6 Protein kinase A governs a RhoA-RhoGDI protrusion-retraction pacemaker in migrating cells.

Tkachenko E, Sabouri-Ghomi M, Pertz O, Kim C, Gutierrez E, Machacek M, Groisman A, Danuser G, Ginsberg MH

Nat Cell Biol. 2011 Jun; 13(6):660-7

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25 Jul 2011 | New Finding

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RECOMMENDED

Most papers studying RhoA regulation focus on Rho guanine nucleotide exchange factors (GEFs) or Rho guanosine triphosphatase (GTPase) activating proteins (GAPs). This paper is interesting because the authors find that Rho guanosine diphosphate (GDP)-dissociation inhibitor (GDI) is critical for regulation of cycles of RhoA activation at the leading edge of migrating kidney epithelial cells.

They have used elegant microscopy methods, using fluorescent biosensors, to track the activity of RhoA and protein kinase A (PKA) at the leading edge. They find a surprising temporal and spatial correlation. They develop a model whereby PKA phosphorylates RhoA (Serine 188), which facilitates RhoA's binding to RhoGDI, resulting in inhibition of RhoA activity. While RhoGDI inhibition of RhoA has been known for some time, this is one of the few cases where it has been shown to be involved in temporal regulation of RhoA. These components form a beautiful cycle for activation and inhibition of RhoA at the leading edge, resulting in protrusion and retraction of the cell membrane and, ultimately, cell migration. First RhoA is activated, then inhibited by PKA phosphorylation and binding of RhoA to RhoGDI and, finally, they show that lack of adhesiveness can lead to inactivation of PKA.