Kravitz and Livingstone had linked to aggressive behavior in lobsters and crayfish 15 years ago.

Edwards's group doesn't know yet whether the neuron also triggers a serotonin burst in crayfish, but they suspect that it might. If it does, then a "feed-forward loop" would operate in dominant animals, says Kravitz, in which triggering the lateral giant neuron would cause a burst of serotonin, which would make the neuron even more likely to be triggered again, causing more serotonin to be released. All that serotonin would pump up the animals' aggressive behavior. In contrast, subordinate crayfish are better served by not acting truculent and inviting a fight they are likely to lose, so it is adaptive for them to put the brakes on that cycle, which is what happens when the burst of serotonin caused by the lateral giant's firing makes the neuron less likely to fire again and trigger the release of more serotonin.

Despite the appeal of that explanation, Kravitz and others point out that the lateral giant neuron alone is unlikely to be the full explanation for the behavioral changes. "You can't say this particular [neuron] ... is causally responsible for any behavioral changes," says Brandeis's Marder. "It is probably only a piece of the story."

To fill out the remaining pieces of that story, Edwards and others are eager to learn what other neurons may be influenced by the switch in social status, and whether some of those neurons show a change in serotonin receptors, or in receptors for other molecules. One target for study is the neurotransmitter octopamine, which Kravitz's group has shown to have the opposite effect to serotonin, producing submissive rather than aggressive behavior.

In addition, the researchers plan to take a closer look at the lateral giant neuron itself, focusing on the specific pathways through which social position gets translated into cellular and molecular changes in the neuron. With all these possibilities for future work, says Kravitz, the Edwards group has opened "a potentially incredibly exciting area of investigation."

–Marcia Barinaga

DEVELOPMENTAL BIOLOGY

Choreographing the Bacterial Cell Cycle

A bacterial cell's life cycle resembles a carefully choreographed dance, with particular movements, such as cell division or the development of particular cell structures, occurring only after previous steps are completed. But while scientists reason that this dance must depend on a few master choreographers—molecules that trigger several steps, ensuring that they proceed in proper sequence—researchers have been unable to find them. Now, however, biologists have come upon a gene that may coordinate several developmental events with the progress of the cell cycle in the aquatic bacterium *Caulobacter crescentus*.

In the 12 January issue of *Cell*, developmental biologists Lucy Shapiro and Kim Quon of Stanford University and Gregory Marczynski of McGill University describe the identification of *ctrA*, a gene whose product regulates not only the formation of a propellerlike flagellum but several other critical events in the *Caulobacter* life cycle, including DNA replication.

CtrA, the protein encoded by the gene, is part of a system of sensor enzymes and so-called "response regulator" proteins that are thought to respond to external and internal events in these cells. "This is the first demonstration of a direct role for a response regulator in global cell cycle events" in any bacterium, says Shapiro. Researchers in molecular biologist Austin Newton's lab at Princeton University reported last year that a response regulator called DivK influences a late cell division event in the *Caulobacter* cell cycle, but Shapiro's group is the first to document a mechanism for how such a protein might perform its integrative functions.

Other scientists are impressed. "Here the protein is being used to drive things the cell does all day long," says Richard Losick, a developmental biologist at Harvard University, and it unveils an important part of the cycle's "underlying pathway." And once molecules that activate *ctrA* have been identified, says Bert Ely, a bacterial geneticist at the University of South Carolina, "we can then ask how general this mechanism is. Does it work for other kinds of bacteria? Does it apply in eukaryotic cells [those with distinct nuclei] as well?"

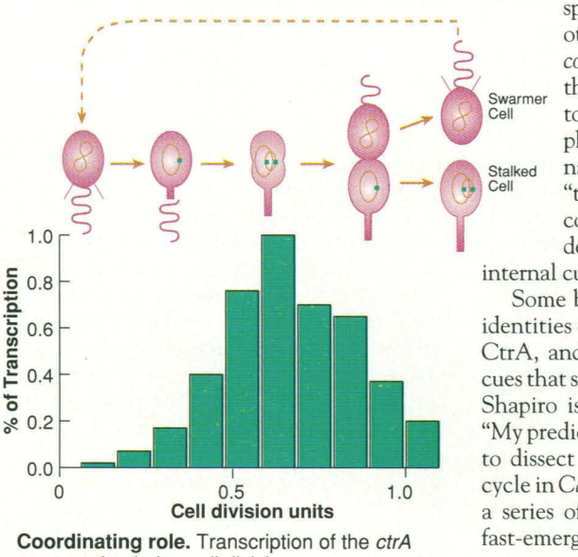
Shapiro's group found *ctrA* while studying *Caulobacter*'s flagellum, which forms at a crucial point in the bacterium's life cycle. Only after its assembly at one pole of a cell does the cell divide in two. The propeller-driven progeny cell then swims off in search of a new home in which to settle down and reproduce, while the other progeny cell stays in place and produces more swarmer cells. Although Shapiro's group has spent years studying mutations affecting flagellar assembly in *Caulobacter*, "we could never find the top of the hierarchy, the gene that turns the thing on," she says. Quon reasoned that this top-level gene might have been so difficult to find because it has some additional essential function. In that case, mutating the gene might kill off the bacteria. So 2 years ago the group began to look for heat-sensitive mutations that might be just slightly perturbed by altered temperatures, upsetting transcription of genes affecting flagellar assembly without killing the cell.

The strategy succeeded. The group found one mutation, in *ctrA*, that not only caused overproduction of FliQ—a protein required for the initial steps of flagellar synthesis—but also prevented cell division. And CtrA, the protein product of normal *ctrA*, binds to a specific DNA sequence in one of the regions that control *fliQ* gene transcription. That same sequence is present in regulatory regions for other genes, including one that contributes to the control of the initiation of DNA replication at different times in both new progeny cells.

The researchers then found that CtrA's amino acid sequence resembles that of response regulator proteins found in other bacteria, including *Escherichia coli*, and that it is readied for action in the same way as these other regulators: through the addition of a phosphate group by so-called "sensor kinases." The work helps confirm that "these two-component systems are controlling essential cell-cycle and developmental events in response to internal cues," says Newton.

Some big unknowns remain, such as the identities of the enzymes that phosphorylate CtrA, and the exact nature of the cellular cues that send these enzymes into action. But Shapiro isn't daunted by these challenges. "My prediction is that we are going to be able to dissect the complete control of the cell cycle in *Caulobacter*, and that it's going to use a series of these response regulators. It's a fast-emerging field."

–Wade Roush



SOURCE: L. SHAPIRO

Coordinating role. Transcription of the *ctrA* gene peaks during cell division.