Histidine-rich glycoprotein regulates neutrophil condition in sepsis

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Reactive oxygen species (ROS) play important roles in the progression of septic pathogenesis. Recent studies revealed that neutrophil adhesion on vascular wall followed by neutrophil extracellular traps (NETs) release may trigger platelet aggregation and immunothrombus formation in septic organ failure. Additionally, the adherent neutrophils-produced ROS induce the immunothrombus formation and tissue damage. Our previous study indicated that plasma histidine-rich glycoprotein (HRG) levels significantly decreased in cecal ligation and puncture (CLP) septic mice model and administration of HRG dramatically improved the survival rate of CLP mice. However, the role of HRG on neutrophil ROS production and immunothrombosis in septic condition was poorly understood. In this study, we showed that HRG inhibited immunothrombus formation in pulmonary vasculatures by keeping neutrophils quiescent morphologically and functionally using immunohistochemical staining and in vivo imaging methods and suppressed excess extracellular ROS production from neutrophils using isoluminol method. These results suggested that HRG may regulate the uncontrolled activation of circulating neutrophils in septic condition.