P#09

Abstract Title:	**Systemic Expression Of Damage Associate Molecule Pattern (DAMP)s In ARDS Due To Smoke Inhalation And Burns In Swine Treated With Extracorporeal Life Support**
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Objective:	1) Describe the effect ECLS treatment has on systemic expression of DAMPs after smoke inhalation injury and thermal burns.
Abstract:	**Background**: Acute respiratory distress syndrome (ARDS) is the most severe form of acute lung injury. It is characterized by acute onset of hypoxemia, bilateral radiographic pulmonary infiltrates with lack of cardiogenic pulmonary edema and leads to multi-organ failure (MOF). Various symptomatic adjunct treatment methods have been explored to attenuate ARDS severity. Our purpose here was to determine the systemic level of damage associated molecular patterns (DAMPs) such as high mobility group protein 1 (HMGB1), toll-like receptor 4 (TLR4), proinflammatory cytokines, and acute kidney injury (AKI) marker neutrophil gelatinase-associated lipocalin (NGAL) to identify evidence for the efficacy of such treatments. To this end, we investigated the effects of low-flow extracorporeal life support (ECLS) as forms of symptomatic ARDS treatment by assessing their effects on innate immune responses as measured by changes in DAMPs expressions. We hypothesized that ECLS treatments result in different patterns of innate immune responses compared to untreated subjects. **Methods**: Female Yorkshire swine (weight: 40-50 kg) were anesthetized and received tracheostomy, mechanical ventilation (MV), arterial and venous catheters, fluids and pressors as needed. Following smoke inhalation injury (SII), animals received a full-thickness flame burn covering 40% total body surface area. The animals were randomized to one of four groups: CTR (uninjured, untreated animals, n = 4), ICTR (injured, untreated, n = 8), Hemo (injured animals treated with Hemolung, n = 10), and Nova (injured animals treated with NovaLung, n = 7). The Hemolung (Alung Technologies, Pittsburgh, PA) and Novalung (Xenios AG, Heilbronn, Germany) are both forms of low flow ECLS which remove CO2 and permit reduction in mechanical ventilator settings.

	Blood samples were collected at baseline (BL), post-injury (PI), 24 hours (24H), 48 hours (48H) and 72 hours (72H) post-injury and stored at 80°C until analysis. Enzyme-linked immunosorbent assays (ELISA) was performed to define systemic expression of HMGB1, TLR4, NGAL. Multiplex assays were performed for IL1β, IL6, IL8, IL10 and TNFα. Statistics by SAS Cary, NC, v. 9.4. Statistical significance was established at $p < 0.05$; data are represented as mean ± SEM. **Results**: While looking at HMGB1 over time, ICTR was higher in Hemo at Baseline. At 24 hours, Hemo and ICTR were both higher than Nova and CTR ($p<0.05$). When looking at TLR4 over time, Hemo and Nova were higher than CTR and ICTR at PI, 24H, 48H, and 72H ($p<0.05$). NGAL IL1β, IL6, IL8, IL10 and TNFα had no change statistically. NGAL was correlated with IL-6, IL-8, and TNFα (r2: 0.5248, -0.3550, -0.4686 respectively, $p<0.05$). TLR4 was correlated with: IL1β, IL8, and TNFα (r2: -0.3883, 0.2313, 0.5316 respectively, $p<0.05$). **Conclusion**: Systemic expression of DAMPs and cytokines show that different ECLS devices, used in adjunct with MV, produced differing effects in CTR and ICTR groups. The NovaLung device cause the least activation of DAMPs. We conjecture that bedside assessment of DAMPs confirms injury and may provide a useful monitoring capability at point of care. Further studies will elucidate the role of combination therapies of ECLS with as comprehensive treatments for ARDS.