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Aspergillus fumigatus melanin subverts host immunity in human airway epithelium

The respiratory epithelium is a complex tissue, composed of distinct cells arranged in a pseudostratified architecture that actively participates in the host response to pathogens. However, the role of the airway epithelium in modulating the immune response to *Aspergillus fumigatus* (Af) is poorly understood. Recognition of Af by human airway epithelial cells (HAEC) leads to transepithelial migration of neutrophils. Using both a human epithelial cell line, NCI-H292, and a fully pseudostratified primary HAEC model grown at air-liquid interface, we demonstrate that purified Af melanin ghosts potently, and actively, inhibits transmigration of neutrophils across the airway epithelium. Af melanin blocks the production of pro-inflammatory neutrophil chemo-attractants, CXCL8 (IL-8) and CXCL1 (Gro-alpha). Melanin does not block either transcription or translation of IL-8 but blocks post-translational secretion of IL-8 by epithelial cells abolishing the transepithelial cytokine gradient. Our results demonstrate that melanin actively down-regulates airway epithelial mediated pro-inflammatory responses toward Aspergillus and reveals a new strategy by which aspergillus evades the immune system.