Comparative study of the pathogenicity and humoral response of *Lomentospora*, *Scedosporium* and *Aspergillus* infections in a murine model

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INTRODUCTION

Lomentospora (Scedosporium) prolificans is an emerging pathogen that causes, above all, disseminated infections in immunocompromised patients with very high mortality rates. This is mainly associated with the kind of infections, the fungal intrinsic drug resistance and the difficulties to perform an accurate and rapid diagnosis. Therefore, an improvement in diagnostic tools, resulting from the identification of new markers or antigens, is essential to establish a proper treatment and reduce the unacceptable morbimortality caused by this fungus.

OBJECTIVE

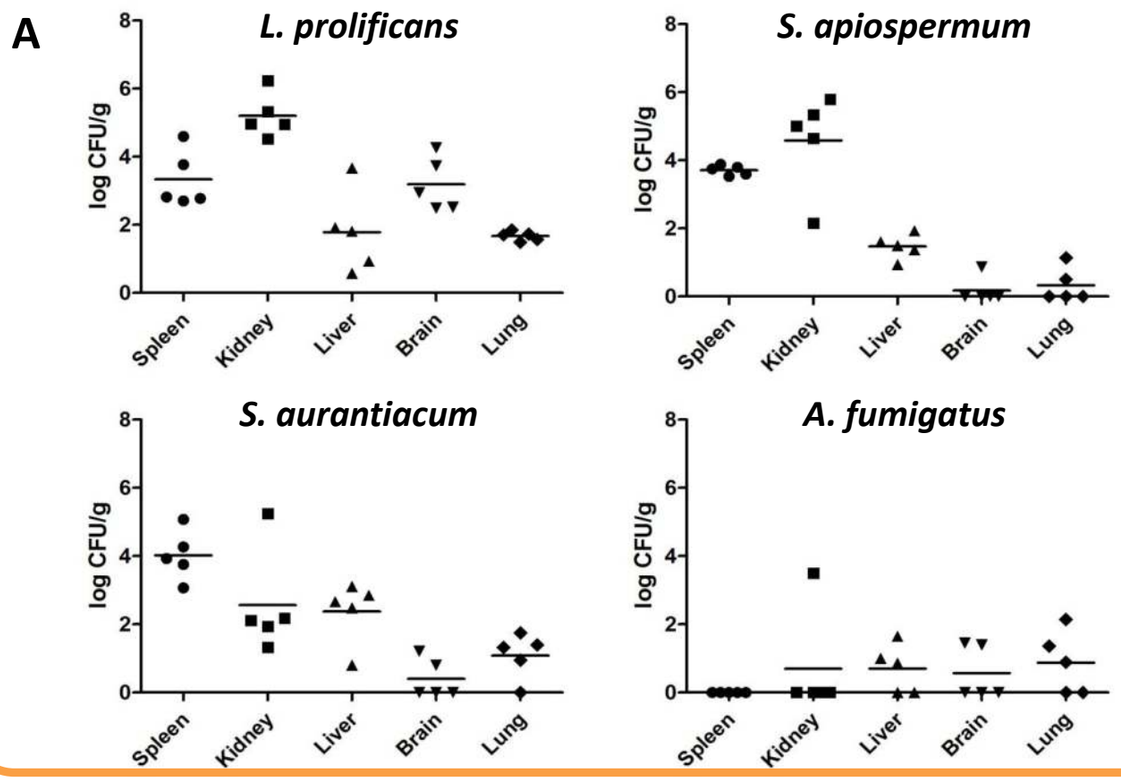
To compare the pathogenicity of *Lomentospora prolificans, Scedosporium apiospermum, S. aurantiacum* and *Aspergillus fumigatus* in a murine model, and to study the cross-reactivity with *L. prolificans* of the serum IgGs from mice infected with the other fungal species, identifying the major antigens.

RESULTS

1. Murine infection by *Lomentospora, Scedosporium* and *Aspergillus* fungi

Methods

Swiss female 8-week-old immunocompetent mice were infected intravenously with 10^5 conidia/animal of *L. prolificans*, *S. apiospermum*, *S. aurantiacum* and *A. fumigatus* (clinical isolates). Twenty eight days after infection, animals were sacrificed for blood and organ extraction.



Results

Mice infected with *Lomentospora* and *Scedosporium* species developed signs associated with infection, while no signs were observed in *A. fumigatus* group. Survival rates were **50%** in ***L. prolificans*** group, **83.3%** in ***S. apiospermum*** and ***S. aurantiacum***, and **100%** in ***A. fumigatus***. In *Lomentospora* and *Scedosporium* infected groups high CFU counting were obtained, while in *A. fumigatus* group very few CFUs were collected (Fig. 1A). Moreover, the histological analysis showed renal affectation on *Lomentospora/Scedosporium* groups (Fig. 1B).

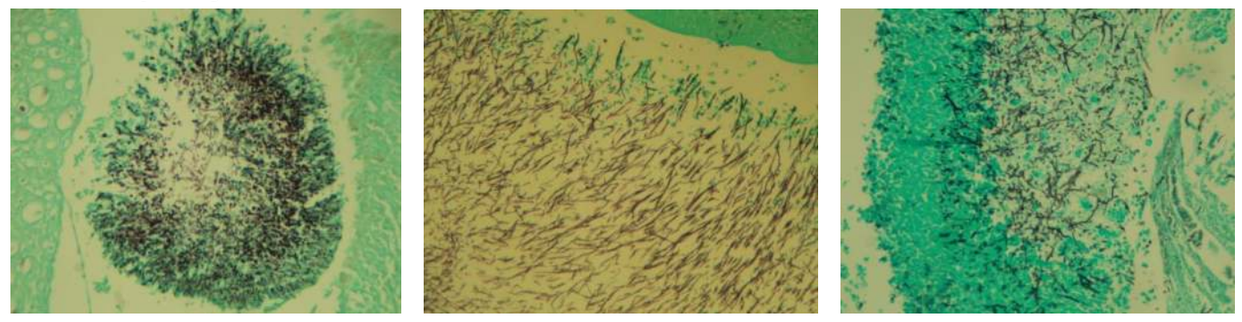


Fig. 1. Number of CFU/g of mice infected with *Lomentospora, Scedosporium* and *Aspergillus* (A); and histological study of kidneys of mice infected with *Lomentospora/Scedosporium* (B).

2. Cross-reativity study of the humoral response

Methods

Pooled sera of 5 mice of each group were used over *L. prolificans* cell extract proteome (hyphae and conidia) to detect antigens by immunoblotting (Fig. 2). The most important antigens of *L. prolificans* were identified by LC-MS/MS (Table 1).

Table 1. Identified antigens of *L. prolificans* in total cell extract.

Spot	Identified protein
1,2	**Heat shock protein 70**
3	Hypothetical protein SAPIO_CDS2096
4,5,6	Proliferating cell nuclear antigen
7,8,9,10	Heat shock protein 70 (fractions)

Results

The Heat shock protein 70 (Hsp70) was identified as the major antigen, being identified in different spots as the full protein or fragments of it.

All the most immunoreactive antigens showed cross-reactivity with the sera from mice infected with *Scedosporium* species but not with *Aspergillus*, which showed a completely different immunome pattern (Fig. 2).

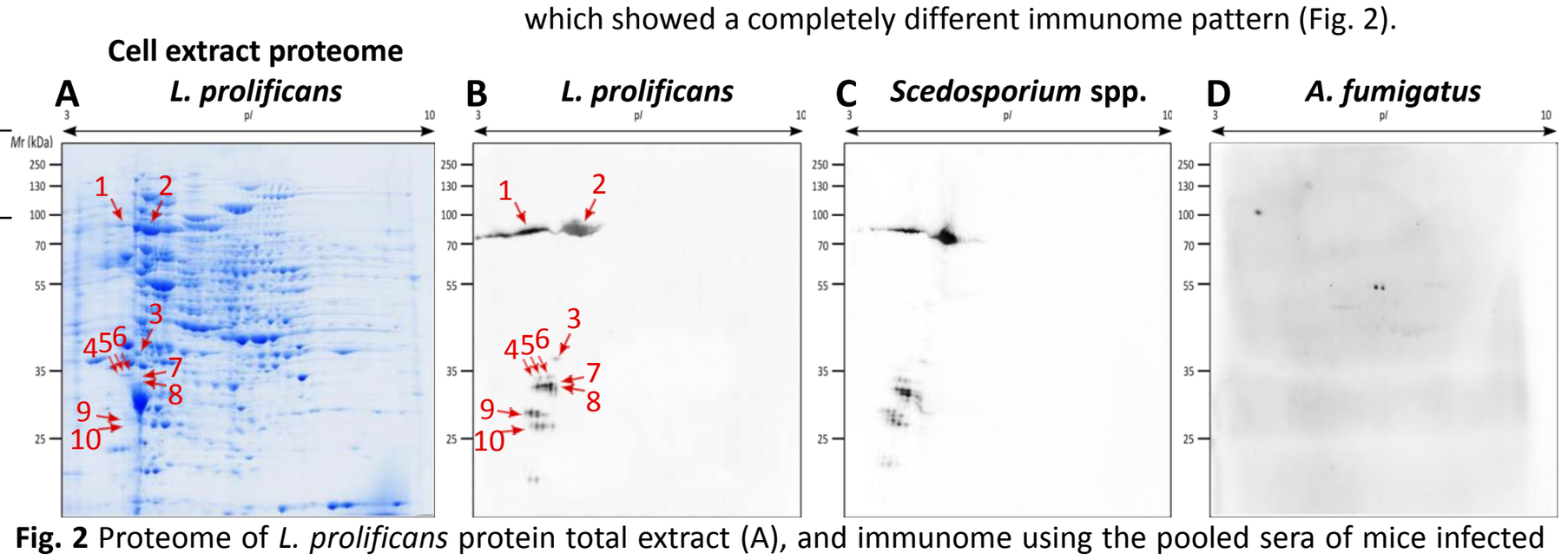


Fig. 2 Proteome of *L. prolificans* protein total extract (A), and immunome using the pooled sera of mice infected with *L. prolificans* (B), *Scedosporium* spp. (C) and *A. fumigatus* (D). Marked spots were identified by LC-MS/MS.

CONCLUSIONS

- Hsp70 stands out as interesting candidate to be evaluated as diagnostic marker of infections caused by *Lomentospora/Scedosporium*.

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