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Activation of the Aryl Hydrocarbon Receptor is involved in the pathogenesis of CDH

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Background:

Every 10 minutes a baby is born with congenital diaphragmatic hernia (CDH). The involvement of environmental chemicals may explain 70% of CDH cases. The aryl hydrocarbon receptor (AHR) protein, an environmental chemical sensor, may be involved in the development of CDH. Interactions between AHR and associated CDH pathways have been linked, but not proven. We hypothesize that the activation of AHR by environmental factors is involved in the pathogenesis of CDH.

Objective:

AHR expression in CDH patients will be compared to the associated established nitrofen rat model. The activation of known CDH inducing pathways by AHR will be studied.

Methods:

We compared the expression of AHR in lung sections near birth from human CDH patients (n = 3, Weeks 39 - 40) and the nitrofen treated rats (n = 3, E21) to age-matched controls using immunofluorescence (IHC/IF). We assessed the response of AHR to nitrofen and known ligands; benzo[α]pyrene and resveratrol in the BEAS-2B human epithelial cell line (n =3). AHR activity within a 24 hour exposure period was assessed with immunocytochemistry (ICC/IF).

Results:

Both CDH patients and rat lung sections have increased AHR abundance in the mesenchyme and smaller airways compared to controls. AHR activation was observed by ICC/IF in BEAS-2B cells within one hour of treatment. The signal transition from the cytoplasm to the nucleus indicates activation through ligand binding. After 24 hours of treatment, the signal detected was strictly cytosolic and decreased.

Conclusion:

The dysregulated expression of AHR is involved in CDH. Lung sections exhibited increased abundance of AHR in CDH patients and the rat model. A comparison of nitrofen to known ligands implicates environmental activators of AHR in the development of CDH.