ORAL ABSTRACTS

118. Transcriptional Profiling Discriminates Complete and Incomplete Kawasaki Disease (KD) from Adenovirus infection (HAdV)

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Background. The diagnosis of Kawasaki disease (KD) is solely based on clinical findings and auxiliary laboratory tests, and is difficult to distinguish from HAdV. Objective: 1) To characterize the specific transcriptional profiles of KD patients versus acute HAdV infection 2) To determine whether the molecular distance to health (MDTH) score (a molecular score that reflects the perturbation derived from whole genome transcriptional analysis) correlates with response to therapy.

Methods. RNA samples from peripheral whole blood were analyzed using Illumina chips and GeneSpring software from 76 pediatric patients with complete KD, 13 with incomplete KD, and 19 patients with HAdV and age- and sex-matched healthy controls (HC). We used class comparison algorithms (Mann-Whitney $p < 0.01$, Benjamini-Hochberg, and 1.25 fold change filter) and modular analysis to define the KD profiles.

Results. Statistical group comparisons identified 7,899 genes differentially expressed in 39 complete KD patients versus HC, and was subsequently validated in another 37 patients with complete KD and in 13 patients with incomplete KD. Using the KD biosignature, modular analysis demonstrated overexpression of inflammation, neutrophils, myeloid cell, coagulation cascade, and cell cycle genes in KD. To differentiate KD from HAdV, we used 25-classifier genes; cross-validation of the training set correctly classified 21 of 22 samples. In the validation analysis (test set) classifier genes correctly categorized 20 of 22 independent patient samples. Thus, the KNN algorithm demonstrated a sensitivity of 92% (95% CI [73%-99%]) and a specificity of 90% [67%-98%] to differentiate KD from HAdV. KD patients that remained febrile 36 hours after treatment with IVIG had higher baseline, pre-treatment MDTH values compared with responders [5572 in responders versus 12,290 for non-responders, $p = 0.009$]. MDTH score significantly correlated with the baseline c-reactive protein ($R = 0.29$, $p = 0.008$), and was inversely related to the days of fever at the time of sample acquisition of the ($R = -0.2$, $p = 0.03$). MDTH in KD patients was significantly higher than in HAdV patients 5097 [IQR 2772-8152] vs. 1331 [IQR 638-2058].

Conclusion. Transcriptional signatures can be used as a tool to discriminate between KD and HAdV infection, and may also provide prognostic information.

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