Leukocyte Adhesion

Edited by

Klaus Ley

Current Topics in Membranes, Volume 64

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Klaus Ley
Division of Inflammation Biology
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La Jolla, CA, USA

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Leukocyte Adhesion

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Foreword

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Studies of leukocyte adhesion have come a long way in the last 20 years, when leukocyte adhesion was still considered a nonspecific process. The discovery of leukocyte integrins (Harlan et al., 1985; Hemler et al., 1987; Springer, Thompson, Miller, Schmalstieg, & Anderson, 1984), their main endothelial ligands (Osborn et al., 1989; Rice & Bevilacqua, 1989; Rothlein, Dustin, Marlin, & Springer, 1986), the three selectins (Bevilacqua, Stengelin, Gimbrone, & Seed, 1989; Camerini, James, Stamenkovic, & Seed, 1989; Johnston, Cook, & McEver, 1989; Siegelman, van de Rijn, & Weissman, 1989; Tedder et al., 1989), and their main ligands PSGL-1 (Moore et al., 1992; Sako et al., 1995) and peripheral node addressins (Rosen, 1993) paved the way for a molecular understanding of leukocyte adhesion. This volume in the series *Current Topics in Membranes* presents a detailed account of our current understanding of the function of these molecules in leukocytes and endothelial cells. In keeping with the tradition of this series, the emphasis is on biophysical rather than biochemical or molecular biology aspects of this process.

In order for cells to discharge their functions, they must be able to sense and recognize their immediate surroundings. As the plasma membrane is the interface between the environment and the cell interior, its components, both proteins and lipids, are central to this recognition process. The leukocyte epitomizes membrane–substrate interactions, and therefore is a good model system with which to study these interactions and the proteins that mediate them. This volume's focus on the leukocyte coalesces novel experimental approaches and summarizes recent knowledge and controversies surrounding the phenomenon of adhesion that easily extends to other cell types. The contents of this volume provide new perspectives on one of the most fundamental properties of membranes, namely, recognition. Thus, it fits nicely into the *Current Topics in Membranes* series.

One of the most useful techniques in determining the spatial relation between different proteins, between subunits of heteromers, or between proteins and the lipid membrane is fluorescence resonance energy transfer.

Minsoo Kim and Craig Lefort provide a detailed account of this and related methods and their uses in leukocyte adhesion studies. The reader may find this chapter particularly useful to determine which experimental approach to take for a specific scientific question. In their chapter "Activation of Leukocyte Integrins," Eun Jeong Park and Motomu Shimaoka integrate data from crystallography, electron microscopy, mutagenesis, and epitope mapping studies to arrive at a model of how leukocyte integrins are activated. Their model is largely based on the $\alpha_L\beta_2$ integrin LFA-1, which is the best-studied leukocyte integrin in terms of its conformational changes. Ronen Alon then takes these integrin models and integrates them with chemokine receptors and signal transduction pathways to outline a mechanism by which chemokine binding to their ligands may activate leukocyte integrins. These membrane-cytoskeletal platforms for rapid chemokine signaling to integrins are of key importance for adhesion under flow. In most organs and tissues, selectins are indispensable to achieve leukocyte adhesion under flow. Cheng Zhu and Rodger McEver explore the biophysical regulation of selectin–ligand interactions under flow, with an emphasis on catch bonds. Catch bonds are characterized by a counterintuitive behavior in which the bonds become stronger when loaded with a force.

The main ligand for the endothelial E- and P-selectins is P-selectin Glycoprotein Ligand-1 (PSGL-1), also known as CD162. This molecule is expressed on the tips of leukocyte microvilli—thin structures that initiate the first contact with the endothelium. When pulling on PSGL-1, membrane tethers can be formed, which tend to reduce the force on the selectin–PSGL-1 bond by dissipating energy into pulling a tether away from the microvillus. Richard Waugh has studied this process in erythrocytes and leukocytes and provides a very lucid account of how pulling tethers works and why it matters for leukocyte adhesion. This chapter is complemented by Jin-Yu Shao's chapter on "Biomechanics of Leukocyte and Endothelial Cell Surface," which adds endothelial tethers to the mix and explains the relationship between microvilli and tethers.

Pulling tethers and extending microvilli only works because adhesion molecules are attached, in highly regulated and versatile ways, to the cytoskeleton. Fred Pavalko explores cytoskeletal interactions with leukocyte and endothelial cell adhesion molecules. The continuum between adhesion molecules and the viscoelastic cell body lends itself to modeling studies. Damir Khismatullin shows how the cytoskeleton and deformability of white blood cells can be integrated into a model of leukocyte adhesion. Maria Pospieszalska and Klaus Ley explore the different approaches to modeling leukocyte rolling, which constitutes one form of leukocyte adhesion. In recent years, the modeling efforts have yielded important predictions that were tested experimentally, but it is clear that much more needs to be done to fully understand the process of leukocyte rolling.

The next step in leukocyte–endothelial interactions is transendothelial migration. The current volume provides three accounts of this from different perspectives. Bill Muller explores how endothelial cells regulate transendothelial migration of leukocytes and discusses the molecules and mechanisms involved. His perspective comes from *in vitro* transmigration assays in which monocytes crawl through endothelial cell monolayers in the absence of flow. Olga Barreiro describes how endothelial adhesive platforms organize receptors to promote leukocyte extravasation. Her chapter integrates cell biology with biophysical data. In chapter 10, Chris Carman discusses how these structures form transmigratory cups and invadosome-like protrusions that ultimately allow the leukocyte to penetrate the endothelium and arrive at the site of inflammation or immune response.

Of course, a volume on leukocyte adhesion can never be complete. At least 38,820 articles on leukocyte adhesion have been published to date (PubMed, August 12, 2009), and it is impossible to cover all aspects. Nevertheless, we hope that the reader will find this volume a useful addition to the existing armamentarium of reviews on leukocyte adhesion. Finally, we would like to thank Gayathri Venkatasamy, the developmental editor for this volume, for putting it all together; Daisy Varbanova, the volume editor's assistant, for keeping track of the different versions of volume and all the figures; and the unnamed reviewers who spent their time to review all chapters.

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