# In Brief

## *Novel Functions for Adhesion Molecules*

### *Translation Induced by Integrins*

Cell adhesion can result in dramatic changes in cell motility, growth, and differentiation. These functional responses are often initiated by integrins, the very molecules that tether some cells. Integrin signaling modulates cell physiology by a number of mechanisms, including the regulation of transcription. The strength of these transcription-based effects, however, has made it difficult to determine if gene expression is controlled by other pathways. In this issue, Pabla et al. (page 175) use activated platelets, a cell type without nuclei, to examine how integrin engagement affects protein expression in the absence of transcription. The results show that outside-in signaling by integrins controls protein production at the level of translation.

In a previous study, these authors made the surprising finding that platelets undergo new protein synthesis upon activation, despite their lack of nuclei. Now Pabla et al. show that engagement of the platelet integrin $\alpha_{IIb}\beta_3$ by fibrinogen is sufficient to induce the translation of a platelet mRNA. Protein expression does not occur in platelets that have been preincubated with peptides or antibodies that block integrin $\alpha_{IIb}\beta_3$ engagement, or in platelets from a patient with Glanzmann thrombasthenia. These platelets are defective in integrin $\alpha_{IIb}\beta_3$ outside-in signaling, suggesting a functional role for the protein expression induced by integrin signals.

"Inducing changes in cell physiology through the translation of preformed mRNAs may be well suited to cells like platelets, leukocytes, and other cells that must respond very, very quickly upon adhesion," says senior author Guy Zimmerman, but the range of cell types and proteins that use these translational controls remain to be identified.

### *Additional Selectin Bonds Provide the Brakes*

The accumulation of leukocytes is required for the host response to tissue damage or infection. Initially, leukocytes survey the endothelium for inflammation through a unique rolling interaction. Adhesive bonds are rapidly formed and broken as the leukocyte is propelled along the vessel wall by the flow of blood. The velocity of these rolling leukocytes varies little in vivo, despite dramatic differences in the force, or shear stress, applied on the cell by the flow of blood. This constant rolling velocity is particularly puzzling in the light of recent studies on the selectin–ligand bonds that mediate leukocyte rolling. The dissociation rate of these bonds increases exponentially with increasing force. In the absence of a mechanism to counterbalance this increased rate of bond dissociation, leukocyte rolling would become destabilized in areas where blood flows at a rapid rate. On page 185, Chen and Springer provide evidence that increasing numbers of adhesive interactions may constitute the required "braking" mechanism.

Chen and Springer compare the behavior of individual selectin–ligand bonds, termed transient tethers, to the behavior of cell attachments that occur during cell rolling, called rolling tethers. At low shear, the average lifetime of rolling tethers is similar to that of transient tethers. At higher shear, however, the average lifetime of rolling tethers is much longer than that of transient tethers.

The kinetics of dissociation suggest that, at higher shear, rolling cells attach to the substrate through multiple selectin bonds. The authors test this more directly by comparing cells that are subjected to a decrease in shear after rolling at different shear values. Bond-dissociation time increases proportionally with the magnitude of shear initially applied, and the kinetics again suggests this increase can be explained by the presence of multiple bonds at higher shear. The authors propose that this increase in the number of selectin bonds formed at higher shear stress may be the mechanism by which leukocyte rolling is stabilized as bond dissociation rates increase.

### *PINCH Proteins at Adherens Junctions*

For muscle contraction to be converted into animal locomotion, muscles must be attached to the epidermis. This attachment occurs through adherens junctions, structures that anchor cytoskeletal adapter proteins such as vinculin, talin, and α-actinin to the extracellular matrix via integrins. On page 45, Hobert et al. report the identification of the PINCH proteins, a novel protein family involved in the assembly and maintenance of adherens junctions.

Hobert et al. describe the characterization of the *C. elegans* PINCH family member unc-97. Mutants in UNC-97 exhibit defects in movement and egg laying, indicating a role for this gene in muscle development or function. Hobert et al. find that these animals have aberrant adherens junctions and that UNC-97 colocalizes with β-integrin and vinculin to adherens junctions. The phenotype induced by inhibition of UNC-97 function by RNA interference mimics that of loss of function alleles of known adherens junction components.

UNC-97 has homologues in several other species, including humans. These genes are highly conserved, consisting entirely of five LIM domains. Hobert et al. find that a *Drosophila* PINCH protein localizes to two integrin-containing cell types (muscle cells and muscle-attached epidermal cells), suggesting the function of PINCH family proteins in the assembly and maintenance of adherens junctions may be conserved.

## *Roles for Coronin in the Actin, and Possibly Microtubule, Cytoskeleton*

Actin-binding proteins modulate the stability and structure of actin filaments. Coronin—an actin-binding protein

with homologues in budding yeast, sea urchin, *C. elegans*, mice, and humans—was originally identified as an actin-associated protein in *Dictyostelium*, where it is required for efficient cell migration, cytokinesis, and endocytosis. But the role of coronin in these actin-dependent processes has been unclear. Goode et al. (page 83) show that Crn1p, the yeast homologue of coronin, can promote the rapid assembly and cross-linking of actin filaments.

When the polymerization of purified actin is followed using light-scattering or pyrene actin fluorescence, there is an initial lag phase as new filaments are nucleated. This lag phase is reduced in the presence of Crn1p, suggesting that this protein may nucleate actin polymerization. This activity is not dependent on filament cross-linking, severing, or capping, leading the authors to propose that Crn1p may promote actin assembly by a novel mechanism. Consistent with this hypothesis, coronin localizes to regions of dynamic actin assembly in a number of cell types including *Listeria* tails, cortical patches in budding yeast, and the leading edge of migrating *Dictyostelium*.

In cells, Goode et al. find that deletion of *CRN1* is synthetic with mutations known to reduce actin filament turnover rates. Remarkably, in the absence of other mutations, *crn1Δ* cells exhibit slight defects in the microtubule, not actin, cytoskeleton. As described here and in a recent paper in *Current Biology* (Heil-Chapdelaine, R.A., N.K. Tran, and J.A. Cooper. 1998. *Curr. Biol.* 8:1281–1284), cells deleted for *CRN1* have an increased sensitivity to the microtubule-depolymerizing drug benomyl, and an increased number of cells with short spindles. Goode et al. demonstrate that Crn1p can bind to microtubules and that this interaction is enhanced in the presence of actin filaments. Though the functional relevance of this interaction remains unclear, an exciting possibility is that Crn1p serves as a cortical attachment site for astral microtubules during spindle elongation.

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