Altered DNA methylation profile in idiopathic pulmonary fibrosis.

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Abstract

RATIONALE: DNA methylation is an important epigenetic mechanism, which often occurs in response to environmental stimuli and is crucial in regulating gene expression. It is likely that epigenetic alterations contribute to pathogenesis in idiopathic pulmonary fibrosis (IPF).

OBJECTIVES: To determine the DNA methylation changes in IPF and their effects on gene expression.

METHODS: Total DNA methylation and DNA methyltransferase expression were compared in IPF and normal control lung tissues. IPF and normal tissues were subjected to comparative analysis of genome-wide DNA methylation and RNA expression using DNA hybridization to the Illumina HumanMethylation27 BeadChip and RNA hybridization to Illumina HumanHT-12 BeadChip. Functional analyses of differentially expressed and differentially methylated genes were done. Selected genes were validated at DNA, RNA, and protein levels.

MEASUREMENTS AND MAIN RESULTS: DNA methylation status was altered in IPF. IPF samples demonstrated higher DNA methyltransferase expression without observed alterations in global DNA methylation. Genome-wide differences in DNA methylation status and RNA expression were
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...demonstrated by array hybridization. Among the genes whose DNA methylation status and RNA expression were both significantly altered, 16 genes were hypermethylated in DNA associated with decreased mRNA expression or vice versa. We validated CLDN5, ZNF467, TP53INP1, and DDAH1 genes at the level of DNA methylation status, RNA, and protein-level expression.

CONCLUSIONS: Changes in DNA methylation correspond to altered mRNA expression of a number of genes, some with known and others with previously uncharacterized roles in IPF, suggesting that DNA methylation is important in the pathogenesis of IPF.

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