# Repurposing an endogenous mRNA packaging protein from the maternal-fetal interface for in utero gene therapy

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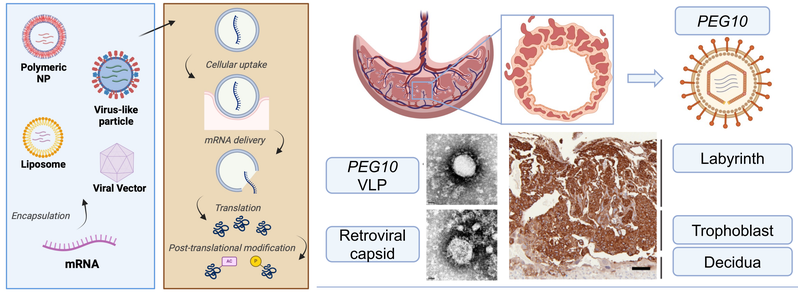
## Introduction

- In utero gene therapy aims to correct congenital disease via the delivery of deficient transgenes to developing fetuses
- Existing delivery vector for fetal gene therapy incur risk of immunogenicity, insertional mutagenesis, and have limited targetability
- **The placental protein PEG10** encapsulates specific mRNA flanked with own untranslated regions within virus-like particles (VLPs)[3]
- PEG10 highly expressed within placenta during fetal development



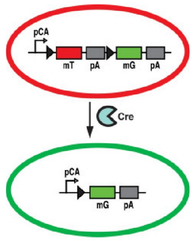


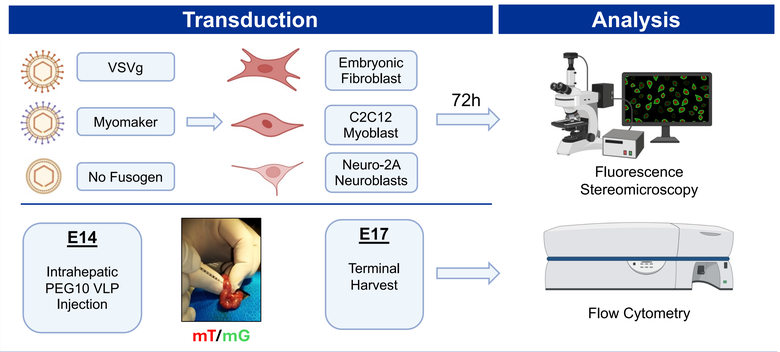


- **Hypothesis:** PEG10 VLPs are capable of packaging and delivering mRNA to the fetal environment with minimal fetal toxicity

## Methods

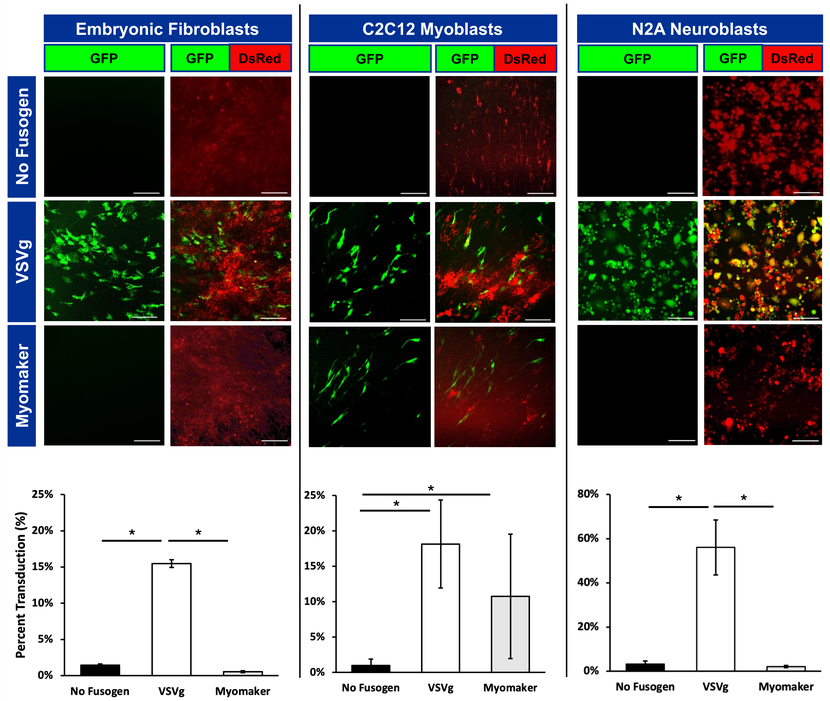
- Generated PEG10 VLPs of various pseudotypes: VSVg (broad tropism), myomaker (restricted tropism), nonpseudotyped
- In vitro co-culture of VLPs with embryonic precursor cell lines
- In vivo delivery of VLPs to mT/mG Cre-reporter mice (right) at E14 via fetal intrahepatic injection



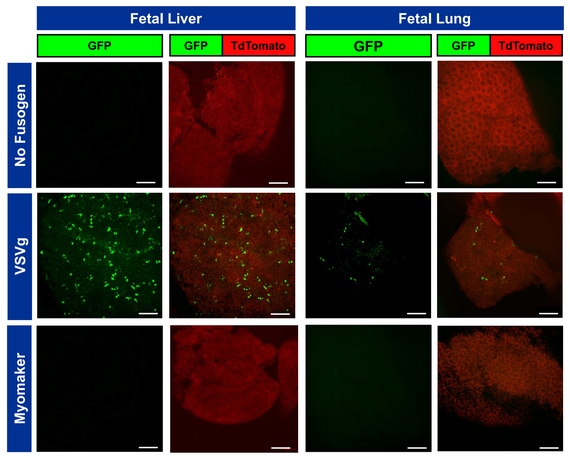



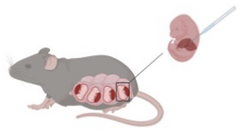

## Results

**PEG10 VLPs can be functionalized to enable cell specific delivery to various embryonic precursor cell lines**




**PEG10 VLPs deliver functional mRNA to the fetal liver and fetal lung when pseudotyped with VSVg fusogen**



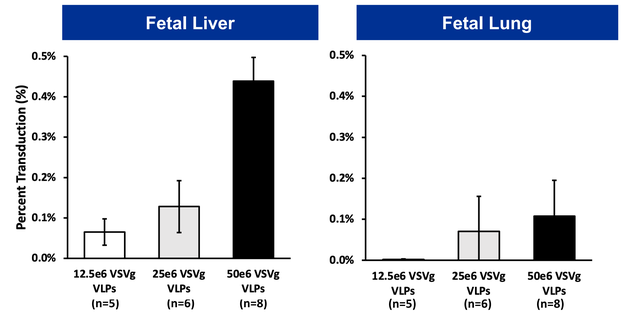



**Other harvested tissues with no detectable transduction**

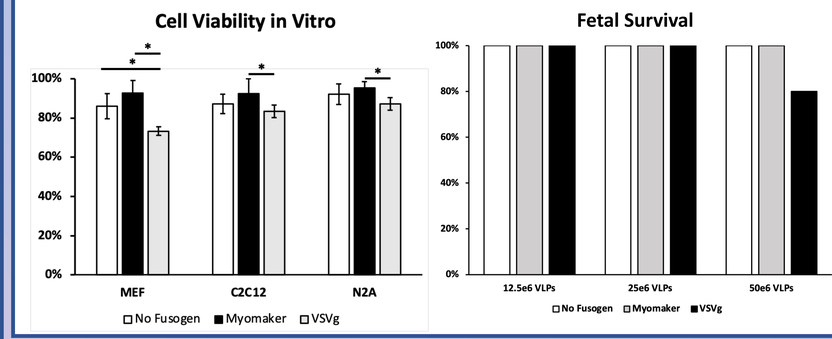
- Peripheral muscle
- Brain
- Heart
- Intestine

## Results

**Transduction efficiency approaches established levels of potential therapeutic efficacy in vivo**

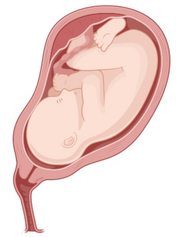



**Minimal increase in cell toxicity with VSVg-pseudotyped VLPs, but no difference in toxicity with entirely endogenous VLPs**




## Conclusions

- PEG10 VLPs **can be functionalized to enable cell-specific delivery**
- Myomaker-PEG10 is the **first entirely endogenous delivery system for muscle cells**
- VSVg PEG10 VLPs can deliver mRNA to **fetal liver and lung,** but targeted delivery in utero awaits further study



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