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Dysregulation of Yes-associated Protein Reduces Proliferation in Nitrofen-induced Hypoplastic Lung Development and Congenital Diaphragmatic Hernia (CDH

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Background:

CDH is the developmental defect that results in developing stiff lungs and less airway branching. Yap is a transcription co-activator which controls organ size by regulating cell proliferation. Recent data showed that Yap is essential for airway branching in normal lung developmentbut the role of Yap in CDH is unknown, yet.

Objective:

We hypothesize that disrupted expression of Yap is associated with abnormal lung development in the nitrofen rat model of CDH.

Methods:

To test our hypothesize, we propose the following experiments: **1)**inducing abnormal lung development and CDH by gavaging nitrofen, a herbicide, to dams on embryonic day (E) 9, **2)**isolating lungs at early and late lung development, **3)**performing Western Blot and total protein normalization,**4)**performing immunofluorescent (IF) and imaging by using Zeiss epi-florescent microscope to better distinguish the localization of Yap, **5)**statistics by using Prism-graphpad

Results:

WB data show that activated form of Yap is significantly (p-value:0.05) lower and inactivated form of Yap (p-Yap) is significantly higher (p-value:0.05) in late development of nitrofen-induced hypoplastic lungs in compare to normal lung tissue. Also, “IF” results show that in nitrofen-induced hypoplastic lung in compare to control lung, Yap localization is more concentrated in nuclei of mesenchymal cells and airway epithelium in early development, and is more inactive and sequestered in the cytoplasm in the late stage.

Conclusion:

In normal lung development, Yap translocate to the nuclei in low cell density to increase cell proliferation. Therefore, in early lung development, Yap is more active in the mesenchymal cells and in late development, it becomes more active in airway epithelial cells. In nitrofen-induced abnormal lungs, the expression pattern of Yap is the same as normal lungs in early development, but it dysregulates in epithelial cells which results in less airway branching in late development.