

Cunha C, Carvalho A, Esposito A, Bistoni F, Romani L. (2012). DAMP signaling in fungal infections and diseases. *Front Immunol.* 3:286.

Fungal infections and diseases predominantly affect patients with deregulated immunity. Compelling experimental and clinical evidence indicate that severe fungal diseases belong to the spectrum of fungus-related inflammatory diseases. Some degree of inflammation is required for protection during the transitional response occurring temporally between the rapid innate and slower adaptive response. However, progressive inflammation worsens disease and ultimately prevents pathogen eradication. The challenge now is to elucidate cellular and molecular pathways distinguishing protective vs. pathogenic inflammation to fungi. In addition to fungal ligands of pattern recognition receptors (pathogen-associated molecular patterns, PAMPs), several host-encoded proteins, the damage-associated molecular patterns (DAMPs), are released during tissue injury and activate innate recognition receptors. DAMPs have been shown to regulate inflammation in fungal diseases. The DAMP/receptor for advanced glycation end-products axis integrated with the PAMP/Toll-like receptors axis in the generation of the inflammatory response in experimental and clinical fungal pneumonia. These emerging themes better accommodate fungal pathogenesis in the face of high-level inflammation seen in several clinical settings and point to DAMP targeting as a novel immunomodulatory strategy in fungal diseases.