Involvement of TET in the Pathology of Diffuse Lung Diseases

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RATIONALE: DNA methylation is an epigenetic mechanism involving the transfer of a methyl group onto the C5 position of the cytosine to form 5-methylcytosine and it affects various biological phenomena. The Ten-eleven translocation (TET) gene has been shown to be involved in DNA demethylation. DNA methylation has been reported to be associated with diffuse lung diseases, but the role of the TET gene in diffuse lung diseases has not been studied. We examined how TET gene affects the pathophysiology of diffuse lung diseases.

METHODS: We analyzed TET gene expression in lung tissues of the patient with diffuse lung diseases and of mouse lung from bleomycin (BLM)-induced fibrosis model. We suppressed TET gene expression in cultured human airway epithelial cells using small interfering RNA and examined changes after TGFβ exposure.

RESULTS: In the lung tissues of patients with diffuse lung disease, TET1 gene expression tended to be decreased in tissues with severe fibrosis compared to tissues with mild fibrosis and control tissues. In addition, in the lung tissue of BLM pulmonary fibrosis model, the expression of TET1 gene was decreased compared to naïve mice. In cultured human airway epithelial cells, the expression of the Col1α2 gene induced by TGFβ exposure was further enhanced by suppressed TET1 gene expression.

CONCLUSION: These findings suggest that the expression of TET1 gene is related to the pathophysiology of diffuse lung diseases.

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