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Poster

Trichophyton rubrum infection on reconstructed human epidermis induces simultaneous epidermal barrier disruption and keratinocytes activation

Dermatophytosis is a superficial fungal infection of keratinized structures, with a prevalence around 25% in humans. Consequences of dermatophytosis on epidermal barrier functions, and cell responses elicited in keratinocytes remain unclear. To gain mechanistic insight, an in vitro model of reconstructed human epidermis (RHE) infected by arthroconidia of Trichophyton rubrum has been investigated. Assays of trans-epithelial electrical resistance and dye permeation through infected RHE revealed a sudden loss in barrier function after four days of infection. The disruption of this barrier could result from disorganized tight junctions, since simultaneous internalization of claudin-1 immunoreactivity was monitored. Electron microscopy illustrated that fungal hyphae progressively invade the stratum corneum of RHE by sneaking into intercellular spaces, down to the granular layer. Also on the fourth day of infection, pro-inflammatory cytokines (IL-1α, IL-1β, TNFα, IL-8, TSLP) and antimicrobial peptides (β-defensin-2, β-defensin-3, S100A7) were increasingly expressed and released by keratinocytes. Simultaneous observation of barrier disruption and keratinocyte activation triggered investigation towards prospective causal relationship. While assessing potential role of p38 MAPK activation in consequence of fungal infection, the use of inhibitor PD169316 indicated that fungal homolog of p38 might be involved in growth of arthroconidia. Indeed, RHE treated with PD169316 were protected against invasion and growth of T. rubrum colonies on Sabouraud agar was altered, as observed by SEM. Altogether, these data identify fungal p38 MAPK signaling as a potential target to counteract dermatophytosis, while supporting requirement for improved knowledge in biology of such infecting species.