Neuronal growth cones have detergent-resistant membranes (DRMs), specialized cell membrane fractions enriched in GPI-anchored proteins and intracellular signaling molecules. But are the DRMs involved in regulating neurite outgrowth? Yes, say Nakai and Kamiguchi (page 1097), who developed a new technique for selectively disrupting DRMs, and used it to demonstrate the functional importance of these structures in neuronal growth cones for the first time.

The authors modified a technique called micro-scale chromophore-assisted laser inactivation (micro-CALI) to specifically disrupt the integrity of DRMs in living cells. A ligand with attached dye was bound to GM1 ganglioside in the DRMs. Upon laser irradiation, the dye produced short-lived free radicals that disrupted nearby membrane structures.

Disrupting DRMs in the peripheral domain stops growth cone migration on L1 or N-cadherin substrates, but not on a laminin substrate. The cell adhesion molecules L1 and N-cadherin apparently require DRMs for normal functioning, whereas B1 integrin, which mediates growth on laminin and is not found in DRMs, does not. Disrupting DRMs in the central domain of the growth cone instead of the peripheral domain has no effect on growth cone migration.

The findings imply that homophilic binding of L1 or N-cadherin in the peripheral domain of the growth cone generates DRM-dependent signals that direct growth cone motility and shape. The new micro-CALI technique should be useful in studying other DRM-dependent signals, and the authors also hope to determine whether the growth cone DRMs are similar or identical to lipid rafts.

**Making Dictyostelium stick**

Using a clever genetic screen, Fey et al., reporting on page 1109, have identified the first cell–substrate adhesion molecule in the social amoeba *Dictyostelium discoideum*. The protein shares some structural features with adhesion molecules in higher eukaryotes, suggesting that the relatively simple amoeba will be a useful model system for understanding the contributions of substrate adhesion to cell movement.

The authors generated a panel of *Dictyostelium* insertional mutants, and then screened the transformants by repeatedly transferring them to new culture dishes. Only mutants that lacked the ability to attach to the dish were transferred. This screen identified nine independent substrate adhesion deficient (*sad*) mutants, one of which has now been characterized. *sadA* defines a novel gene encoding a molecule critical for cell–substrate adhesion in vegetative cells. GFP-tagged SadA protein localizes to the plasma membrane. In addition to multiple membrane-spanning regions, the protein’s predicted structure includes three EGF-like domains, suggesting that these domains may be an evolutionarily conserved feature of adhesion molecules.

Mammalian cell–substrate adhesion is more complex than one molecule, but the identification of nine genes essential for adhesion in *Dictyostelium* is an encouraging start. The authors are now characterizing the other Sad genes in an effort to determine how their gene products interact.

**Arp2/3 gets inhibited**

The Arp2/3 protein complex is a central regulator of actin assembly. Although a number of Arp2/3 activators have been identified in recent years, Humphries et al., on page 993, are the first to find a direct inhibitor of the complex: the highly conserved actin cytoskeleton component coronin. Using a combination of biochemical and genetic strategies, the authors found that the yeast coronin protein Crn1 physically and functionally interacts with the Arp2/3 complex in vivo via an evolutionarily conserved coiled-coil domain of Crn1. Although Crn1 strongly inhibits Arp2/3-mediated nucleation of actin in vitro, the addition of preformed actin filaments overrides this inhibition.

Based on the results, Humphries et al. propose that Crn1 may spatially restrict the activity of Arp2/3, permitting nucleation of new filaments only from the sides of existing filaments. This would promote the growth of a branched actin filament network like those often seen at the leading edges of motile cells. The mechanism by which coronin exerts this effect is not clear, although biochemical experiments have ruled out a simple steric block of Arp2/3 binding to either activators or actin.