Serum Versus Peripheral Blood Mononuclear Cells (PBMCs): Different MicroRNA Profiles in Sarcoidosis Patients

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Introduction: Sarcoidosis is a granulomatous disease that involves the lungs in more than 90% of the affected individuals. The overall prevalence of sarcoidosis in the US is estimated to be around 15 in 100,000 population/year. Noncoding RNAs (ncRNAs) isolated from PBMCs of pulmonary sarcoidosis subjects were found diagnostic when compared to healthy controls. NcRNAs are implicated in the physiological processes that maintain cellular homeostasis. microRNAs (miRNAs), a group of small ncRNAs <200 nucleotides, have been studied in several diseases because of their potential use in diagnosis and monitoring during therapy. However, the role of serum circulatory miRNAs in sarcoidosis, particularly in subjects with pulmonary fibrosis remains unclear. We questioned whether serum miRNA profiles are similar to or different from PBMC miRNA profiles. Therefore, we conducted this study to compare expression patterns of serum and PBMC miRNAs and to find out if serum miRNA can be used as a biomarker of sarcoidosis. Methods: We selected 5 subjects with confirmed pulmonary sarcoidosis to compare their miRNA profiles in serum and PBMCs. Sarcoidosis was confirmed based on clinical, radiological and pathological findings based on ATS guidelines. All subjects had pulmonary fibrosis in chest CT scans, were male, and their mean age was 55 years. miRNA from PBMCs were sequenced using the Illumina TruSeq Small RNA Library Kit on the NextSeq500 in single end 75bp reactions. Due to low concentration of miRNA, the targeted HTG EdgeSeq miRNA WT Assay containing 2,102 probes, including 13 housekeeper genes, five negative process controls, and one positive process control was used for serum. Results: We found a total of 50 miRNAs expressed significantly different between samples from serum and PBMCs after correcting for multiple comparisons, with a false discovery rate < 0.05. Figure 1 shows the miRNA expression patterns between serum and PBMC samples in sarcoidosis patients with pulmonary fibrosis. Pathway analysis showed that miRNA-222, miRNA-let-7g, miRNA-20a, miRNA-16, miRNA-221, miRNA-126, and miRNA-146a which inhibit inflammatory response, were all down-regulated in serum samples, and not in PBMC samples. Conclusions: We found that serum miRNA profiles are different from PBMC miRNAs in sarcoidosis patients with pulmonary fibrosis. This may lead to develop a novel diagnostic tool for pulmonary fibrosis with a simple blood test at the point of care.

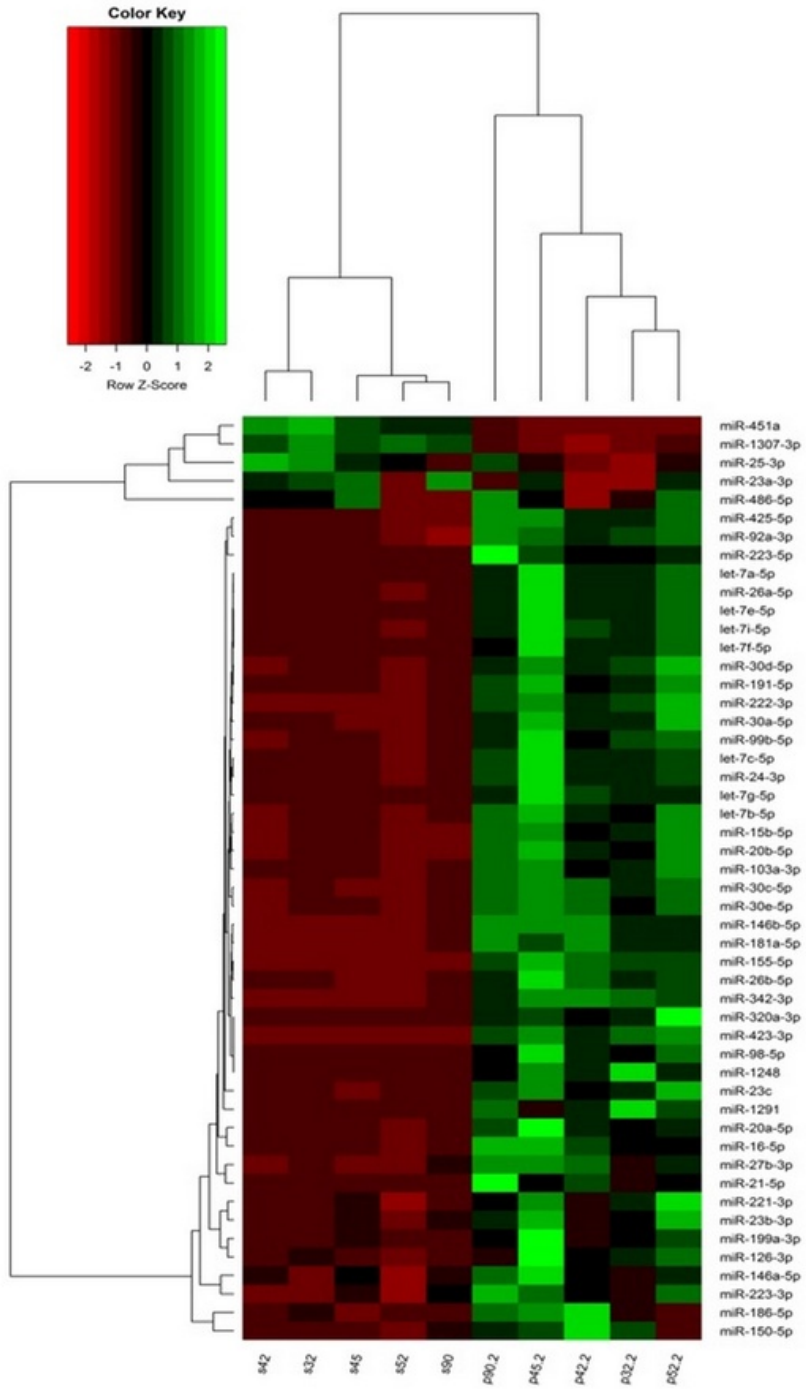

Figure 1: Heatmap of miRNA profile in serum and PBMC samples in sarcoidosis patients with pulmonary fibrosis.

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