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218. Pathogenic mechanisms of lung transplant complications: a focus on CLAD

PA1791

System biology (SB) allows the identification of pathogenic micro RNA (miR) in BOS

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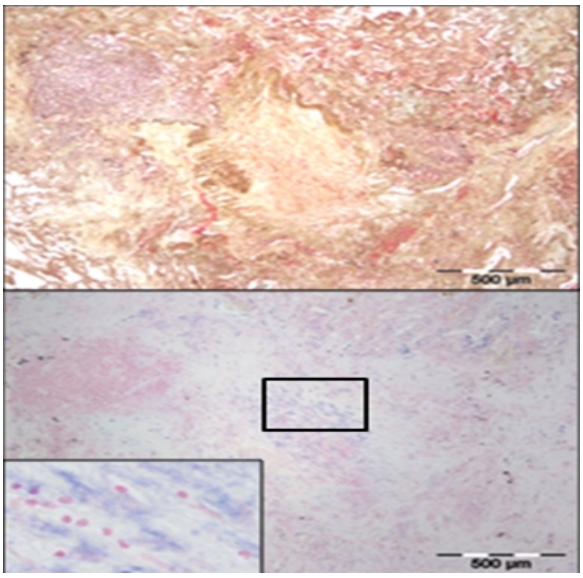
BOS is characterized by fibrotic bronchiolar obliteration. MicroRNAs (miRs), are small, non-coding, single stranded RNAs playing a role in many biological processes including EMT. Recent studies demonstrated a role of miRs in fibrotic disorders but evidence on BOS are lacking. We applied an SB approach and computationally identified and scored a limited panel of miRs potentially relevant in BOS. All pathways involved in BOS were included, enhanced using the ReNEs software, then list of intronic miRs was extracted. The initial panel of 54 candidates was scored (Coverage and ValCov scores) considering miR activity on pathways and previous validation. To validate SB analysis we selected, among miR with ValCov score >0.4, **miR21** (2° rank: 0.047) that was assessed by ISH on 3 samples: 3 mesenchimal cell lines (MC) derived from BAL of BOS pts, 2 lung BOS grafts of orthotopic rat lung Tx model (outbread CD SPF/VAF) and one explanted human BOS lung. MC lines expressed high level of miR21 with slight variation among lines. In addition, while native rat lung had no miR21 expression, a high degree of miR21 was documented in myofibroblasts of the OB lesion developed 15 days after Tx. Finally a very high degree of miR21 was documented in OB lesions of the BOS lung, while normal human lung had minimal miR21 positivity.



Our SB approach is validated and recognizes miR21 as a pathogenic factor and a possible therapeutic target in BOS.