients with AD sensitized to Mala s 13 and hTrx. Patients with AD not sensitized to *Malassezia* species, healthy subjects, and patients with psoriasis served as control subjects. Mala s 13-specific T-cell clones (TCCs) were generated from TCLs. TCCs were characterized by antigen specificity, phenotype, and cytokine secretion pattern. Human keratinocytes were stimulated with IFN- γ , TNF- α , and IL-4, and the release of hTrx was determined by means of ELISA.

Results: Mala s 13-specific TCLs and TCCs from the blood and skin of patients with AD sensitized to Mala s 13 and hTrx were fully cross-reactive with hTrx. Mala s 13- and hTrx-specific TCCs could not be generated from control subjects. The majority of cross-reactive TCCs were CD41 and coexpressed cutaneous lymphocyte antigen. In addition to TH1 and TH2 TCCs, we could also identify TCCs secreting IL-17 and IL-22. After stimulation with IFN- γ and TNF- α , keratinocytes released substantial amounts of thioredoxin.

Conclusion: In patients with AD sensitized to *Malassezia* species, cross-reactivity at the T-cell level to Mala s 13 and the homologous hTrx is detectable. hTrx autoreactive skin-homing T cells might be relevant for cutaneous inflammation in patients with AD.