Transamniotic Stem Cell Therapy Impacts Cardiac Remodeling in the Nitrofen Model of Congenital Diaphragmatic Hernia

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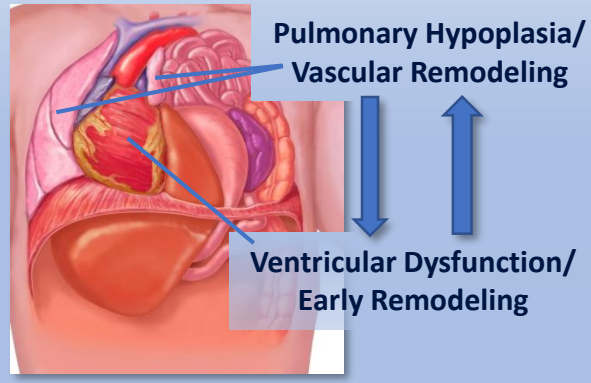
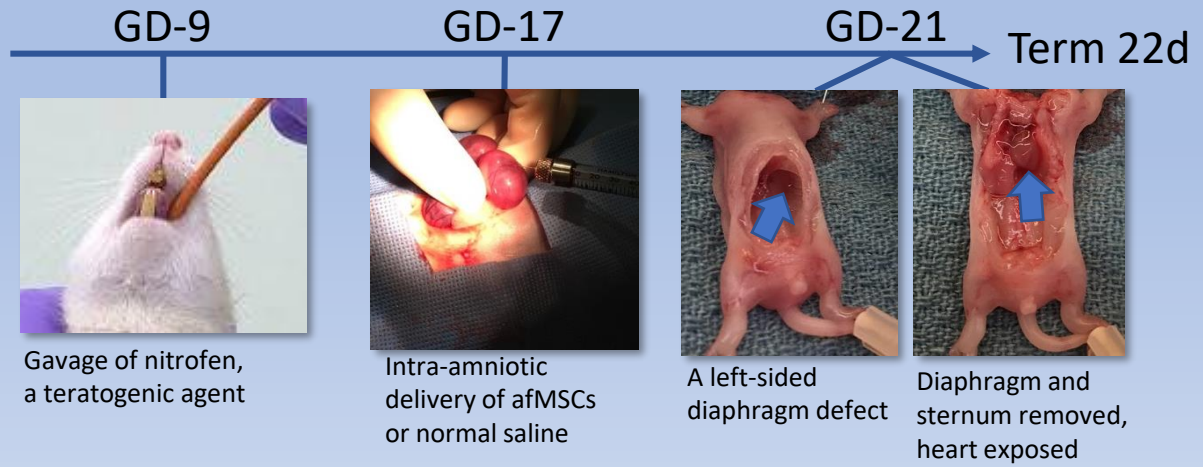
Objective

- Cardiac dysfunction plays a critical role in the physiology of congenital diaphragmatic hernia (CDH) and increases mortality
- Evidence of cardiac remodeling and immaturity in the rat nitrofen model of CDH
- Prior studies have shown potential affect of transamniotic stem cell therapy (TRASCET) on pulmonary remodeling[1]
- We hypothesize this approach could affect cardiac remodeling as well



Methods

- Nitrofen model of CDH (teratogenic gavage gestational day 9 (GD-9))
- Amniotic fluid derived mesenchymal stem cells (afMSCs) delivered via TRASCET
- CDH confirmed, whole heart removed GD-21
- Mann-Whitney U test accounting for maternal effects, conservative Bonferroni p $\leq$0.01

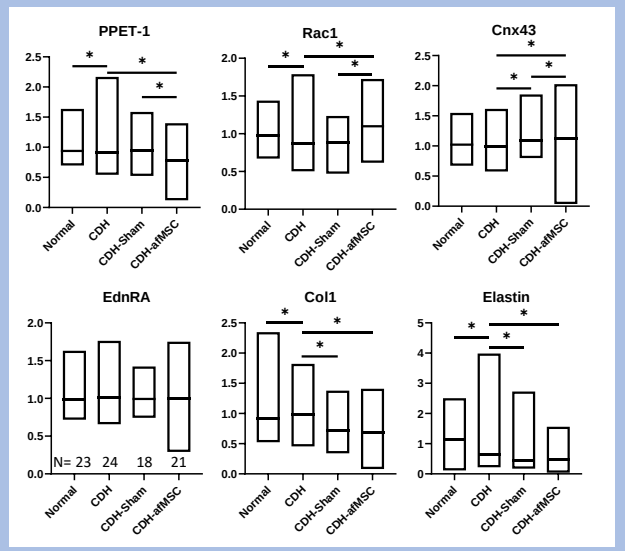


Markers

- Pre-proendothelin-1 (**PPET-1**) and endothelin-1 receptor A (**EndRA**): terminal cardiomyocyte maturation, upregulated in times of stress
- Ras-related C3 botulinum toxin substrate (**Rac1**): fetal cardiac maturation signal
- Connexin 43 (**Cnx43**): gap junction, expressed in mature, functioning cardiomyocytes
- Extracellular matrix: collagen (**Col1**) and elastin (**Elastin**)

Results:

- Evidence for decreased fetal cardiac stress (↓**PPET-1**) with increased cardiomyocyte development/maturation (↑**Rac1,** ↑**Cnx43**) in TRASCET compared to both CDH and sham
- No change in EndRA expression
- No change in expression of extracellular matrix components compared to sham



Conclusions: Transamniotic stem cell therapy impacts cardiac remodeling in experimental congenital diaphragmatic hernia. Further scrutiny into the physiologic effect is warranted.

References:

[1]Chalphin AV, Tracy SA, Lazow SP, Kycia I, Zurakowski D, Fauza DO. Congenital diaphragmatic hernia as a potential target for transamniotic stem cell therapy. *J Pediatr Surg*. 2020;55(2):249-252. doi:10.1016/j.jpedsurg.2019.10.033