CIS-10

Neutrophil infiltration during inflammation is regulated by PILRα via modulation of integrin activation

Jing Wang[1,2], Ikuo Shiratori[1], Junji Uehori[1,2], Masahito Ikawa[3] & Hisashi Arase[1,2]

[1]Department of Immunochemistry, Research Institute for Microbial Diseases, Osaka University, Osaka, Japan.
[2]Laboratory of Immunochemistry, WPI Immunology Frontier Research Center, Osaka University, Osaka, Japan.
[3]Department of Experimental Genome Research, Research Institute for Microbial Diseases, Osaka University, Osaka, Japan.

Abstract

Acute inflammatory responses are important in host defense, whereas dysregulated inflammation results in life-threatening complications. Here we found that paired immunoglobulin-like type 2 receptor alpha (PILRα), an inhibitory receptor containing an immunoreceptor tyrosine-based inhibitory motif (ITIM), negatively regulated neutrophil infiltration during inflammation. *Pilra*$^{-/-}$ mice had increased neutrophil recruitment to inflammatory sites and were highly susceptible to endotoxin shock. *Pilra*$^{-/-}$ neutrophils showed enhanced transmigration ability and increased adhesion to the ligand ICAM-1. PILRα expressed on neutrophils constitutively associated in *cis* with its ligands, resulting in clustering of PILRα during stimulation with a chemoattractant. Clustering of PILRα enhanced ITIM-mediated signaling, thus modulating β_2 integrin inside-out activation. These data demonstrate that neutrophil recruitment in inflammatory responses is regulated by PILRα via modulation of integrin activation.