from the target, while two newly built proton detectors track protons knocked from oxygen nuclei in the target. A scattered electron and two protons emitted all at once signal a rare double knockout event; the group spotted about 5000 of these in all.

From the momenta and energies of the scattered electron and emitted protons, the researchers can determine the protons' original relationship inside the nucleus. Particular patterns of momentum mark proton pairs that were originally close neighbors, on the point of being flung apart by the repulsion between their quark cores.

Focusing on those events that involved closely interacting protons, Onderwater and his colleagues were able to reconstruct the energy states of the original nuclei, which correspond to the energy of the closely interacting proton pairs. "This is the first experiment of this kind that is really able to make a distinction between the different states," he says.

By comparing their results with recent calculations that attempt to accommodate SRCs, Onderwater's team concludes that about 70% of the proton pairs they detected were originally interacting very closely. The finding supports a picture of the nucleus in which many nucleons have a higher momentum than a mean-field approach alone would predict. That would explain why earlier single-proton knockout experiments, looking at only low momenta, could not see many of the protons.

The technique should eventually reveal even more details about SRCs, says Onderwater. "It's aimed at providing more information on how the mean-field model should be extended in order to incorporate this strong repulsive core in [nucleons]," he says. Soon, the private lives of nucleons may be a mystery no more.

–Andrew Watson

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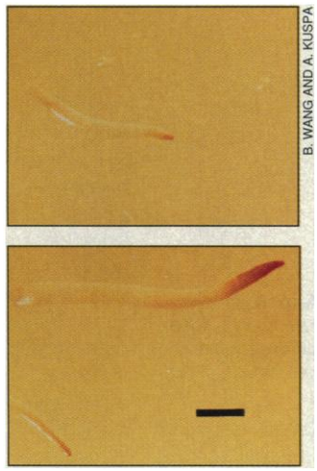
DEVELOPMENTAL BIOLOGY

One Molecule Orchestrates Amoebae

For a mere soil-dwelling amoeba, *Dictyostelium* manages some impressive feats of organization. When food is scarce, individual cells band together with their comrades to form a mound that crawls to better pastures and disperses by building a stalk and a spore body. Researchers have struggled for years to understand the signals that coordinate this multifarious behavior, hoping to gain insights into the development of more complex organisms. Now, with a paper in this issue, the picture has been dramatically simplified.

On page 251, Bin Wang and Adam Kuspa of Baylor College of Medicine in Houston show that a single molecule—an enzyme called PKA—can single-handedly drive all steps of development: clumping together; forming the cell cluster or slug; and differentiating into stalk or spore cells. The finding narrows the role of another molecule, cyclic AMP (cAMP), which activates PKA and can also act as a signal in its own right. Researchers had suspected that cAMP might work via many other pathways, says longtime *Dictyostelium* researcher William Loomis of the University of California, San Diego (UCSD). Now, "the paper shows that essentially all of the internal cAMP responses are mediated by PKA."



Migratory slugs. *Dictyostelium* mutants lacking cAMP *(top)* behaved like normal organisms. (Bar equals 0.25 millimeter.)

Besides telling *Dictyostelium* researchers that they needn't look for alternative cAMP signaling pathways to drive development, the finding also has an important message for researchers studying higher organisms. There, PKA and cAMP are key actors in everything from embryogenesis in fruit flies to memory in mice, and the new finding suggests that PKA may have the leading role. Says Loomis, "The universality of this is very important."

For decades, cAMP has been the center of attention in the study of *Dictyostelium* development. The molecule, synthesized by an enzyme called adenylyl cyclase, initially seemed to have many faces. Inside individual cells, it binds to PKA and sparks it into action to trigger cell differentiation. Outside the cells, it acts as a molecular magnet, drawing single cells into well-integrated structures. Many other roles for cAMP had been proposed, but no one had been able to pin them down or gauge their importance.

Kuspa and Wang had run across mutant amoebas that hinted that cAMP might be less crucial than many researchers had thought. These mutants had inactive adenylyl cyclase enzymes, yet they managed to develop normally. Given the many open questions about cAMP's roles, Kuspa says he and Wang, a graduate student in his lab, decided to take a closer look at such mutants. "We had been staring at the data for 2 years, and we just had to test this the best way we knew how."

They began with a well-characterized adenylyl cyclase mutant—one that essentially made no traces of the enzyme—provided by Peter Devreotes at Johns Hopkins University in Baltimore. Next, the Baylor researchers genetically engineered the mutant so that its cells produced high levels of a mutant PKA that was permanently turned "on," even without cAMP to activate it. The Baylor team then watched how these microorganisms developed over the course of 24 to 30 hours.

To their surprise, the mutants looked and behaved virtually the same as normal organisms. Moreover, when the researchers tested the activity of specific genes that are turned on and off at particular times in *Dictyostelium* development, they observed a normal pattern. "The cell-type specific genes were turned on at the same time as wild-type," says Kuspa. "That was probably the most shocking thing."

Not only was the cells' internal signaling taking place normally, but the collective behavior of the cells also appeared normal. They bunched together and formed stalks and spores—events that researchers had thought could only be orchestrated by pulses of cAMP. Only when the density of cells was low did the lack of cAMP seem to prevent the mutants from building normal mounds.

"The intriguing thing is that the organism can bypass a number of events that normally require cAMP in the wild," says developmental geneticist Richard Firtel of UCSD. Kuspa believes the mutants can get around the need for the chemical signal by bumping into each other, triggering alternative signaling pathways that require only PKA.

At first sight, the results appear at odds with Firtel's own findings. He and his colleagues had created similar mutants and found that they failed to develop normally. But Firtel thinks the discrepancy may stem from "too much of a good thing." While Kuspa's mutants produced twice the normal levels of PKA, Firtel's organism overproduced the enzyme in much greater amounts. "It just means that you need a specific amount of PKA ... to produce the observed phenotype," he says.

If PKA in just the right amount can serve as a master coordinator of development, "the subtleties go way beyond Wang and Kuspa," says Loomis. "The findings could be used as a guideline for studies of all vertebrate and invertebrate development—in addition to being fascinating for *Dictyostelium* in and of itself."

–Trisha Gura

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