Complement System Targets and Models

Complement Inhibition Ameliorates Blast-induced Acute Lung Injury in Rats

Complement is a network of proteins in the plasma that target and mark pathogens in the body for destruction by other immune processes. Complement inhibition by protein decay-accelerating factor (DAF) was found to protect the brain from blast-overpressure (BOP)-induced damage (*Li et al., 2013*). Thus, researchers at U.S. Army Institute of Surgical Research (USAISR; Fort Sam Houston, Texas) conducted a study to determine the effect of DAF on acute lung injury induced by BOP exposure and to elucidate its possible mechanisms of action (Figure 1).

BOP exposure significantly increased the production of pro- and anti-inflammatory proteins (cytokines), and pathological changes such as swelling of the lungs, inflammation, blood vessel damage, and hemorrhage in the lungs (Figure 2). These alterations were ameliorated by early administration of DAF (Figure 3). The DAF treatment significantly reduced the levels of pro-inflammatory and complement proteins HMGB1, RAGE, NF-[κ]B, C3a, and C3aR and reversed HMGB1 and complement protein C3a activities (Figure 4). These findings indicate that early administration of DAF efficiently inhibits systemic and local inflammation and mitigates blast-induced lung injury. The underlying mechanism might be attributed to its potential modulation of C3a and HMGB1. Therefore, complement and/or HMGB1 may be potential therapeutic targets in amelioration of acute lung injury after blast injury.

This effort was supported by the DMRDP.

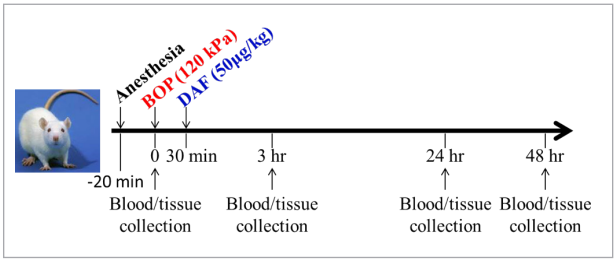

FIGURE 1: Experimental design and timeline.

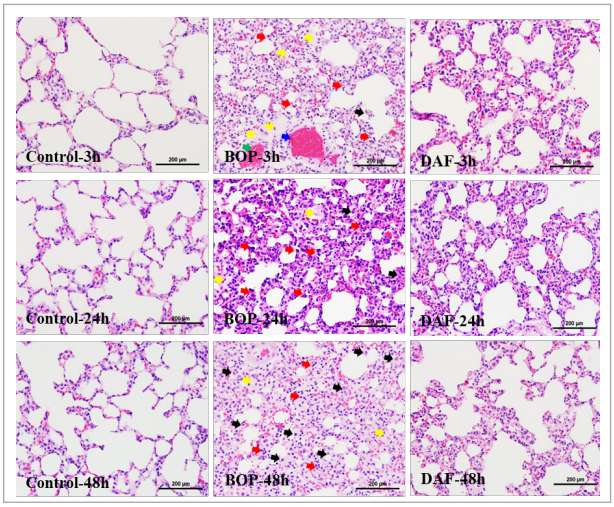

FIGURE 2: DAF treatment mitigated lung tissue injury induced by BOP in a rat model.

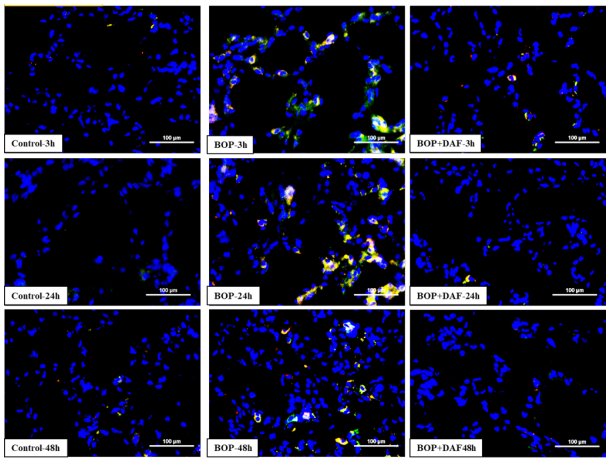

FIGURE 3: Effect of DAF on interaction of C3a and C3aR in lungs of rats after BOP exposure.

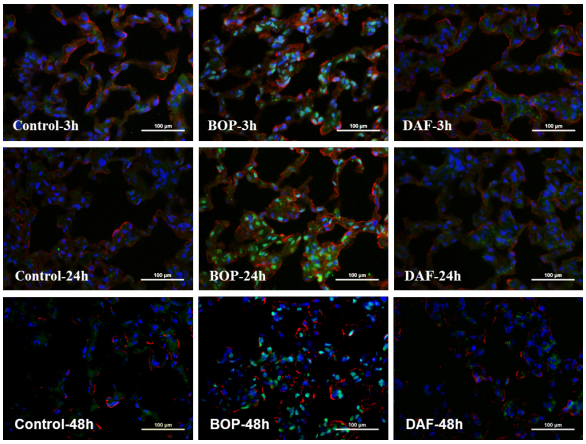

FIGURE 4: Effect of DAF on HMGB1 and RAGE expression and translocation in rats exposed to BOP.

REFERENCES:

Li, Y., Chavko, M., Slack, J. L., Liu, B., McCarron, R. M., Ross, J. D., & Dalle Lucca, J. J. (2013). Protective effects of decay-accelerating factor on blast-induced neurotrauma in rats. Acta Neuropathol Commun, 1, 52. doi:10.1186/2051-5960-1-52