LPS induces NEAT1 expression in acute kidney injury via TLR4/NF-κB signaling

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Background

TLR4/NF-κB signaling has been implicated in the pathogenesis of acute kidney injury(AKI). Nuclear Paraspeckle Assembly Transcript 1 (NEAT1) is a long non-coding RNA that plays key roles in a variety of biological processes and is involved in many inflammatory diseases. Beyond its fundamental role of maintaining function of the nucleus, it remains unknown whether NEAT1 is involved in TLR4/NF-κB signaling in the development of AKI.

Methods

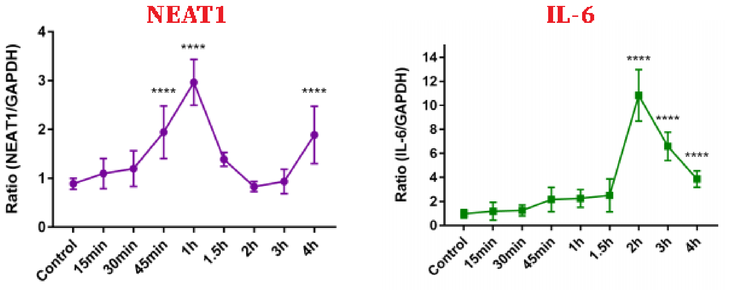
Septic AKI model was established with injection of LPS into mice. Mouse tubular cells (C1.1) were stimulated with LPS for the study of tubular inflammation. NEAT1 was knocked down by injection of shRNA via ultrasound-mediated microbubble gene transfer method. The role and upstream regulatory mechanisms of NEAT1 in inflammatory processes were studied by using signaling inhibitors.

Conclusion

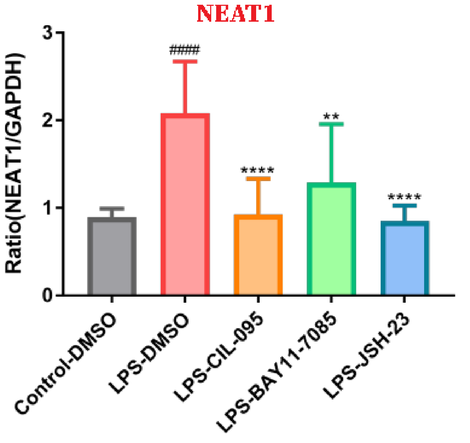
NEAT1 expression was induced in LPS-induced AKI model via TLR4/NF-κB signaling, suggesting its potential role in the inflammatory process.

Results

1. NEAT1 and IL-6 mRNA levels were upregulated by LPS in C1.1 cells.

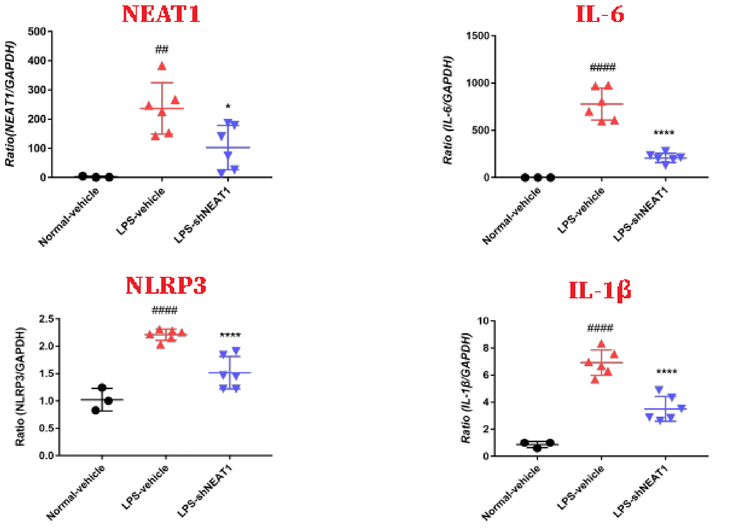


2. LPS-induced NEAT1 expression was suppressed by TLR4 and NF-κB inhibitors.

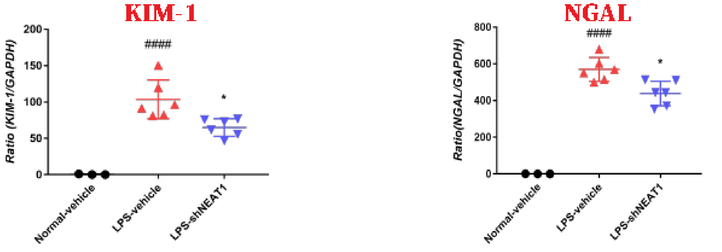


*CIL-095 is the inhibitor of TLR4
*BAY11-7085 and JSH-23 are inhibitors of NF-κB

3. Knock down of NEAT1 by shRNA gene transfer reduced renal inflammation in 12h LPS-induced septic mouse model.



4. Mice with knock down of NEAT1 had reduced tubular injury at 12h after LPS injection.



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