Adhesion Mechanisms of Endothelial Cells

P. F. Bradfield (✉) · B. A. Imhof

Department of Pathology, Faculty of Medicine, CMU, University of Geneva, 1 rue Michel Servet, Geneva 4, CH1211 Switzerland
paul.bradfield@medecine.unige.ch

1 Immune Surveillance and Homeostasis: The Role of the Endothelium . . . 406
2 Cell Adhesion Molecules ................................................... 406
3 Targeting Leukocyte Adhesion ................................................. 408
  3.1 Primary Adhesion ............................................................ 409
  3.2 Activation ...................................................................... 410
  3.3 Secondary Adhesion ........................................................... 410
  3.4 Diapedesis ..................................................................... 410
4 Regulation of Cell Trafficking by Distinct Populations of Endothelial Cells. 413
  4.1 Recirculation of Leukocytes: Deciphering the Role of the Lymphatic Endothelium .......................................................... 415
5 Inflammation and Wound Healing: Synergy Between the Endothelium and the Extra-vasculature ......................................................... 416
6 Cell Adhesion Molecules, the Players in Mediating Endothelial Function . 418
  6.1 Selectins and Their Ligands .................................................. 418
  6.1.1 Selectins .................................................................... 418
  6.1.2 Selectin Ligands: Sialomucins and Carbohydrate Moieties ............. 419
  6.1.3 Function and Patterns of Expression ...................................... 420
  6.2 Integrins ....................................................................... 421
  6.3 The Immunoglobulin Superfamily .......................................... 424
  6.3.1 ICAM and VCAM .......................................................... 425
  6.3.2 Mucosal Adressin Cell Adhesion Molecule 1 ............................. 426
  6.3.3 CD31 ....................................................................... 426
  6.3.4 Junctional Adhesion Molecules ............................................ 427
  6.4 CD99 .......................................................................... 428
  6.5 CD44 ........................................................................... 428
  6.6 Vascular Adhesion Protein-1 .................................................. 429

References .................................................................................. 429

Abstract Endothelial cells express a diverse and exquisite array of adhesion molecules and cell surface receptors. Adhesion molecules expressed on endothelial cells not only maintain structural integrity of the vasculature, but also mediate more dynamic processes such as the highly regulated movement of leukocytes from free flow into different tissue compartments. Recent studies have focused on the molecular processes that mediate endothelial cell function and their ability to respond rapidly to changes in their immediate microenvironment, as well as maintaining routine cell trafficking through specialist
tissue compartments. Adhesion molecules expressed on the endothelium mediate the movement of leukocytes into the underlying extravasculature to mediate a diverse array of functions including immune effector responses, cellular interactions in specialist lymphatic microenvironments and recirculation back into the vasculature. The true diversity and capacity of adhesion molecules capable of being expressed on the endothelium is now beginning to emerge, demonstrating new levels of complexity as specialist subsets of endothelium are characterised that define specific, yet diverse functions. In this chapter, the role of cell adhesion molecules in mediating endothelial cell function is discussed, from how their different physiochemical properties contribute to function, to how specific ligand interactions expressed on leukocyte cell populations contribute to functions ranging from constitutive cell trafficking to inflammation.

**Keywords** Endothelium · Leukocyte · Migration · Vascular junctions · Adhesion molecules · Trafficking · Inflammation

1 **Immune Surveillance and Homeostasis: The Role of the Endothelium**

Immune responses are optimised by constant monitoring and tight control of cell positioning to ensure a rapid and effective immune response when required. Integral to immune surveillance is cell trafficking, a process that confines cells to different routes of cell movement, dependent on cell type and function. This also allows cells with specific functions to move from the extravasculature and exist within defined compartments, optimising relevant interactions and effector responses, but minimising encounters with other cell types. Cell trafficking also ensures that cells involved with immunosurveillance have a much higher degree of contact with a potential antigen, and are therefore able to initiate a more rapid effector response.

Leukocytes as well as other cell types express a number of cell surface molecules that are able to bind to a wide range of ligands expressed on endothelial cell and stromal cell populations which provide an ‘address code’, allowing a cell to determine its position as well as direction and function. These include cell adhesion molecules that can physically anchor cells and allow migration through tissue, and chemokines, which provide cells with information about direction leading to recruitment, proliferation, apoptosis and retention (Imhof and Dunon 1995; Butcher and Picker 1996; Campbell and Butcher 2000).

2 **Cell Adhesion Molecules**

The ability of an individual cell to assimilate information about its immediate environment is critical in maintaining the integrity of multicellular or-