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Basic Science

Abstract Title
Synthetic immunomodulatory peptides can improve abnormal lung development in the nitrofen rat model of congenital diaphragmatic hernia

Background
Congenital diaphragmatic hernia (CDH) occurs in approximately1 in 2500 live births and is associated with impaired lung development. However, the underlying pathogenesis remains poorly understood. Previous studies have shown that pro-inflammatory responses are involved in CDH. We recently demonstrated that a cathelicidin-derived peptide can rescue inflammation and enhance lung branching using the nitrofen-induced CDH explant model in vitro.

Objective
In this study, we evaluated the pro- and anti-inflammatory effects in vivo, as well as the impact on epithelial mesenchymal transition (EMT), of two synthetic peptides, including a cathelicidin-derived peptide, in the nitrofen-induced CDH rat model. Our aim was to assess their effects on fetal lung growth and repair.

Methods
Pregnant rats received nitrofen by oral gavage at embryonic day (E)9. Synthetic peptides were injected subcutaneously at E7, E9, E11, E13, and E15; controls received saline. Fetuses were harvested at E21. Body and lung weights were recorded, and diaphragmatic defects were graded (A–D). Lung morphology was assessed using hematoxylin–eosin staining. Immunofluorescence was performed to evaluate cathelicidin, NF-κβ nuclear translocation, E-cadherin and vimentin. Data were analyzed using t-tests ($p<0.05$).

Results
Peptide treatment did not change CDH incidence. In left CDH, the left lung-to-body weight ratio did not differ between the cathelicidin-derived peptide and saline groups overall. However, in severe left CDH, this ratio was significantly higher with the cathelicidin-derived peptide ($p=0.03$). In contrast, the other peptide showed a lower left lung-to-body weight ratio versus saline in left CDH ($p=0.02$). Lung morphology in left CDH did not differ between peptide and saline groups. The NF-κB nuclear translocation ratio was higher with peptide treatment ($p<0.01$). Vimentin/E-cadherin ratio in alveolar areas was lower in the cathelicidin-derived peptide group.

Conclusion
Synthetic immunomodulatory peptides may impact lung development in nitrofen-induced CDH. Further studies are required to elucidate the underlying mechanisms and advance prenatal regenerative therapy for CDH.

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