A new *in vivo* murine model of dermatophytosis reveals that infection dynamics are influenced by the ecological niche of dermatophytes

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Introduction

Dermatophytes are the most common pathogenic fungi of the skin. Depending on their ecological niche (anthropophilic, zoophilic, and geophilic), they most often cause distinct clinical presentations. However, it remains unclear whether these differences reflect fundamentally distinct pathogenic mechanisms. To date, no study has directly compared the infection dynamics of dermatophytes according to their ecological niche within a same *in vivo* model. Our specific objective was to use a validated experimental mouse model to compare host-dermatophyte interactions according to their ecological niche, based on clinical and histopathological criteria, and the expression of fungal and murine target genes.

Material & Methods

Three dermatophyte species representing ecological niches were used: *Trichophyton rubrum* (anthropophilic), *Microsporum canis* (zoophilic), and *Nannizzia gypsea* (geophilic). For infection, a mixed inoculum combining spores, germ tubes, and mycelium was applied epicutaneously to scarified skin. Infection kinetics were monitored using a semi-quantitative clinical score (0 to 4) based on the intensity of three parameters: erythema, scaling, and crusting. Histopathological analyses were performed to assess epidermal invasion and inflammatory infiltrates. Host-pathogen interactions were further evaluated by measuring fungal protease gene expression (deuterolysin, *DEUT*; subtilisin 6, *SUB6*; and subtilisin 10, *SUB10*) and host Th17-associated cytokines (*IL-1β, IL-17A, IL-22*) by RT-qPCR at day 3 post-infection (PI).

Results

Our murine model proved effective for comparing the three species of dermatophytes. Combined clinical and histopathological analyses revealed clear differences in terms of infection dynamics and tissue invasion: *T. rubrum* induced moderate and transient lesions associated with superficial epidermal invasion; *M. canis* caused persistent lesions and extensive skin infiltration; *N. gypsea* triggered symptoms of severe inflammation associated with pronounced tissue damage. At day 3 PI, all three species strongly upregulated fungal proteases (*DEUT, SUB6, and SUB10*), although DEUT and SUB6 expression was comparatively reduced in the geophilic species. Host responses were dominated by a Th17 cytokine profile, with significant overexpression of *IL-1β, IL-17A*, and *IL-22* regardless of fungal species.

Discussion & Conclusion

For the first time, a standardized murine model was successfully used to compare dermatophytes representative of the three ecological niches. Distinct infection dynamics characterized by differences in symptom severity, tissue invasion, and infection-associated fungal gene expression suggest differences in pathogenic mechanisms related to ecological group. These findings underscore the value of our standardized murine model as a robust tool to further studying host-pathogen interactions of dermatophytosis.

Keywords: dermatophytes; murine model; ecological niche; host–pathogen interaction