Host-parasite relationship: clinical manifestations and immune responses during experimental hyalohyphomycosis by *Purpureocillium lilacinum*

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Abstract

Purpureocillium lilacinum is a filamentous fungus reported as an emerging pathogen in humans. Both, immunosupressed and immunocompetent patients may have the infection. Our aim was to evaluate the clinical manifestations and immune response of immunocompetent (CPT) and chemically immunosupressed (SPS) C57BL/6 mice infected with two isolates of *P. lilacinum*. Blood sample was collected and lungs and liver were removed for histopathological studies. Splenocytes recovered from spleen for surface flow cytometry analysis. Sera of mice were used to analyze the specificity of antibodies by indirect immunofluorescence and flow cytometry assays. Our results showed a maximum recovery of fungal cells at 7 dpi, in CPT and SPS inoculated with both isolates, with a higher mean of fungal cells recovered from spleen of the mice inoculated with PL.P isolate. CPT and SPS mice inoculated with PL.P presented histological changes, however, only the SPS mice inoculated with PL.T isolate showed fungal structures and some mice presented abdominal nodules, filled with fungal cells. The SPS group presented higher percentage of CD4+CD69+ cells when compared with CPT groups. At day seven after infection the percentage of CD8+CD69+ cells were higher in the CPT group infected with the PL.P isolate when compared with the animals infected with PL.T. The expression of CD25 decreased over time in CD4+ T cells from SPS and CPT animals infected with both PL.P and PL.T. The expression of CD62L in CD8 T cells dropped significantly 21 days after infection in both animals infected groups with both isolates. For both CD4 and CD8 T cells the expression of CD62L was higher in the SPS group infected with PL.P than in the SPS group infected with PL.T. At day 21 of infection, the expression of CD62L enhanced in all groups. IgG antibodies were evaluated in CPT and SPS animals after infection with PL.P isolate. The humoral response was considered specific, since virtually no antibodies were detected in the serum of control mice. In summary, PL.P was more virulent than PL.T due histological alterations and higher quantity of cells recovered from spleen, and *P. lilacinum* infection is able

to activate CD4+ and CD8+ T cells that probably are able to migrate to tissues. We also observed that the expression of activation and migration markers was higher in cells of immunosupressed mice and PL.P seems to induce a higher degree of activation in CD 4+ and CD8+ T cells when compared with PL.T.

Keywords: *Purpureocillium lilacinum*, hyalohyphomycosis, clinical manifestations, immune response, murine model.

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