Abstract

Histidine-rich glycoprotein (HRG) is a multifunctional plasma protein and maintains the homeostasis of blood cells and vascular endothelial cells. In the present study, we demonstrate that HRG and recombinant HRG concentration-dependently induced the phagocytic activity of isolated human neutrophils against fluorescence-labeled *E. coli* and *S. aureus* through the stimulation of CLEC1A receptors, maintaining their spherical round shape. The phagocytosis-inducing effects of HRG were inhibited by a specific anti-HRG antibody and enhanced by opsonization of bacteria with diluted serum. HRG and C5a prolonged the survival time of isolated human neutrophils, in association with a reduction in the spontaneous production of extracellular ROS. In contrast, HRG maintained the responsiveness of neutrophils to TNF-α, zymosan and *E. coli* with regard to ROS production. The blocking Ab for CLEC1A and recombinant CLEC1A-Fc fusion protein significantly inhibited the HRG-induced neutrophil rounding, phagocytic activity and prolongation of survival time, suggesting the involvement of the CLEC1A receptor in the action of HRG on human neutrophils. These results as a whole indicated that HRG facilitated the clearance of *E. coli* and *S. aureus* by maintaining the neutrophil morphology and phagocytosis, contributing to the anti-septic effects of HRG *in vivo*.