

Specific and novel microRNAs are regulated as response to fungal infection in human dendritic cells.

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Abstract

Within the last two decades, the incidence of invasive fungal infections has been significantly increased. They are characterized by high mortality rates and are often caused by *Candida albicans* and *Aspergillus fumigatus*. The increasing number of infections underlines the necessity for additional anti-fungal therapies, which require extended knowledge of gene regulations during fungal infection. MicroRNAs are regulators of important cellular processes, including the immune response. By analyzing their regulation and impact on target genes, novel therapeutic and diagnostic approaches may be developed. Here, we examine the role of microRNAs in human dendritic cells during fungal infections. Dendritic cells represent the bridge between the innate and the adaptive immune systems. Therefore, analysis of gene regulation of dendritic cells is of particular significance. By applying next-generation sequencing of small RNAs, we quantify microRNA expression in monocyte-derived dendritic cells after 6 and 12 h of infection with *C. albicans* and *A. fumigatus* as well as treatment with lipopolysaccharides (LPS). We identified 26

microRNAs that are differentially regulated after infection by the fungi or LPS. Three and five of them are specific for fungal infections after 6 and 12 h, respectively. We further validated interactions of miR-132-5p and miR-212-5p with immunological relevant target genes, such as FKBP1B, KLF4, and SPN, on both RNA and protein level. Our results indicate that these microRNAs fine-tune expression of immune-related target genes during fungal infections. Beyond that, we identified previously undiscovered microRNAs. We validated three novel microRNAs via qRT-PCR. A comparison with known microRNAs revealed possible relations with the miR-378 family and miR-1260a/b for two of them, while the third one features a unique sequence with no resemblance to known microRNAs. In summary, this study analyzes the effect of known microRNAs in dendritic cells during fungal infections and proposes novel microRNAs that could be experimentally verified.

Beteiligte Forschungseinheiten

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