The temporal dynamics of differential gene expression in *Aspergillus fumigatus* interacting with human immature dendritic cells *in vitro*.

Morton CO, Varga JJ, Hornbach A, Mezger M, Sennefelder H, Kneitz S, Kurzai O, Krappmann S, Einsele H, Nierman WC, Rogers TR, Loeffler J (2011) The temporal dynamics of differential gene expression in *Aspergillus fumigatus* interacting with human immature dendritic cells *in vitro*. *PLOS One* 6(1), e16016-e16016.

Abstract

Dendritic cells (DC) are the most important antigen presenting cells and play a pivotal role in host immunity to infectious agents by acting as a bridge between the innate and adaptive immune systems. Monocyte-derived immature DCs (iDC) were infected with viable resting conidia of Aspergillus fumigatus (Af293) for 12 hours at an MOI of 5; cells were sampled every three hours. RNA was extracted from both organisms at each time point and hybridised to microarrays. iDC cell death increased at 6 h in the presence of A. fumigatus which coincided with fungal germ tube emergence; >80% of conidia were associated with iDC. Over the time course A. fumigatus differentially regulated 210 genes, FunCat analysis indicated significant up-regulation of genes involved in fermentation, drug transport, pathogenesis and response to oxidative stress. Genes related to cytotoxicity were differentially regulated but the gliotoxin biosynthesis genes were down regulated over the time course, while Aspf1 was up-regulated at 9 h and 12 h. There was an up-

regulation of genes in the subtelomeric regions of the genome as the interaction progressed. The genes up-regulated by iDC in the presence of A. fumigatus indicated that they were producing a pro-inflammatory response which was consistent with previous transcriptome studies of iDC interacting with A. fumigatus germ tubes. This study shows that A. fumigatus adapts to phagocytosis by iDCs by utilising genes that allow it to survive the interaction rather than just up-regulation of specific virulence genes.

Involved units

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Details

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