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The Sars-Cov-2 E Protein Induces Pro-Inflammatory Tlr Signaling, Lung Injury And Alveolar Remodeling In The Neonatal Lung

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The SARS-CoV-2 E protein induces pro-inflammatory TLR signaling, lung injury and alveolar remodeling in the neonatal lung

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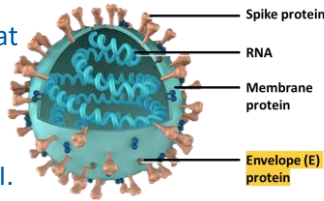
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Background and Methods

Background:

- SARS-CoV-2 can cause severe acute lung injury (ALI) in neonates. Neonates with COVID-19 can exhibit a hyper-inflammatory response with vascular injury.
- The mechanisms by which SARS-CoV-2 structural proteins induce ALI in neonates is unclear.
- Emerging data suggest that the envelope (E protein, E) of the SARS-CoV-2 activates Toll Like Receptor (TLR)-mediated immune hyperactivation and cytokine storm.

- We tested the hypothesis that SARS-CoV-2 E protein (E) can induce TLR-mediated inflammation and ALI in a neonatal mouse model of ALI.



Primary Human Pulmonary Microvascular Endothelial Cell (HPMEC, ScienCell) experimentation

Around 18wks gestation, passages 3 to 4 used.
Control cells or Silencing (siTLR2, siTLR4) or scRNA (SCBT)
Incubation with 500ng E protein (E) (Abclonal), 24hr

Cells processed for:
Trypan blue quantification
PCR, Western Blot (WB)

Mouse (C57BL6) lung experimentation

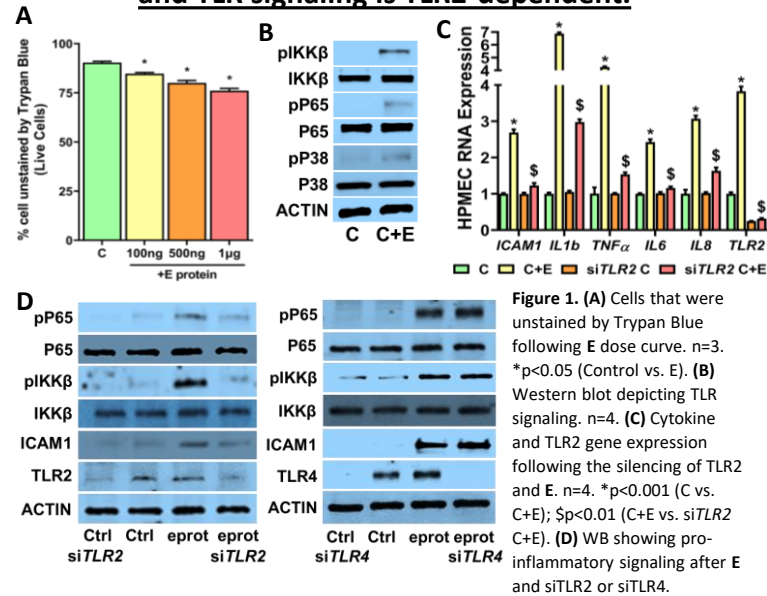
i.p injection with 10ug E protein (E), typically 48hr

Lungs harvested for

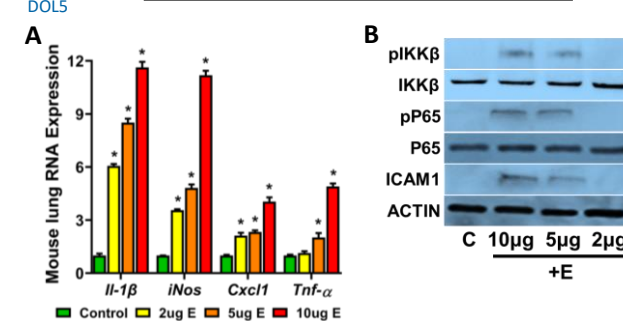
- DOL7- RNA, protein → PCR, WB
- DOL11- Bronchoalveolar Lavage (BAL)
- DOL15- Lung inflations → Morphometry

Results

E protein (E)-induced HPMEC injury, inflammation, and TLR signaling is TLR2-dependent.

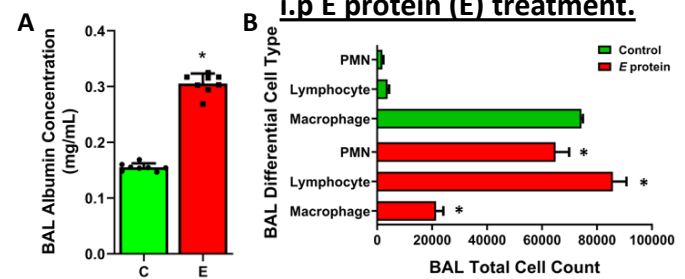


E protein (E) induces lung cytokine expression and TLR signaling in DOL7 mice.

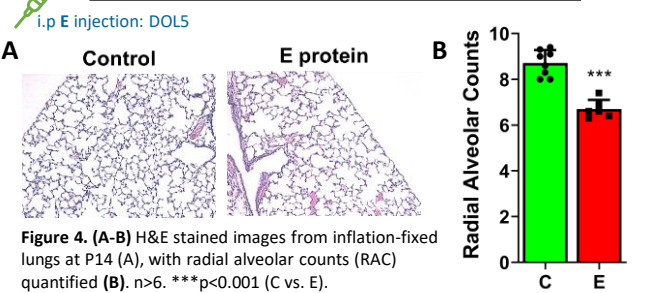


Results and Conclusion

Immune cell infiltration and vascular leak measured in DOL11 mice 48hr post i.p E protein (E) treatment.



The effects of systemic E protein (E) on alveolar simplification in DOL14 mouse lungs.



Conclusion:

- The SARS-CoV-2 E protein (E) induces TLR signaling, ALI, and alveolar remodeling in the neonatal lung.
- Ongoing *in vitro* studies suggest that E induced EC injury and inflammation is TLR2-dependent in HPMEC.
- This study provides mechanistic insight into neonatal immune activation and lung injury seen in infants with COVID-19.

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