Circulating miRNA in Idiopathic Pulmonary Fibrosis: A Pilot Study

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RATIONALE Idiopathic pulmonary fibrosis (IPF) is a chronic progressive fibrotic disease characterized by exertional dyspnea and non-productive chronic cough. Although the pathogenesis of IPF is unknown, genetic and environmental factors could be implicated in the development of the fibrotic process. Currently, early and/or minimally invasive biomarkers are not available for this disease. In this context, liquid biopsy techniques are gaining an increasingly important role in the evaluation of such biomarkers. Particularly, circulating microRNAs (miRNAs) can provide valuable insights into theunderlying pathogenetic mechanisms of complex and multifactorial diseases. In this study, we aimed at investigating the profile of circulating miRNAs in patients with IPF.METHODS We analised the profile of circulating miRNAs through small RNA sequencing (RNASeq) in the plasma of 14 patients with IPF and 7 healthy subjects. All patients aged between 59 and 88 years, and had high-resolution CT features suggestive for definite or probable usual interstitial pneumonia (UIP).RESULTS Thirty differentially expressed miRNAs were identified, including 21 up-regulated and 9 down-regulated. This profile was found to be unique for this type of pathology, showing no overlap with circulating miRNAs identified in other fibrotic diseases such as liver cirrhosis and autoinflammatory diseases such as Systemic Lupus Erythematosus and vasculitis like Behçet's syndrome. Functional analysis using Gene Ontology (GO) revealed several terms related to fibrosis, particularly signaling mechanisms mediated by GTPases and cell adhesion molecules. Analysis conducted through the KEGG ontology showed significant enrichment for the term Non-Small Cell Lung Cancer (NSCLC).Specifically, among the target genes and miRNAs deregulated in patients with IPF, we identified genes relevant to the pathophysiology of this type of tumor (ALK, EGFR numerous kinases, genes related to apoptosis, etc.).CONCLUSIONS Overall, the results of the present study, albeit preliminary, open up interesting views for studying pathophysiological mechanisms and lay the groundwork for the use of miRNAs as early biomarkers of IPF and its progression

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