Abstract

MiR-221 plays essential role in Epithelial-Mesenchyme Transition (EMT). HMGA2 is a key regulator of EMT. However, the role of miR-221 in pulmonary fibrosis, and the relation between miR-221 and HMGA2 remain largely unknown. Here we detected the expression of miR-221 and HMGA2 in human idiopathic pulmonary fibrosis (IPF) tissue and pulmonary cells, including adenocarcinoma A549 and human bronchial epithelium (HBE) cells, and found that expression of miR-221 was inhibitedin both tissues and cells, while high expression of HMGA2 was observed in mRNA and protein level. Additionally, TGF-β1 induced the upregulation of EMT, characterized byupregulated mesenchyme markers, including N-cadherin, Vimentin, α-SMA, Collagen I, and Collagen III, anddownregulated epithelial marker in A549 and HBE. We then performed miR-221 mimics transfection, and found that expression of p-Smad3 in miR-221-overexpressed cells was significantly downregulated, compared with TGF-β1 treated cells without transfection. Furthermore, overexpression of miR-221 led to the decreased expression of HMGA2, the downregulated EMT, and the inhibited proliferation in A549 and HBE. HMGA2 was directly targeted by miR-221 using Dual Luciferase Reporter Gene assay, which negatively regulated the expression of HMGA2. Finally, bleomycin (BLM)-induced pulmonary fibrosis model was used to confirm the effect of miR-221 on EMT. H&E staining showed that BLM induced thicker alveolar walls and more collagen deposition, while miR-221 treatment reduced lung fibrosis, and tissuesshowed thinner alveolar wallsand normal lung alveoli. Besides, EMT process was downregulated after miR-221 injection. Conclusively, miR-221 targets HMGA2 to inhibitbleomycin-induced pulmonary fibrosis through TGF-β1/Smad3.