The Role of a Panel of Pro-Fibrogenic miRs in Fibrotic Lung Disorders

Original
The Role of a Panel of Pro-Fibrogenic miRs in Fibrotic Lung Disorders / Meloni, Federica; Inghilleri, Simona; DI CARLO, Stefano; Cova, Emanuela; Calabrese, Fiorella; Piloni, Davide; Zorzetto, Michele; Divizia, Laura; Politano, GIANFRANCO MICHELE MARIA; Benso, Alfredo; Vanaudenaerde, Bart; Kessler, Romain; Porzio, Michele; Morbini, Patrizia; Rossi, Elena. - In: AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE. - ISSN 1535-4970. - ELETTRONICO. - 195:A6415(2017), pp. 1-1.

Availability:
This version is available at: 11583/2674536 since: 2017-06-13T09:31:31Z

Publisher:
ATS Journals

Published

Terms of use:
openAccess
This article is made available under terms and conditions as specified in the corresponding bibliographic description in the repository

(Article begins on next page)
The role of a panel of pro-fibrogenic miRs in fibrotic lung disorders.

Simona Inghilleri\textsuperscript{1}, Patrizia Morbini\textsuperscript{2}, Elena Rossi\textsuperscript{2}, Stefano Di Carlo\textsuperscript{3}, Emanuela Cova\textsuperscript{1}, Fiorella Calabrese\textsuperscript{4}, Davide Piloni\textsuperscript{1}, Michele Zorzetto\textsuperscript{1}, Laura Divizia\textsuperscript{1}, Gianfranco Politano\textsuperscript{3}, Alfredo Benso\textsuperscript{3}, Bart Vanaudenaerde\textsuperscript{5}, Romain Kessler\textsuperscript{6}, Michele Porzio\textsuperscript{6} and Federica Meloni\textsuperscript{1}.

\textsuperscript{1}Respiratory Diseases Dpt., IRCCS San Matteo Foundation, Pavia, Italy; \textsuperscript{2}Molecular Medicine, University of Pavia, Pavia, Italy, \textsuperscript{3}Control and Computer Engineering Dpt., Politecnico di Torino, Torino, Italy, \textsuperscript{4}Thoracic and Cardiovascular Sciences Dpt., University of Padua, Padua, Italy, \textsuperscript{5}Dept. of Clinical and Experimental Medicine Division of Respiratory Diseases Lung Transplant Unit Leuven University of Leuven \textsuperscript{6}Department of Pneumology University Hospital of Strasbourg

\textbf{Rationale} Pulmonary idiopathic fibrosis (IPF), Cryptogenetic organizing pneumonia (COP) and bronchiolitis obliterans syndrome (BOS) are rare pulmonary disorders, linked by the presence of fibrotic lesions. In our previous work (Di Carlo, 2016) on BOS we computationally identified a panel of candidate miRNAs and demonstrated by \textit{in situ} hybridization analysis (ISH) and qRT-PCR, a dysregulation of two highly ranked miRNAs, miR-21 and miR-34a; ISH confirmed abnormal miR-21 and miR-34a expression in BOS lesions; other miRNAs where indicated as potential candidates in BOS by computational analysis.

\textbf{Aim} We extended our previous work by analyzing the expression of miR-21, miR-34a and three other highly ranked miRNAs (miR-145, miR-146b-5p and miR-381) in BOS and other lung diseases associated with fibroblast activation/proliferation and collagen deposition. Identifying a specific profile of dysregulated miRNAs could provide useful diagnostic markers and potential therapeutic target.

\textbf{Methods} We evaluated miRNAs expression profile by ISH and RT-PCR quantification in a series of formalin-fixed and paraffin-embedded lung samples obtained from patients with IPF (n. 8), OP (n. 8), BOS (n. 12) and normal lung from organ donors.

\textbf{Results} In BOS, COP and IPF/UIP miR-21 and miR-145 were expressed in fibroblasts of BO lesions, OP plugs and in fibroblast foci respectively, and in reactive alveolar epithelia; miR-146b expression correlated to the amount of inflammatory cell infiltrates and epithelial activation in all cases, while a weak expression was evident in OP and IPF/UIP lesions. miR-34a overexpression was associated with the activation of alveolar epithelia and to a lesser extent with fibroblast lesions in OP. miR-381 showed a weak expression in all diseases, and was localized especially in inflammatory cells. ISH data have been confirmed by qRT-PCR analysis obtained on same samples.
**Conclusions** miR-21, miR-145 and miR-146b are over-expressed in fibroblasts in all the cases analyzed, but their expression is not disease-specific, although some differences are observed in different diseases. This finding underlies their role in non-specific fibrotic lung processes. ISH complements the results of qPCR, allows the precise cellular localization of miR expression, and improves correlations with cell-specific pathways.