Alternative Splice Variant Expression of MCIDAS Does Not Induce Ciliated Cell Differentiation

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Mucociliary clearance of toxins from the respiratory tract epithelium depends on a precise ratio of ciliated to goblet cells. If this ratio is low, mucus produced by the goblet cells builds up in the airway, leading to airway pathologies, including asthma and chronic obstructive pulmonary disease. To increase this ratio, more ciliated cells must be differentiated from basal cells, which act as stem cells in the airway. This process, called ciliogenesis, is dependent on the expression of the Forkhead Box J1 gene (FoxJ1), which is induced by the MCIDAS (Multiciliate Differentiation and DNA Synthesis Associated Cell Cycle Protein) gene. Natural splice variants of the MCIDAS gene have recently been discovered, including (delta)exon 3 and (delta)exon 4; a third variant, ORF 2, was artificially synthesized. In order to determine whether these splice variants induce ciliogenesis, western blots, quantitative reverse transcription PCR (RT-qPCR), and immunofluorescence staining were performed to assay the relative expressions of MCIDAS and FoxJ1 in cells transduced with lentiviral vectors containing a specific splice variant of the MCIDAS gene. Cells transduced with (delta)exon 3 or (delta)exon 4 did not express FoxJ1, as the RT-qPCR and the immunofluorescence showed no FoxJ1 expression or FoxJ1 protein synthesis. Conversely, the ORF 2 cells expressed elevated levels of FoxJ1. This suggests that individuals whose splicing mechanisms create (delta)exon 3 and (delta)exon 4 variants are at greater risk of developing mucociliary clearance-related disorders. Further research investigating the role of these MCIDAS splice variants in ciliogenesis opens the potential for new therapeutic avenues in the diagnosis and treatment of lung disease.

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