Genome-wide Expression Profiling Reveals S100B as Biomarker for Invasive Aspergillosis.

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Abstract

Invasive aspergillosis (IA) is a devastating opportunistic infection and its treatment constitutes a considerable burden for the health care system. Immunocompromised patients are at an increased risk for IA, which is mainly caused by the species Aspergillus fumigatus. An early and reliable diagnosis is required to initiate the appropriate antifungal therapy. However, diagnostic sensitivity and accuracy still needs to be improved, which can be achieved at least partly by the definition of new biomarkers. Besides the direct detection of the pathogen by the current diagnostic methods, the analysis of the host response is a promising strategy towards this aim. Following this approach, we sought to identify new biomarkers for IA. For this purpose, we analyzed gene expression profiles of haematological patients and compared profiles of patients suffering from IA with non-IA patients. Based on microarray data, we applied a comprehensive feature selection using a random forest classifier. We identified the transcript coding for the S100 calcium-binding protein B (S100B) as a potential new biomarker for the diagnosis of IA. Considering the expression of this

gene, we were able to classify samples from patients with IA with 82.3% sensitivity and 74.6% specificity. Moreover, we validated the expression of S100B in a real-time reverse transcription polymerase chain reaction (RT-PCR) assay and we also found a down-regulation of S100B in A. fumigatus stimulated DCs. An influence on the IL1B and CXCL1 downstream levels was demonstrated by this S100B knockdown. In conclusion, this study covers an effective feature selection revealing a key regulator of the human immune response during IA. S100B may represent an additional diagnostic marker that in combination with the established techniques may improve the accuracy of IA diagnosis.

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