O0121 Cell wall fucomannan is a biomarker for diagnosis of invasive murine mucormycosis

Caitlyn Orne, Amanda Burnham-Marusich, Clara Baldin, Teclegiorgis Gebremariam, Ashraf Ibrahim, Alexander Kvam, Thomas Kozel

1DxDiscovery, Reno, United States, 2Los Angeles Biomedical Research Institute, Division of Infectious Diseases, Torrance, United States, 3University of Nevada, Reno School of Medicine, Reno, United States, 4DxDiscovery, Reno, United States

Background: Mucormycosis causes severe morbidity and mortality in patients with diabetes mellitus, patients undergoing chemotherapy for hematological malignancies, and patients who have received hematopoietic stem cell transplants. Mucormycosis is difficult to diagnose in these high risk patients. The goal of this study was to develop a lateral flow immunoassay (LFIA) that can aid diagnosis of mucormycosis using BALF, serum, urine or tissue as clinical specimens.

Materials/methods: Monoclonal antibody (mAb) 2DA6 was produced from splenocytes of mice immunized with fungal cell wall fragments. BALF, serum, urine or tissue were obtained from diabetic ketoacidotic (DKA) or neutropenic (cyclophosphamide/cortisone acetate) murine models of invasive pulmonary or wound mucormycosis.

Results: A LFIA was constructed from mAb 2DA6 for detection of cell wall fucomannan of the Mucorales in clinical samples. The antibody is reactive with the alpha-1,6 mannose backbone in mannans of fungi of the Zygomycota and Ascomycota. However, mAb 2DA6 has an exquisite sensitivity for fucomannan due to an apparent low level of side chain substitution found on fucomannan vs. high levels of side chain substitution that occlude the backbone in mannans of most ascomycetes other than the dermatophytes.

BALF, serum, and urine were harvested 3-4 days after intratracheal challenge of immunosuppressed or DKA mice with spores from several Mucorales, including Rhizopus delemar, Lichtheimia corymbifera, Mucor circinelloides and Cunninghamamella bertholletiae. Samples were evaluated for presence of fucomannan with the 2DA6 LFIA. Positive reactions were observed with multiple sample types from all four fungi, demonstrating the ability to detect infection by multiple genera. Samples collected 3 days and 4 days post-infection were positive, demonstrating the ability of the LFIA to produce early positive results. The highest reactivity was found with urine samples. Finally, tissue was collected from a neutropenic mouse model of R. delemar-inflicted wound infection. Extracts from tissue also produced a clear positive result.

Conclusions: Studies in clinically relevant animal models of mucormycosis showed that a lateral flow immunoassay for detection of cell wall fucomannan has the potential for early diagnosis of mucormycosis using BALF, serum, urine and tissue as clinical samples.