EDITORIAL

Sticky Situations: Cell-Cell and Cell-Matrix Interactions

Cell adhesion receptors define how a cell views and interacts with its immediate environment through specific cell-cell and cell-matrix contacts. Cell adhesion is fundamental to multiple biological processes in health and disease, from viral entry into cells and bacterial adherence, through to more complex interactions involving, for example, those occurring in reproduction, development, and tissue organisation. It is now clear that cell adhesion receptors not only mediate attachment, but also act as signalling receptors regulating cell phenotype, proliferation, shape and motility. A common theme of many cell adhesion receptors is their capacity to interact directly with and modulate the structure of the cell cytoskeleton. This issue's Showcase on Research presents three minireviews that explore different aspects of cell adhesion in regulating cell-cell and cell-matrix interactions in pathological or normal physiological situations.

The first review by Jana Yip, Yang Shen and Robert Andrews discusses platelet adhesion receptors regulating haemostasis and thrombosis. The platelet has a complex adhesion receptor system that allows it to bind to damaged blood vessels, even under conditions of high shear flow in the blood. This involves a unique receptor, the GPIb-IX-V complex, a member of the leucine-rich repeat family, binding to a large multimeric matrix glycoprotein, von Willebrand factor. GPIb-IX-V spans the platelet membrane bilayer, providing the primary linkage to a membrane skeleton of short actin filaments bridged by filamin. Platelets tethered to von Willebrand factor translocate about 100-fold slower than platelets in the circulation, allowing secondary adhesive events, such as GPVI adhesion to collagen to occur, leading to stable platelet adhesion.

The second review by Gregory Moseley and Denise Jackson discusses the biological function of PECAM-1, a member of the immunoglobulin family of cell adhesion receptors. PECAM-1 is expressed primarily on platelets, leukocytes and on endothelial cells at the cell junction. It plays an important role in limiting cell responses, particularly those mediated by immunoreceptor tyrosine-based activating motif (ITAM)-containing receptors. It does this by virtue of containing a cytoplasmic immunoreceptor tyrosine-based inhibitory motif, which binds SHP family phosphatases, thus countering the effect of Syk and other tyrosine kinases bound to ITAM-containing receptors such as platelet GPVI or the T cell receptor on lymphocytes.

Another class of important cell adhesion receptors are the cadherins, which mediate cell-cell interactions, primarily in epithelial, neural and vascular endothelial cells. In the third review, Alpha Yap and Marita Goodwin describe recent advances in our understanding of cadherins, particularly with respect to how they direct homotypic interactions and act as cytoskeletal and signal transducers.

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Cover Illustration

Clumping assay showing dispersed CHO cells stably transfected with P-selectin (labelled with Membrane Tracker™ orange) binding to dispersed CHO cells stably transfected with platelet GP Ib-IX (labelled with Membrane Tracker™ green). These assays provided one line of evidence showing these two proteins act as adhesion counter receptors – see Romo *et al.* (1999) *J. Exp. Med.* **190**, 803-814.

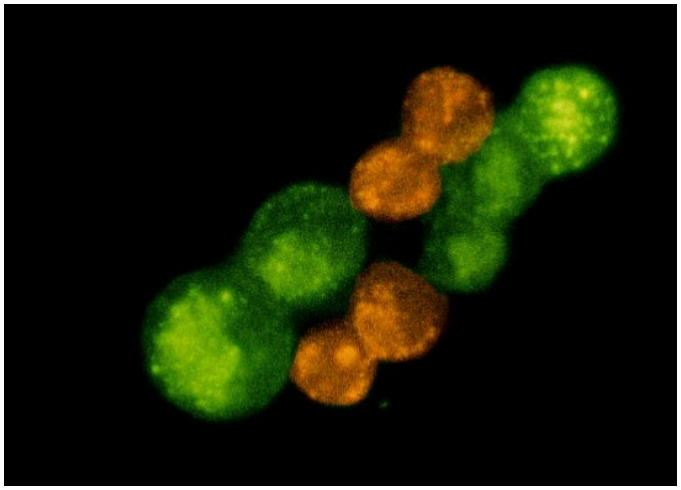
Image courtesy of Dr Jose Lopez, Baylor College of Medicine, Houston, Texas.

Cell Adhesion

Guest Editor: Michael Berndt

In the next issue...

In December, Showcase on Research will be on **Metal Ions in Biology** – *Guest Editor: Greg Anderson*



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