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Effect of Notch1 signaling pathway on the differentiation of alveolar epithelial cells in the nitrofen-induced congenital diaphragmatic hernia rat model

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Abstract

Purpose: Pulmonary hypoplasia remains a major cause of high mortality in congenital diaphragmatic hernia (CDH). Notch1 signaling pathway plays a critical role in alveolar epithelial cells(AECs) differentiation which dominated in the pulmonary hypoplasia of CDH. However, the effect of Notch1 pathway in CDH remains unclear. We design this study to investigate the hypothesis that the aberrant Notch1 pathway leads to the pulmonary dysplasia in nitrofen-induced CDH rat model. Methods: Pregnant rats were designed as follows: Control, CDH, CDH+CUR. Morphological, Immunostaining and qRT-PCR study were performed to determine the expression levels of T1α and TTF1 in AECs and the expression levels of gene including NICD1 and Hes1 associated with Notch1 signaling pathway. Results: Immunostaining of AEC-I marker T1α and AEC-II marker TTF1 showed that the positive area ratio of T1α in CDH group was less in CUR and Control group, TTF1 was larger in CUR and Control than CDH group ($p< 0.05$). NICD1 and Hes1 in CDH group were lager than CUR and Control group ($p< 0.05$). qRT-PCR showed that the expression levels of T1α in CDH group was lower than that in CUR and Control group ($p< 0.05$), and TTF1, NICD1 and Hes1 in CDH group were higher than CUR and Control group ($P < 0.05$). Conclusion: Aberrant Notch1 signaling pathway and AECs differentiation disorders are involved in the pathogenesis of pulmonary hypoplasia in nitrofen-induced CDH rat model. Our data suggest that overexpressed Notch1 signaling pathway may cause pulmonary hypoplasia in CDH by inhibiting the differentiation of AECs.

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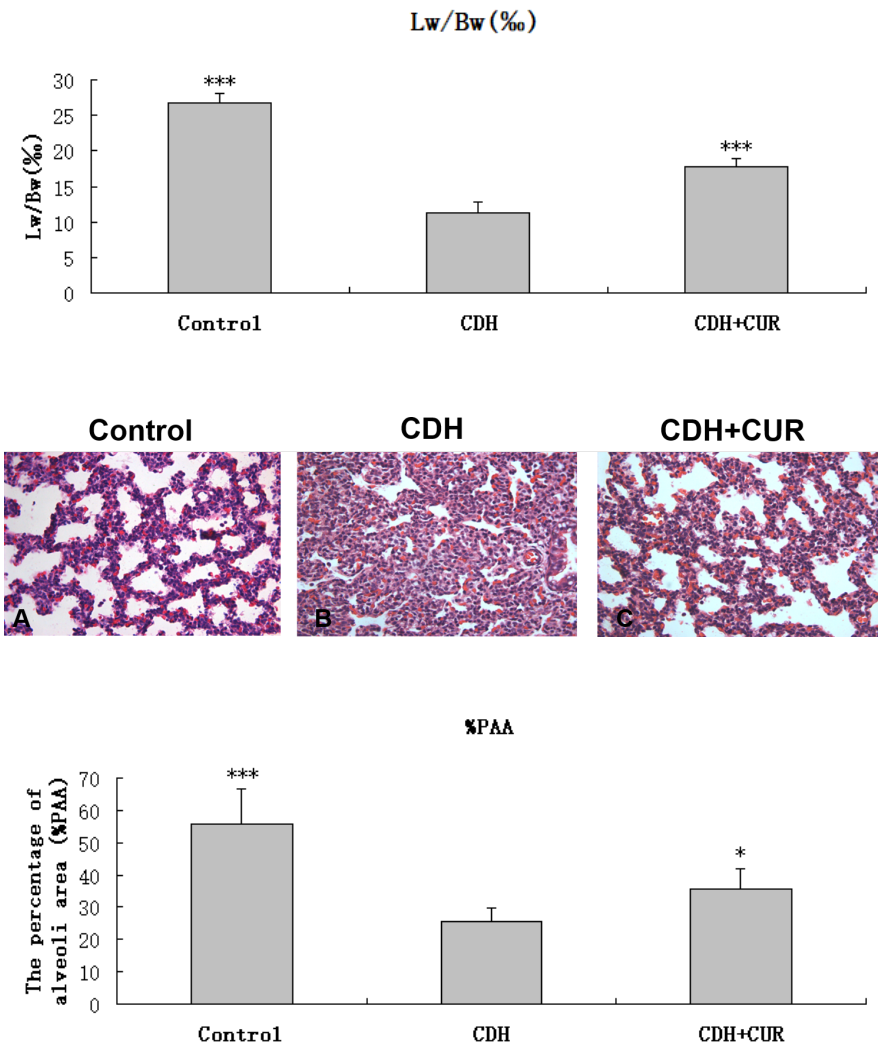

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