

# Immuno-Ethiopia: Genetics of Fungal 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.

This article focuses on a presentation by Prof. Mohamed Ridha Barbouche from the Institut Pasteur de Tunis, Tunisia who gave insights on “**Genetics of the immune response to Fungal Infections**”. In his talk he highlighted the global fungal infection burden (over 14.9 million cases per year with over 1.7 million deaths worldwide). These fungal infections are polyclinical, with well-known forms including:

- Invasive fungal infections (Cryptococcal meningitis, Pneumocystis pneumonia, disseminated histoplasmosis, invasive aspergillosis, Candida bloodstream infection) which are often fatal
- Skin, hair and nail infection (ringworm, tinea capitis, athlete’s foot, onychomycosis)
- Mucosal infection (oral and esophageal candidiasis, Candida vaginitis)
- Allergic fungal disease (allergic bronchopulmonary aspergillosis, severe asthma with fungal sensitization)
- Chronic lung or deep tissue infection (chronic pulmonary aspergillosis, endemic mycoses)

He explained that gene polymorphisms have been associated with

fungal infections. These gene polymorphisms have been studied however, identifying the right population to study is critical for some fungal infection e.g. candida and aspergillosis because there is evidence of genetic susceptibilities to these fungal pathogens.

Specific genetic signatures (combination of variants) may determine the immune responses to those pathogens (Barbouche et al, 2017. *Front.Immunol.*). Gene variants such as TLR1, TLR2, TLR3, TLR4, TLR5, TLR6, TLR9, CARD 9, MBL2, PLG, PTX3 are involved in the susceptibility to fungal infections like invasive pulmonary aspergillosis (IPA), recurrent vulvovaginal candidiasis (RVVC), chronic pulmonary aspergillosis (CPA) and allergic bronchopulmonary aspergillosis (ABPA) (Campos et al., 2018 *Current Topics in Microbiology and Immunology*). As lessons are being learnt, we understood that:

1. Identification of variants (polymorphisms) in pattern recognition receptors associated with susceptibility to fungi is helping decipher their contribution to disease
2. Specific genetic signatures may determine the immune responses to these pathogens
3. Understanding how these molecules are regulated at the genetic level may enable the possibility of targeted "therapy" that may restore defective pathways.

In addition to gene variants, inborn errors in immunological pathways also contribute to genetic susceptibility to fungal infections. Inborn errors of the phagocyte NADPH oxidase complex (chronic granulomatous disease), severe congenital neutropenia (SCN) and leukocyte adhesion deficiency confer a predisposition to invasive aspergillosis and candidiasis. In addition, inborn errors of IL-17 immunity have recently been shown to underlie chronic mucocutaneous candidiasis (CMC), while inborn errors of caspase recruitment domain-containing protein 9 (CARD9) immunity underlie deep dermatophytosis and invasive candidiasis (Li et al, 2017; Lanternier et al., 2013 *Curr Opin Pediatr*).

*By Arthur D Djibougou*