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Protein disulfide isomerase plays an important role in αMβ2 integrin-mediated neutrophil recruitment during vascular inflammation

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Protein disulfide isomerase (PDI), a cell-surface localized oxidoreductase, plays an important role in regulating integrin-mediated platelet functions. PDI is detected on the neutrophil surface. However, its role in neutrophil recruitment during inflammation remains unknown. Using intravital microscopy, we demonstrated that infusion of PDI inhibitors impairs neutrophil adhesion to the TNF-α-inflamed cremaster muscle venule wall in living mice. The inhibitory effect of blocking anti-PDI antibodies on neutrophil recruitment was further enhanced in αLβ2 but not αMβ2 null mice. PDI inhibitors dose-dependently diminished human neutrophil adhesion to TNF-α-activated endothelial cells under shear and to intercellular adhesion molecule-1 (ICAM-1)-coated surfaces under static conditions. There was additive inhibitory effect on neutrophil adhesion when anti-PDI was combined with anti-αL but not anti-βM antibodies under shear and static conditions. When PDI is knocked down in HL60 cells, αMβ2 activation and cell adhesion to activated endothelial cells under shear were significantly reduced. Immuno precipitation assays and confocal microscopy revealed that surface PDI interacts with αMβ2 integrin and that such interaction was enhanced by neutrophil activation and reduced by inhibition of isomerase activity. Our results indicate that surface PDI regulates αMβ2-ligand interaction, thereby playing an important role in neutrophil adhesion to the activated endothelium during vascular inflammation.

Biography

Jaehyung (Gus) Cho has completed his Ph.D from University of Wisconsin-Madison School of Medicine and postdoctoral training from Harvad Medical School. He is an Assistant Professor at Department of Pharmacology, University of Illinois College of Medicine. He has published more than 12 papers and is serving as an editorial board and peer-review member of several journals including Journal of Clinical Toxicology, Thrombosis and Haemostasis, and Journal of Biological Chemistry. He has been serving as a member of AHA Vascular Wall Biology Basic Research Study Section. Currently, his research is supported by NIH P30 and RO1, and AHA Scientist Development Grant.