



# Treatment with Placenta-Derived Mesenchymal Stem Cells Mitigates Development of Bronchiolitis Obliterans in a Murine Model

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**We have no disclosures**



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## Introduction

- Bronchiolitis Obliterans (BO) limits the long-term success of lung transplantation
- Mesenchymal stem cells (MSCs) under investigation as novel treatment option in lung injury and transplant rejection
- MSC sources include bone marrow, placenta, and adipose tissue



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## Introduction

- MSCs have anti-inflammatory and immuno-modulatory properties
- MSCs have been shown to be beneficial due to their paracrine secretions, cell-cell interactions, and direct incorporation and differentiation
- Investigate MSC treatment in bronchiolitis obliterans



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## Hypotheses

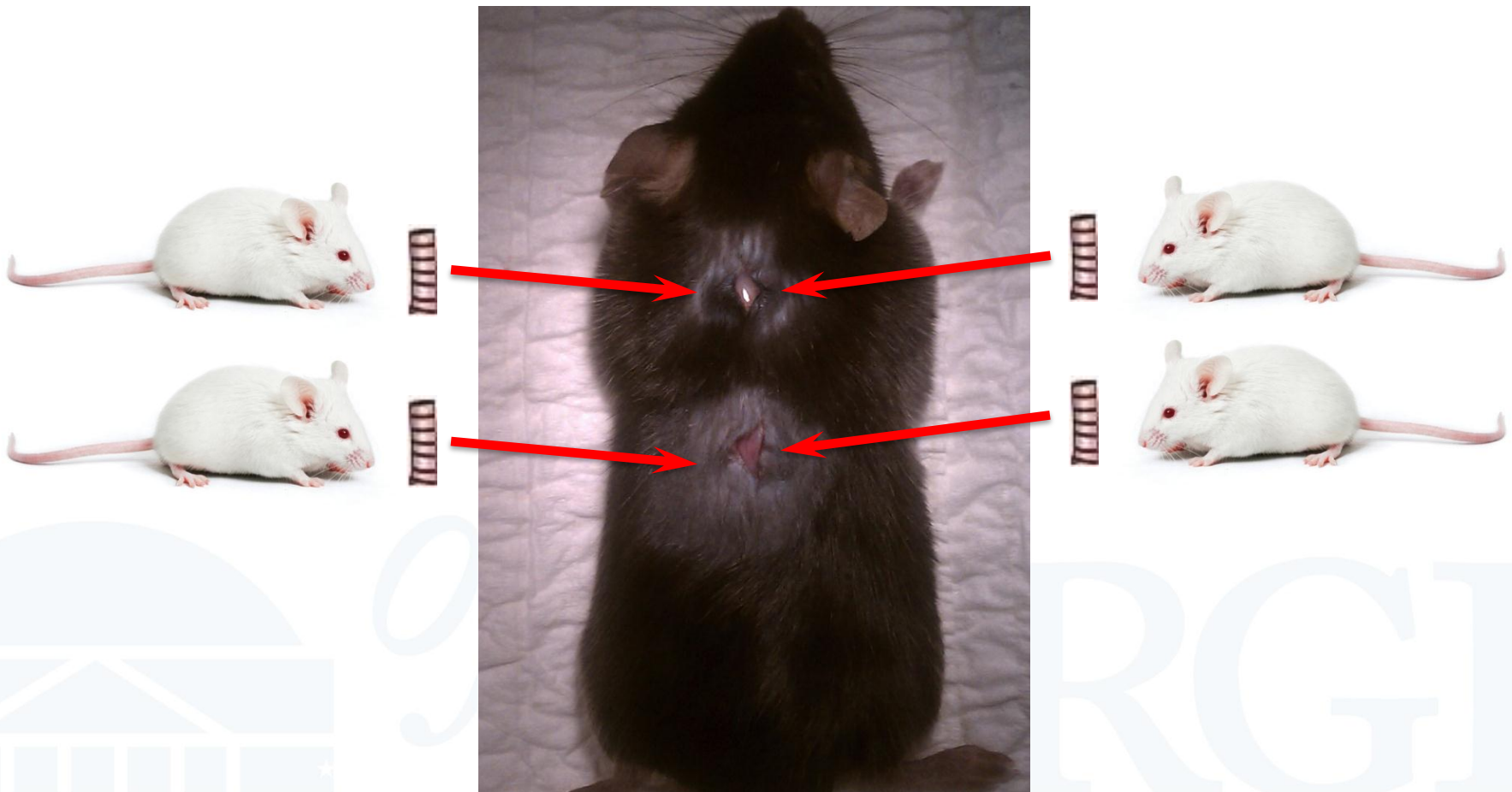
1. *Treatment with Placenta-derived Mesenchymal Stem Cells (PMSCs), or with PMSC-conditioned media, will reduce the development of BO in a murine model*
2. *The protective effects of PMSCs will be predominantly due to paracrine secretions*



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## Methods

- Murine heterotopic tracheal transplant model of BO



## Methods

- 4 treatment groups
  - 1) Placenta-derived mesenchymal stem cells (PMSCs)
  - 2) PBS control
  - 3) Media conditioned by PMSCs (PMSC media)
  - 4) Control media



## Methods

- At 3 days post-transplant, tracheas injected intraluminally with designated treatment
- Tracheas harvested at 14 or 28 days post-transplant
- Assess loss of tracheal epithelium at day 14 (H&E stain)
- Assess luminal deposition of collagen at day 28 (direct red 80 stain)
- Immunohistochemistry for human leukocyte antigen [HLA]
  - PMSCs are from human placenta

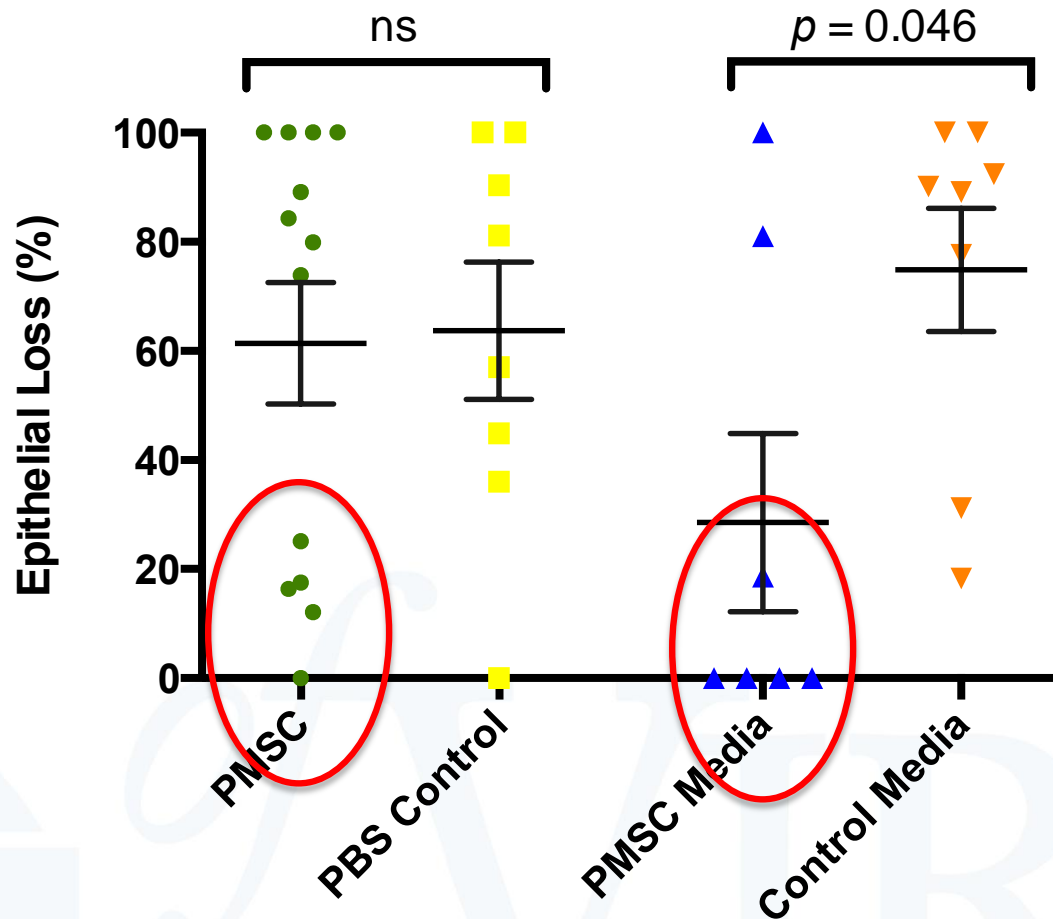


# Results

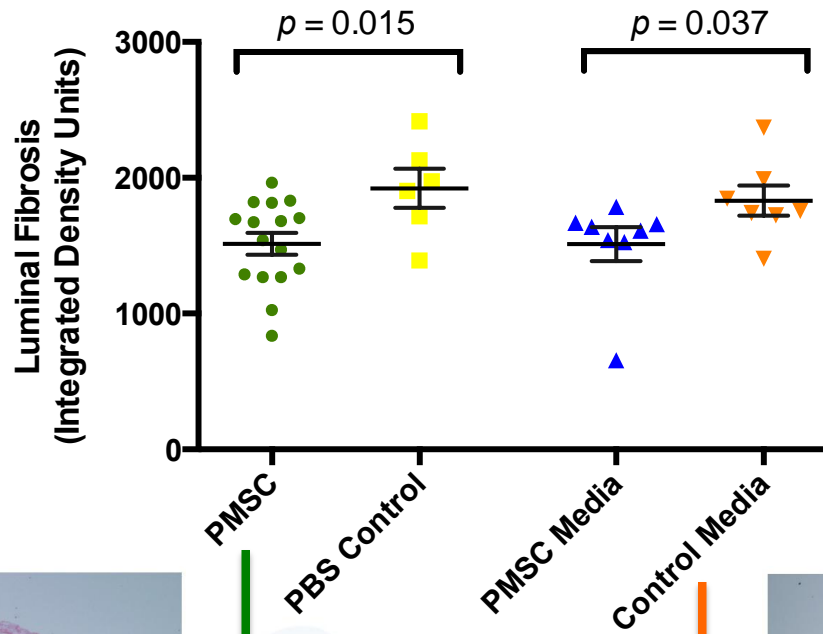


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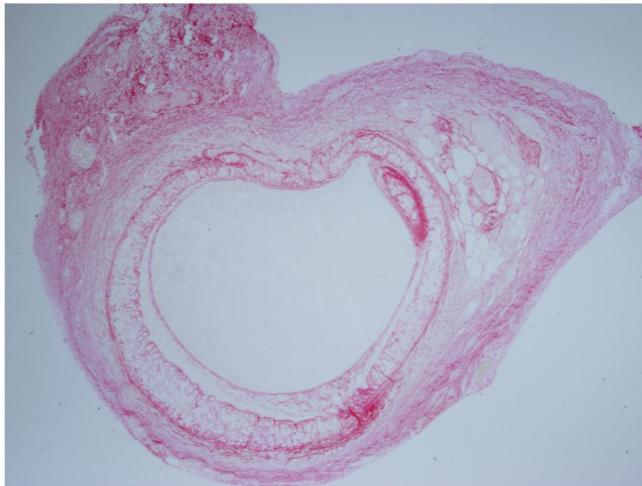
## Loss of Allograft Epithelium at 14 days



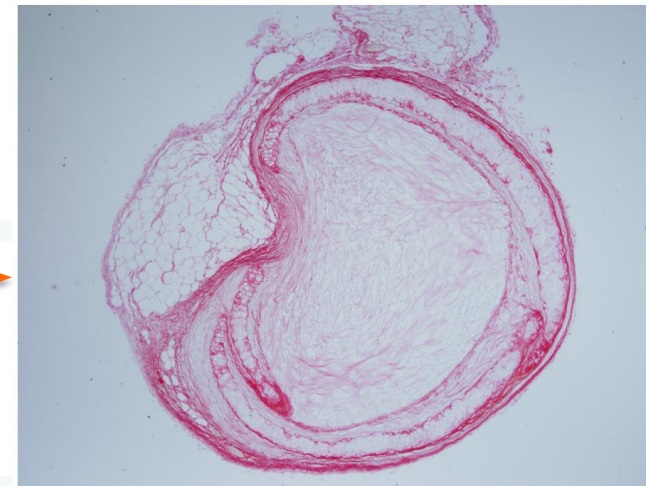
## Collagen Deposition at 28 days



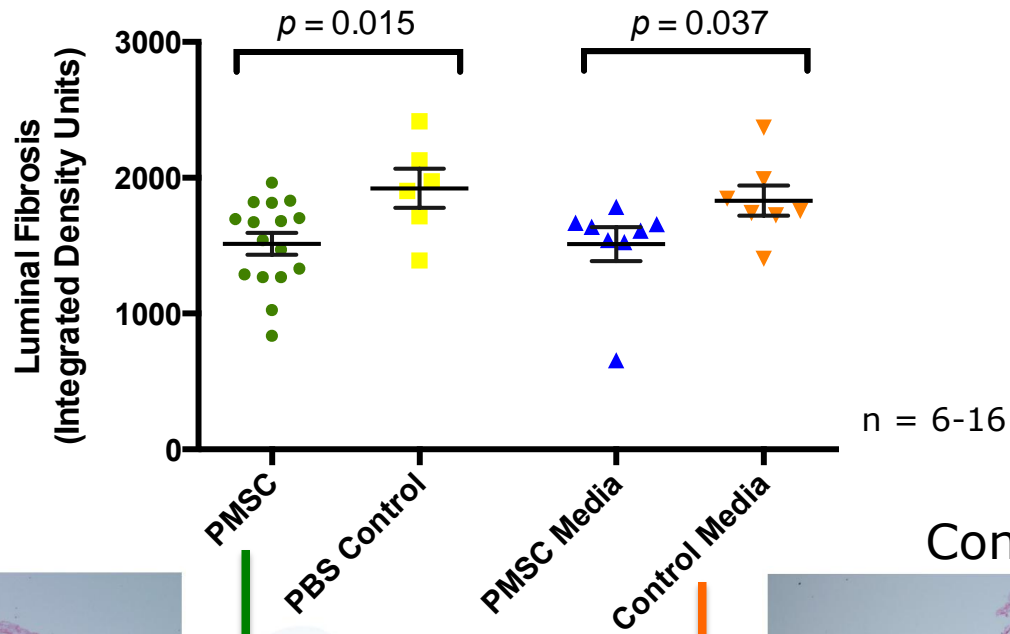
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PMSC



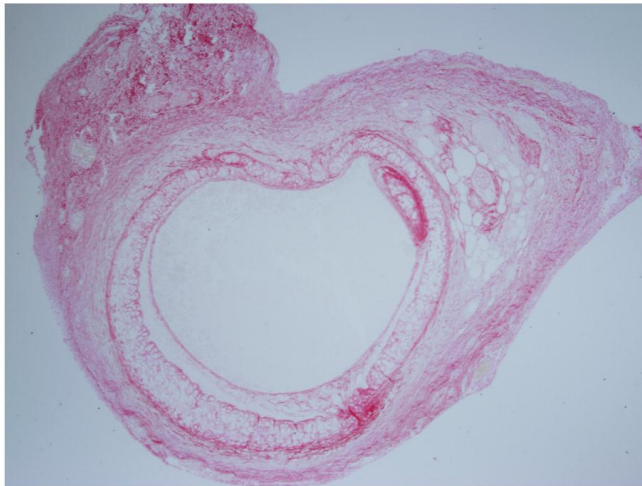
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Control Media



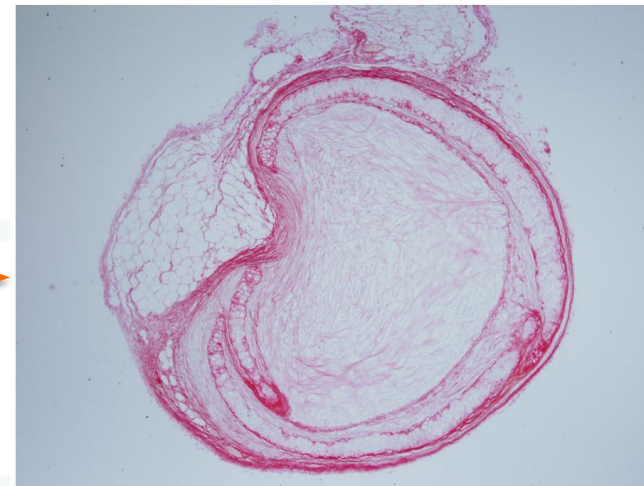
## Collagen Deposition at 28 days



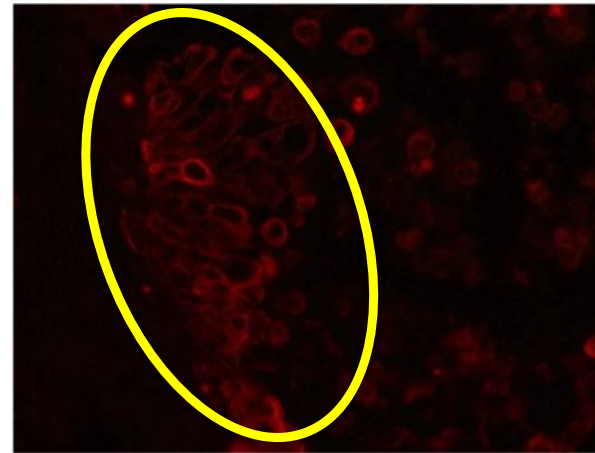
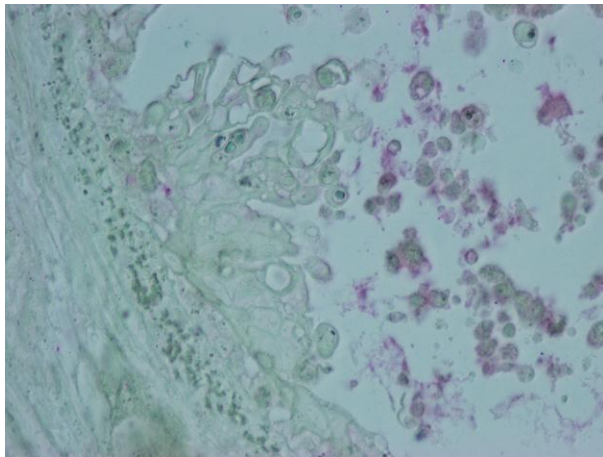
PMSC



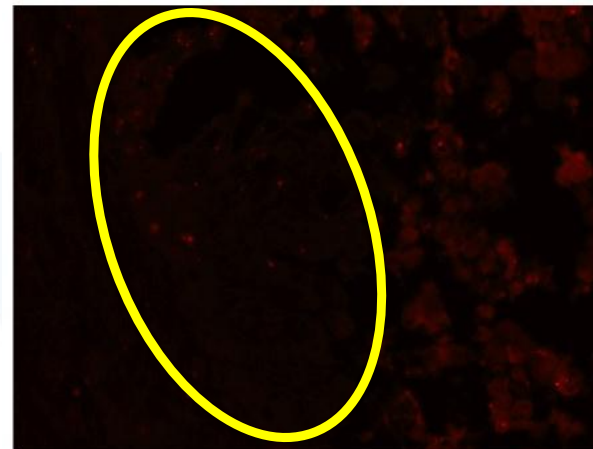
Control Media



## HLA Staining after PMSC treatment at 14 days



Anti-CK14  
[epithelium]



Anti-HLA  
[human PMSCs]

## Summary

- 1) Treatment with PMSCs and PMSC-conditioned media reduces BO development in a murine model
- 2) Protective effects of PMSCs likely due to paracrine effects rather than direct incorporation into epithelium
- 3) PMSCs may serve as a novel treatment modality to prevent BO in lung transplant patients



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**Thank you**



# Immunohistochemistry

- At day 14, PMSC-treated tracheas showed:
  - Fewer neutrophils
  - Fewer CD3+ T cells
  - More Foxp3+ T regulatory cells
  - More macrophages

