Hematology-2013
OMICS Group Conferences
Accelerating Scientific Discovery
International Conference on
Hematology & Blood Disorders
September 23-25, 2013 Raleigh, USA

Tissue homing of inflammatory neutrophils during sepsis is mediated by integrin VLA-3 (CD49c/CD29)

Pranita P. Sarangi
National Institute of Dental and Craniofacial Research, NIH, USA

Abstract

During sepsis there is aberrant activation, migration and sequestration of neutrophils in visceral organs that leads to widespread release of pro-inflammatory mediators contributing to multi-organ failure and death. Interaction of cell surface integrins with their counterpart ligands, results in the adherence of circulating neutrophils and directed migration to infection sites. In our study, we show that administration of a cyclic analog of RGD peptide (Arg-Gly-Asp) significantly reduced the number of tissue-invading neutrophils and the degree of sepsis-induced lethality in mice as compared to control peptide. Secondly, β_1 integrin (CD29) and more specifically VLA-3(CD49c/CD29) is dramatically up regulated on a subpopulation of neutrophils isolated from both human septic patients and mouse sepsis models. Compared with the $Gr1^{high}CD11b^{high}VLA\text{-}3^{low}$ granulocyte population, $Gr1^{high}CD11b^{high}VLA\text{-}3^{high}$ cells from septic animals displayed hyper-inflammatory phenotypes. Administration of VLA-3 antagonist peptides and conditional genetic ablation of VLA-3integrin from granulocytes also improved survival and bacterial clearance in septic animals. Thus, our results indicate that expression of VLA-3integrin is important for modulating neutrophil trafficking during sepsis, and therapeutics specifically targeted against VLA3integrins may be beneficial.

Biography

Dr. Sarangi is a research fellow at the National Institutes of Health. She is a graduate of the University of Tennessee, with postdoctoral training at Center for Vaccine Biology and Immunology, University of Rochester Medical Center. She has published 8 first author and 6 co-author papers in reputed peer reviewed journals including a book chapter.