Aspergillus fumigatus

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Aspergillus fumigatus is an **opportunistic** fungal pathogen. The spores of this fungus, called **conidia**, are found widely in the environment and it is thought that we inhale several conidia daily. When we inhale conidia, resident immune cells in our lungs **phagocytose** and destroy them – preventing them from causing an infection. **Alveolar macrophages** in the lung are the primary line of defence against conidia.

As with many fungal pathogens, when the immune system becomes impaired we become highly susceptible to *A. fumigatus* infection. *A. fumigatus* causes a wide range of infections, including chronic lung disease (chronic pulmonary aspergillosis) and life-threatening systemic infection that can involve multiple organs (invasive aspergillosis). *A. fumigatus* is a major concern for patients undergoing haematopoetic stem cell transplantation, patients with chronic neutropenia (a reduction in circulating neutrophils) and patients receiving high-doses of steroids.

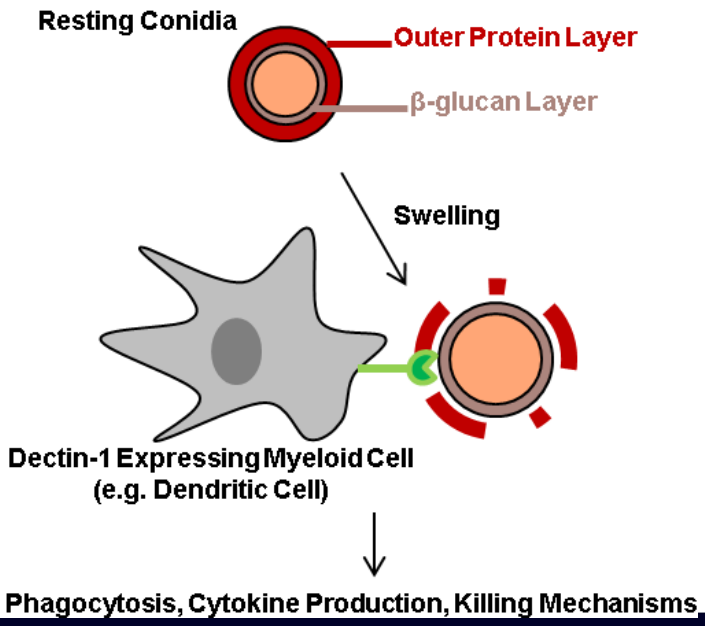
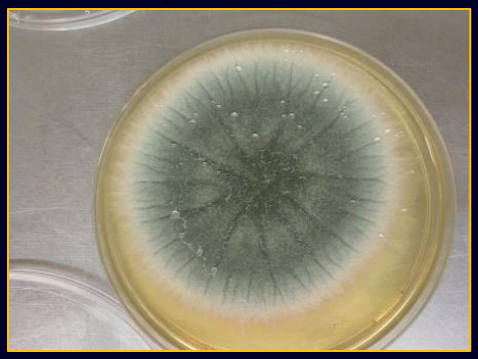


Figure 1. Resting conidia have an outer protein layer 'masking' β-glucans from the immune system. Upon swelling, β-glucans become exposed and are able to be recognised by Dectin-1 on host leukocytes, resulting in the initiation of an immune response.

If the immune system is ill-equipped to deal with inhaled conidia, these spores *can* start to swell and form filamentous forms called **germ tubes** (short tubes) and **hyphae** (long tubes). These elongated cells can penetrate host cells and cause damage. Our immune system also reacts more violently to these forms of the fungus which stimulate production of **pro-inflammatory cytokines and may contribute towards** immunopathology.

Immunity to *A. fumigatus*

When conidia swell and start forming germ tubes/hyphae, the fungal cell wall starts to change. This results in exposure of previously hidden **pathogen-associated molecular patterns** (**PAMPs**); key molecules recognised by receptors of the innate immune system (**pattern recognition receptors, PRRs**).



For example, **β-glucans** primarily make up the cell walls of fungal hyphae but are shielded from the immune system in conidia by a proteinaceous layer. β-glucans are recognised by the PRR, **Dectin-1**, expressed by **myeloid cells**, which initiates inflammatory responses to most types of fungi (**Figure 1**). In *A. fumigatus* infections, Dectin-1 mediates uptake and killing of *A. fumigatus*. Humans with a point mutation in the Dectin-1 gene are highly susceptible to *A. fumigatus* infection following transplants and this is cited as a risk factor.

Lastly, epithelial cells which line the lung can also protect against *A. fumigatus* invasion. Epithelial cells also express PRRs, including the recently charcaterised MelLec. MelLec binds to melanin, which is expressed by conidia (and thus appear green/black; **Figure 2**). MelLec is an important receptor for protecting against *A. fumigatus* infections, and similar to Dectin-1, point-mutations in this gene in humans are a risk factor for invasive *A. fumigatus* infections.