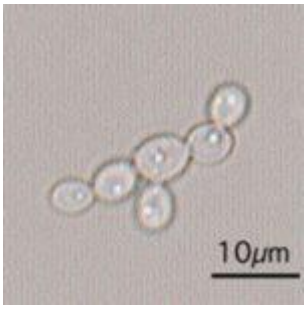
Immuno-Ethiopia: Fungal epidemiology and immunology



IUIS-FAIS Immuno-Ethiopia course co-sponsored by the IUIS, FAIS and Volkswagen Foundation took place between 23rd-29th of February. The theme of this meeting was Neglected Tropical Diseases and Malaria challenges in Sub-Saharan Africa. In this article we shall focus on Fungal immunology talks presented by Dr J. Claire Hoving (University of Cape Town).

Dr Hoving's first talk focused on **"The Epidemiology of fungal infections",** she highlighted that although fungal infections cause more than 1.5 million deaths annually, the impact on human health is not widely recognized and deaths are often overlooked (Brown et al, Sci Trans Med, 2012). The enormous influence fungal pathogens have on plant and animal life is well recognised, especially for food security. However, fungal infections are often not perceived as life threatening to humans. This is not the case. Four major genera cause deaths- *Pneumocystis, Aspergillus, Cryptococcus* and *Candida species*. Public health agencies conduct little to no mycological surveillance, making epidemiological data for fungal infections notoriously poor. Roughly, 25% of the world's population are affected by superficial fungal infections, however these are generally not life threatening. In contrast, invasive fungal infections are associated with a high rate of mortality which often exceeds 50%. In Africa, second only to tuberculosis, fungal infections such as *Cryptococcal meningitis* and *Pneumocystis jirovecii* pneumonia are the leading cause of death of HIV-infected patients. In this

resource limited setting, drug and diagnostic test availability is severely limiting the outcome for infected patients. Understanding how the host responds to infection is key to developing new diagnostic tests or drugs to clear infection.

Dr Hoving's second second lecture titled "**Host Immunity and Fungal pathogenesis**", discussed aspects of fungal immunology including both innate and adaptive host responses. Dr. Hoving explained that fungal pathogens come in many shapes and sizes, and once entering the host, many can change their shape to avoid recognition. This changes how the host immune system responds to infection, for example a large fungal cell may stimulate an extracellular response while a smaller organism will be easier to take up by phagocytes. Innate immune receptors are important in shaping the adaptive immune response. C-type lectin receptors (CLR) are pathogen recognition receptors described for their role in fungal recognition. Synergistic signalling of Toll like receptors (TLR) and CLR has been shown in immune response to pathogens (Brown et al, Cell, 2010). The most prominent CLR in fungal recognition is Dectin-1, known to recognise B-glucan in the fungal cell wall (Brown et al, Nature Rev. 2018). These signalling CLRs trigger an intracellular signalling cascade which induces gene transcription and the production of various inflammatory mediators. This includes uptake and killing by phagocytes and subsequently the development of protective Th1 and Th17 responses. Fungi have developed mechanisms to evade the host immune response such as changing their shape, surface pathogen associated molecular patterns (PAMPS), releasing decoy components or they are able to survive harsh environment within a macrophage.

Compared to TB and HIV, fungal immunology is understudied. Talks by Dr Hoving, highlighted the importance of doing this research. As it will lead to improved care for immunocompromised individuals who at risk of acquiring

“potentially” deadly fungal infection.

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