The geographical region of origin determines the phagocytic vulnerability of *Lichtheimia* strains.

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Abstract

Mucormycoses are life-threatening infections that affect patients suffering from immune deficiencies. We performed phagocytosis assays confronting various strains of *Lichtheimia* species with alveolar macrophages, which form the first line of defense of the innate immune system. To investigate seventeen strains from four different continents in a comparative fashion, transmitted light and confocal fluorescence microscopy was applied in combination with

automated image analysis. This interdisciplinary approach enabled the objective and quantitative processing of the big volume of image data. Applying machine-learning supported methods, a spontaneous clustering of the strains was revealed in the space of phagocytic measures. This clustering was not driven by measures of fungal morphology but rather by the geographical origin of the fungal strains. Our study illustrates the crucial contribution of machine-learning supported automated image analysis to the qualitative discovery and quantitative comparison of major factors affecting host-pathogen interactions. We found that the phagocytic vulnerability of *Lichtheimia* species depends on their geographical origin, where strains within each geographic region behaved similarly, but strongly differed amongst the regions. Based on this clustering, we were able to also classify clinical isolates with regard to their potential geographical origin.

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