

Category : **Renal: extracorporeal support**

**A31 - Scavenging nucleus-derived molecules by polymyxin b membrane inhibits the stimulation of toll-like receptors**

**N Takeyama ; D Ohishi ; T Irahara ; M Tsuda ; S Tanabe ; M Hattori ; Y Kuge ; H Kano**  
*Aichi Medical University, Department of Emergency and Critical Care Medicine, Aichi, Japan*

**Introduction:**

The nucleus-derived molecules elicit various immunostimulatory effects via toll-like receptors (TLRs). Direct hemoperfusion with a Polymyxin B (PMX)-immobilized fiber column (Toraymyxin; Toray Industries, Tokyo, Japan) is an extracorporeal therapy developed for the treatment of endotoxemia. We hypothesize that PMX membrane can absorb nucleus-derived molecules and can block the ability of these nucleus-derived molecules to activate TLRs.

**Methods:**

We first evaluated whether PMX membrane can capture and remove nucleus-derived molecules and then determined whether treatment with PMX membrane can limit the ability of nucleus-derived molecules to activate innate immune response via TLRs using reporter cell lines HEK-Blue hTLR9 and 7. The capacity of PMX-membrane absorption to DNA, RNA, cell-free neutrophil extracellular trap (NET) and nucleosome was estimated by incubation of these components with PMX-membrane. HEK-Blue hTLR7 and 9 cells were incubated with PMX-treated or -untreated nucleus-derived chromatin components. TLR7 and 9 activation of NF- $\kappa$ B were also measured.

**Results:**

One cm<sup>2</sup> PMX membrane can absorb  $3 \pm 0.01$  mg authentic DNA within 5 min and removes DNA from incubation solution in a surface size-dependent manner. One cm<sup>2</sup> PMX membrane significantly absorb  $5 \pm 0.02$  mg authentic RNA,  $6 \pm 0.02$  mg nucleosome and  $1.3 \pm 0.006$  mg cell-free NET as well as DNA when compared with incubation without PMX membrane. HEK-Blue hTLRs cells showed that PMX membrane treatment significantly inhibited the ability of nucleus-derived molecules to stimulate nucleic acid-recognizing TLRs.

**Conclusion:**

We demonstrated that PMX membrane can effectively capture various nucleus-derived molecules. Furthermore, scavenging nucleus-derived molecules by treatment with PMX membrane inhibited the stimulation of TLRs 9 and 7. Removing systemic nucleus-derived molecules from circulation by PMX may ameliorate irrelevant inflammatory complications in patients with sepsis and trauma.