



Effects of T-Cell Immune Modulator AB103 on Experimental Sepsis-induced Acute Kidney Injury

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Background

- Sepsis is a systemic inflammatory response syndrome caused by severe infection. Sepsis-associated acute kidney injury (SA-AKI) is common and is associated with high morbidity and mortality. The underlying mechanisms are not completely understood.
- In response to pathogen-derived molecules, T cell activation plays a crucial role in the immediate immune response.
- CD28 is essential for T cell proliferation and survival, cytokine production, and T-helper type-II development.
- AB103 is a rationally designed short peptide acting as a CD28 co-stimulatory receptor antagonist regulating the host's inflammatory response, improving the host's ability to effectively fight the infection.

Objective

- We sought to understand the role of AB103 in sepsis-associated acute kidney injury.

Methods

- Sepsis was induced by Cecal Ligation and Puncture (CLP) in 22 male Balb/c mice of which 6 received sham surgery.
- Six hours after CLP, mice were randomized to receive either a single dose of intravenous AB103 (5 mg/kg) or vehicle, and survival was followed for 48 hrs. Kidney tissue and blood were collected from surviving animals at that time.
- Creatinine level and kidney histology were determined, assessing vacuolization of the tubular epithelium/perivascular cell and neutrophil gelatinase-associated lipocalin (NGAL) expression.

Results

Figure 1. AB103 treatment significantly improves survival.

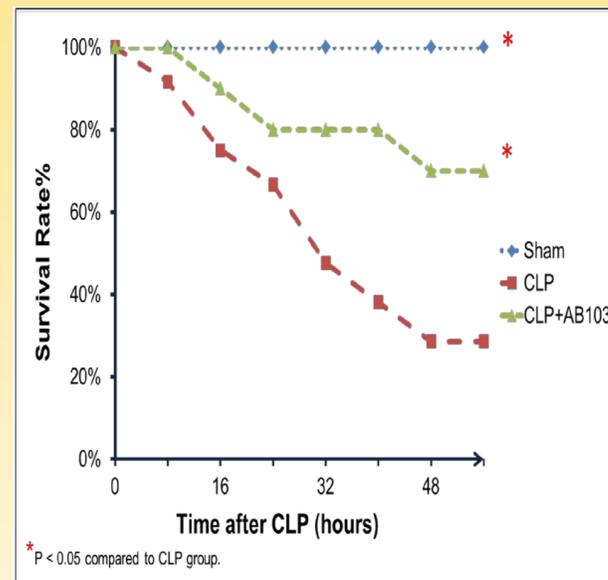
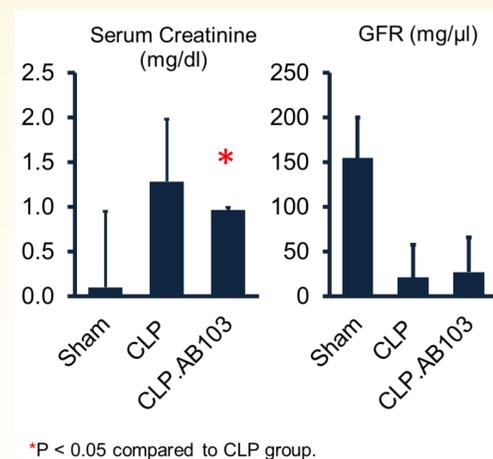


Figure 2. AB103-treated septic animals exhibited an improvement in kidney function.



Results

Figure 3. AB103-treated septic animals displayed variable effects on kidney pathology.

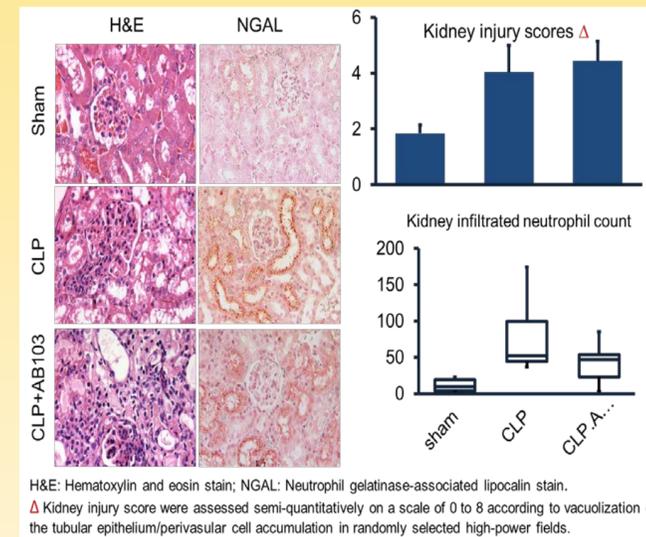
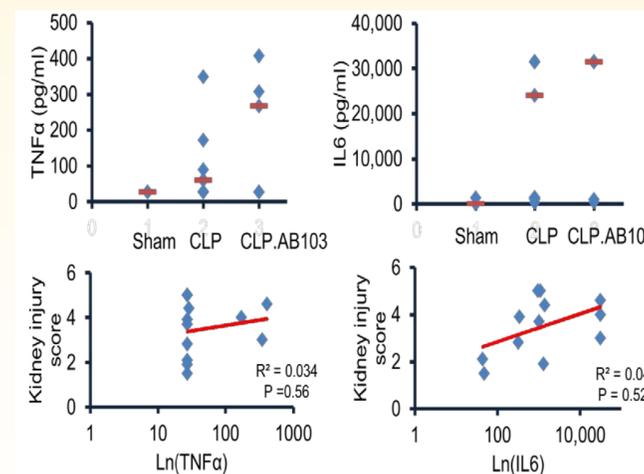


Figure 4. Circulating inflammatory cytokine concentrations had no significant correlation with kidney pathology.



Results

Figure 5. Diagram of CD28 Signaling in T-Helper Cell activation pathway.

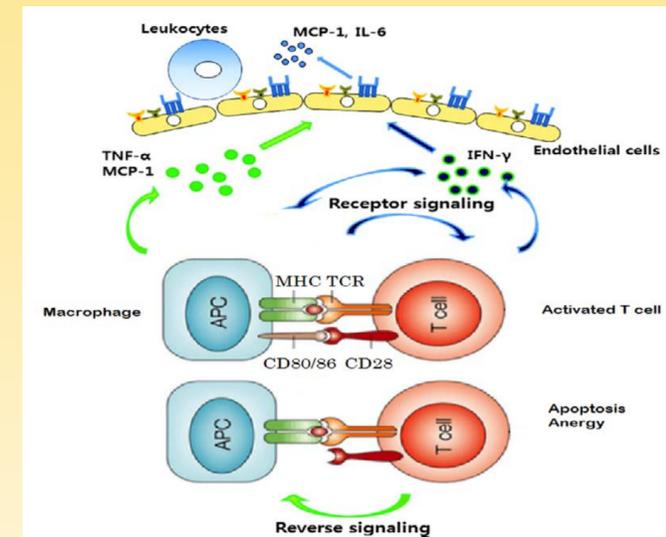


Figure revised from: Jeon H J et al. *Circulation*. 2010;121:1124-1133; Alegre ML et al. *Nat Rev Immunol*. 2001;1(3):220-8.

Conclusions

- AB103 dramatically improved survival from Cecal Ligation and Puncture-induced sepsis in mice.
- AB103 significantly reduced serum creatinine and improved kidney function in this model of sepsis.
- Kidney injury assessed in survivors was not clearly improved by AB103, but given the low survival in control animals, it is not possible to draw a firm conclusion.

