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Spotlight on Leading Edge Research

Frontline Science: HMGB1 induces neutrophil dysfunction in experimental sepsis and in patients who survive septic shock

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Abstract

Sepsis is accompanied by the initial activation of proinflammatory pathways and long - lasting immunosuppression that appears to contribute to late - occurring mortality. Although high - mobility group box 1 (HMGB1) is involved in many aspects of inflammation, its role in sepsis - induced immune suppression remains unclear. In this study, we examined HMGB1's contribution to neutrophil NADPH oxidase activity dysfunction and associated neutrophil - dependent bacterial clearance in mice subjected to sepsis and in patients who survive septic shock. Using a murine model of polymicrobial septic peritonitis, we demonstrated that treatment with anti - HMGB1 Ab significantly diminished sepsis - induced dysfunction of neutrophil NADPH oxidase activity. In a subsequent set of experiments, we found that blocking HMGB1 preserved the ability of neutrophils from patients recovering from septic shock to activate NADPH oxidase. Taken together, our data suggest that HMGB1 accumulation in the late phase of sepsis plays a specific role in the development of postsepsis immunosuppression and specifically affects neutrophil - dependent antibacterial defense mechanisms. Thus, blocking HMGB1 may be a promising therapeutic intervention to diminish the adverse effects of sepsis - induced immunosuppression.