**Background**

- Acute respiratory distress syndrome (ARDS) remains a significant cause of morbidity and mortality in ICU patients. Oxidative stress and inflammation have a significant role in the pathogenesis of lung injury in ARDS.
- Extracellular superoxide dismutase (EC-SOD/SOD3) is the sole extracellular enzymatic defense against superoxide.
- A R213G SNP in the matrix binding region of EC-SOD results in redistribution of EC-SOD from the matrix into extracellular fluids without affecting enzyme activity.
- Carriers of R213G SNP have an attenuated risk of exacerbations of chronic obstructive pulmonary disease and allergic airway inflammation in asthma.
- We have demonstrated the protective effects of R213G SNP in bleomycin-induced lung fibrosis and LPS-induced lung injury.
- While the role of R213G SNP has been investigated in COPD and Asthma in human studies, and LPS- and bleomycin-induced lung injury in animal studies, its role in infectious pneumonia and sepsis remains unknown.

**Hypothesis**

We hypothesized that the R213G variant results in redistribution of EC-SOD to the alveolar compartment with intratracheal *Staphylococcus aureus*, and is protective against *S. aureus*-induced acute lung injury and inflammation.

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**Methods**

- **Staph aureus pneumonia:** C57BL/6 (WT) and R213G mice infected IT with 1x10^8 CFUs of methicillin-resistant *S. Aureus (MRSA)* strain. 24-hrs post-inoculation, lungs, spleen, and broncho-alveolar fluid (BALF) collected.
- **Protein analysis:** EC-SOD protein expression measured in lung and BALF by Western blot.
- **Evaluation of lung injury:** Total cell counts and differentials, total protein and albumin, measured in BALF.
- **Evaluation of inflammation:** IL-1β, IL-6, and TNF-α measured by ELISA in BALF and qPCR in lung homogenates.
- **Bacterial translocation:** Spleens and lung homogenates plated on TSA agar and bacterial CFUs counted after 24hrs.
- **Statistical analysis:** Data were analyzed by unpaired t-test or 2-way ANOVA with Bonferroni post-tests. Significance defined as p<0.05.* p<=0.05, ** p<=0.01, ***p<=0.001, ****p<=0.0001

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**Results**

- R213G mice release EC-SOD into alveolar fluid in response to *S. aureus* infection.
- S. aureus induced lung inflammation is attenuated in R213G mice.
- Increased neutrophilic alveolar infiltration following *S. aureus* infection is blocked in R213G mice.
- R213G mice are protected from *S. aureus* dissemination to extrapulmonary sites.

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**Conclusions**

- R213G variant is protective against lung injury and inflammation in *S. aureus* pneumonia.
- Neutrophils may play a significant role in mediating the severity of injury in this model.
- R213G variant is protective against bacterial translocation potentially due to preserved integrity of alveolar-capillary barrier or enhanced systemic clearance/killing of the bacteria.
- Further studies will interrogate the mechanisms driving this protection and therapeutic implications.

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