Slide this way

When cells of the slime mold *Dictyostelium* sense cAMP, they get the urge to merge, steering toward the source of the chemical and fusing into a slimy blob. By observing labeled cAMP receptors on traveling slime mold cells, Masahiro Ueda (Osaka University, Osaka, Japan) and coworkers were able to document differences in receptor activity between the “front” and “back” ends. The paper marks one of the first uses of a new technique for resolving and monitoring individual molecules.

To label the individual cAMP receptors, the authors fused cAMP molecules to an orange fluorescent dye called Cy3 and then exposed the slime mold cells to the compound. Using a total internal reflection fluorescence microscope, they could track and count the receptors on the cell surface that had bound to the glowing cAMP. “This technique can reveal the dynamics of the individual signaling molecules in living cells,” says Ueda.

The observations confirm previous reports that the migrating cells are polarized. Although there were about the same number of receptors at each end, 12% more receptors were bound to cAMP at the anterior end than at the posterior end. The investigators also found that the receptors at the anterior end released their cAMP more quickly. How the cells become polarized remains a mystery, Ueda says. However, polarity apparently develops independent of the cAMP gradient. “It will be important to determine how cells initially form such a polarity in receptor states and whether chemoattractant gradients can modify it,” Ueda says.  
Reference: Ueda, M., et al. 2001. *Science*. 294:864–867.

Renal budding (left) increases when endostatin is inhibited (right).  

**To branch or not to branch**

A new study identifies a possible new function for endostatin, the potential cancer-killer that checks blood vessel growth. Within the developing kidney, endostatin may help regulate the branching that establishes the network of urine-collecting tubules.

Cells in the ureteric bud divide and change shape to form the plumbing system of the kidney. Because endostatin inhibits blood vessel formation, Lloyd Cantley (Yale University, New Haven, CT) and colleagues suspected that it might also limit the formation of new tubules within the ureteric bud. To find out, they grew ureteric bud tissue in culture, adding exogenous endostatin or blocking endogenous production.

The results were striking. “Endostatin has a profound effect on branching,” says Cantley. The authors found that ureteric bud tissue branches excessively if doused with an anti-endostatin antibody. Buds treated with antibody, for instance, sprouted 75% more branches than the control group. By contrast, adding endostatin to the ureteric bud hampers branch formation.

Earlier studies had shown that inactivation of glypican-3, a receptor for endostatin as well as heparin-binding growth factors, results in excessive proliferation and branching of the ureteric bud. These studies identified bone morphogenetic protein as one of the possible regulators of branching in the ureteric bud. This paper adds endostatin to the list, Cantley says. He adds that endostatin’s role in the kidneys may not be limited to development; it may also help repair injuries.  
Reference: Karihaloo, A., et al. 2001. *Proc. Natl. Acad. Sci. USA*. 98:12509–12514.

Staying connected

Learning spurs axons in the brain to grow and connect with other neurons. However, scientists know little about what maintains these connections, which sometimes last a lifetime. A new study reveals that a protein known as p190 RhoGAP stabilizes the axon. The authors report that p190 works by stifling a built-in “retraction pathway” that causes axons to shrink.

Liqun Luo of Stanford University, Palo Alto, CA, and colleagues investigated p190’s function in the *Drosophila* mushroom body, the part of the brain responsible for olfactory learning and memory. When they inhibited p190 in neurons, the axon branches shrank or even disappeared. They got the same results by activating the RhoA pathway, which p190 normally blocks. “The idea that in mature neurons there is a pathway whose job is to destroy the axon is surprising,” says Luo.

The authors did not look for behavioral abnormalities in flies with inactivated p190. The results suggest, however, that regulation of the protein may have a role in the neural rewiring responsible for learning and memory, Luo says. p190 may also be linked to two other proteins that are necessary for memory formation or storage: Src and integrin. Since Src and integrin likely inhibit p190, their effects on memory may stem from changes in neuronal structure rather than changes in synapse function, says Luo.  
Reference: Billuart, P., et al. 2001. *Cell*. 107:195–207.