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Basic Science

Abstract Title
Exploring Airway Branching in Drosophila melanogaster Through Development of a Novel Nitrofen Model

Background
Congenital Diaphragmatic Hernia (CDH) is a severe birth defect affecting 1 in 2,500 babies, with a 30% mortality rate. CDH involves a diaphragmatic defect and pulmonary hypoplasia (PH) characterized by abnormal airway branching. The CDH rat model administers nitrofen to pregnant rats, resulting in offspring with CDH and PH. Nitrofen-exposed fetal rat lungs show abnormal airway branching even without the diaphragm defect. We aim to examine nitrofen-induced airway branching in an organism without a diaphragm: Drosophila melanogaster. Although flies lack lungs, their branching tracheal system is analogous to mammalian lungs in development and function, offering a simplified system to study disrupted airway branching in CDH.

Objective
To develop a novel Drosophila model of nitrofen-induced airway defects to investigate molecular pathways involved in the abnormal airway branching associated with CDH.

Methods
Wild-type (Canton-Special) flies were fed food containing nitrofen at 5μM, 50μM, and 500μM throughout development and adulthood. The appropriate dose was determined via lifespan assay. Ongoing work includes phenotyping tracheal branching with nitrofen using flies with tracheal specific GFP expression. Additionally, flies with gene knockdowns will be exposed to nitrofen to investigate how genes of interest impact airway branching. Lastly, tracheal cells will be isolated via FACS for RNA sequencing to uncover transcriptional responses to nitrofen.

Results
Flies exposed to 500μM nitrofen showed a significantly reduced lifespan compared to controls, indicating this is an appropriate dose. A clear sex difference was also observed with female flies surviving longer than males, suggesting a potential sex-specific difference in airway response to nitrofen. Preliminary imaging confirms tracheal specific GFP expression, allowing phenotyping to be underway.

Conclusion
This novel Drosophila model of abnormal airway branching provides a simplified yet powerful tool to explore the developmental and genetic mechanisms disrupted by nitrofen. Results of this study may elucidate novel mechanisms and modifiers of abnormal lung development in CDH.

Authors

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