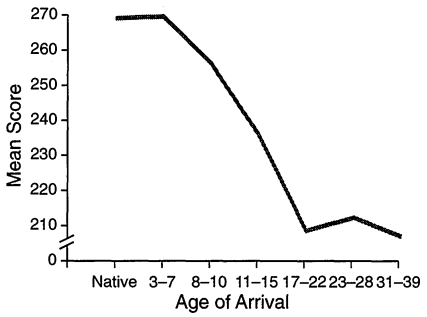
celerate the learning of these concepts by giving children special training that emphasizes the idea that others think differently. That suggests, she says, that there isn't "some maturational event in the brain" that makes the timing right, "but rather that the very things you learn enable you to learn new things."

What it may come down to, at least for some types of complex learning, is a question of whether learning drives changes in the maturing brain, or whether the maturation process controls the ease with which learning occurs. Such questions can be addressed, says Neville, as brain structures associated with different kinds of learning are identified. For example, she is currently experimenting with children to see if training that accelerates their language learning results in measurable changes in brain organization, and several research teams are beginning to use brain imaging to investigate organizational changes in brain areas involved in the formation of bonds of attachment. "The work is going on; we just don't have the answers yet," says Neville. But she predicts that any answers are "not going to be either-or. We have a whole panoply of brain systems. It is likely that the answer is going to be different for each individual system."



Telltale curve. The scores of immigrants on a grammar test decline with the age at which they were immersed in English and level out after puberty, a sign of a sensitive period that ends in the teen years.

As researchers pool their resources to nail down what role critical periods may play in learning, certain themes are emerging: Whereas younger brains may change more readily, older brains have not lost that capacity to change. And although it is clear that childhood is a privileged time for learning and one not to be wasted, there is no reason to give up hope for learning at any age. Indeed, says Rochester's Newport, the work may produce an understanding of whether the mechanisms of late-life learning differ from those of childhood. With a better understanding of such differences, says Newport, "one could think of different approaches and strategies" to improve adult education programs. And that would be good news for eager learners of all ages. **–MARCIA BARINAGA**

MEETING **SOCIETY FOR DEVELOPMENTAL BIOLOGY**

A Mile-High View of Development

BOULDER, COLORADO—Nearly 600 scientists gathered at the base of the Flatirons to discuss the growth and patterning of organisms including plants, worms, fruit flies, fish, and mice at the 59th annual meeting of the Society for Developmental Biology. Among the highlights were clues about how blind cave fish lost their eyes and how a gene that influences cell movement might help cancer spread.

A Fish's Tale

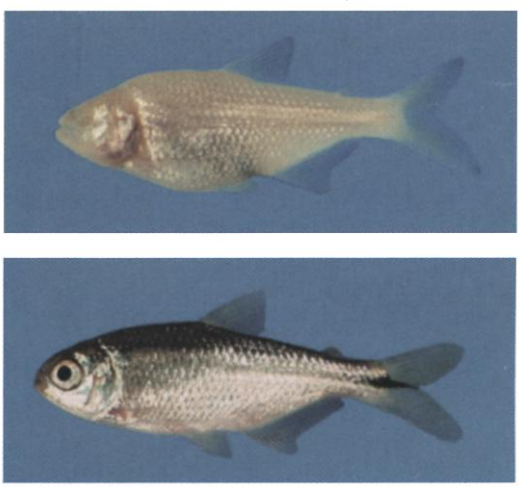
"An eye for an eye and a tooth for a tooth," declares the ancient biblical commandment. But for a population of blind cave fish, the exchange may have been an eye for a tooth—or several teeth. The theory is far from proven, but at the meeting researchers presented evidence that changes in the expression of a key gene involved in facial development might help explain the lost sight in cave fish. They suspect that during the course of evolution, the cave fish may have exchanged its sight—unneeded in underground rivers—for more teeth and taste buds.

The Mexican tetra fish (*Astyanax mexicanus*) thrives in habitats from surface waters to lightless caves in northeastern Mexico. Although technically the same species as their light-dwelling cousins and able to interbreed with them, the *A. mexicanus* from caves are much paler and have no eyes as adults. Intrigued by different-looking fish within the same species, developmental biologist William Jeffery and postdoctoral fellow Yoshiyuki Yamamoto of the University of Maryland, College Park, have been trying to understand how evolutionary changes in the animal's development caused the troglodytic fish to lose its eyes.

The researchers first examined the expression patterns of several eye-related genes in cave fish embryos, hoping to find clues about why the eye, which begins to develop almost normally, eventually degenerates and disappears as the fish matures. When they checked the young fish for the presence of one of the genes switched on early in eye development, called *Pax6*, they found a curious pattern: Throughout almost the entire cave fish embryo, the expression pattern of *Pax6* matched that seen in surface-dwelling *A. mexicanus*. But in the region of the embryo destined to give rise to eventual eye cells, *Pax6* was less prominent and appeared farther from the midline (a precursor of the backbone).

Previous work had shown that *Sonic hedgehog* (*Shh*), a fundamental patterning gene (named for a character from a children's computer game) that is active at the midline, can affect expression of *Pax6*. When *Shh* is missing, for example, the mutants develop so-called cyclopia—an enlarged single eye in the middle of the forehead. To see whether *Shh* might play a role in the loss of eyes, the scientists compared the pattern of *Shh* expression in cave fish and surface fish embryos. In cave fish, they found, *Shh* appeared in a wider swath at the midline, suggesting that the cave fish might have developed a sort of anticyclopia in which extra Shh protein causes smaller—or missing—eyes. "We were very surprised," Jeffery says, "that our initial guess was actually correct."

To see whether they could mimic the suspected evolutionary changes in the lab, the researchers injected excess *Shh* mRNA into surface fish embryos at the two- to



Trade-off. Cave-dwelling *Astyanax mexicanus* (*top*) may have lost eyes but gained teeth as they diverged from their surface-dwelling cousins of the same species.

CREDITS: (GRAPH) E. NEWPORT AND J. JOHNSON; (PHOTOS) YOSHIYUKI YAMAMOTO/UNIVERSITY OF MARYLAND

four-cell stage. Indeed, the fish developed smaller-than-normal eyes. And when Yamamoto exposed early cave fish embryos to ethanol, which is known to interrupt Shh protein signaling, the cave fish seemed to develop slightly larger eyes. The scientists caution that experiments are preliminary—ethanol, especially, is likely having multiple effects on gene expression. Even so, evolutionary developmental biologist Brian Hall of Dalhousie University in Halifax, Nova Scotia, calls the findings "quite suggestive."

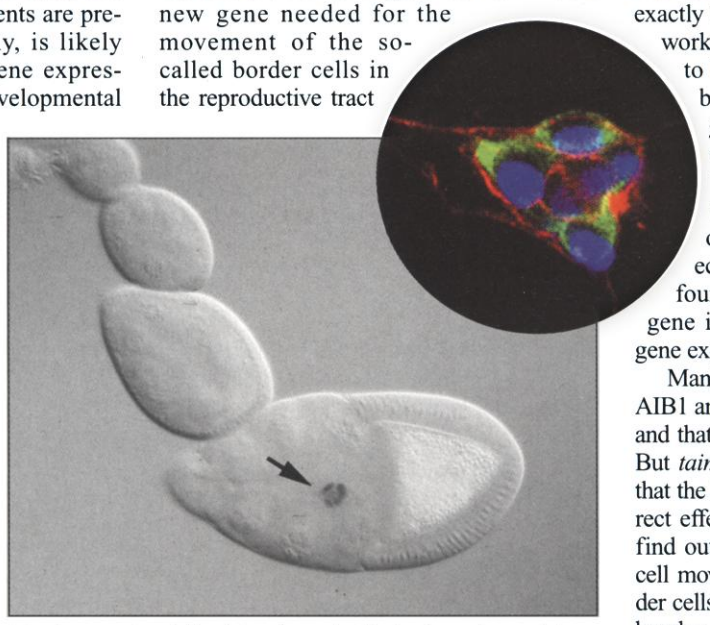
Because the differences in gene expression appear so early, before the cells destined to become eyes have fully differentiated, Jeffery and Yamamoto suspect that the altered *Shh* pattern has caused other changes in cave fish facial development. To find out, the team plans to examine the effect of *Shh* on the development of teeth and taste buds. In a paper published this spring in *Development, Genes and Evolution*, Jeffery's team reported that cave fish have more taste buds than surface-dwelling fish have, and Jeffery says they also have more teeth, based on work with David Stock of the University of Colorado, Boulder. He suspects that during the course of evolution, more teeth and more taste buds may have given the ancestors of the bottom-dwelling cave fish an advantage. An ancestor of today's blind bottom-dwellers might have inherited an up-regulated signal from *Sonic hedgehog*, which resulted in more teeth but smaller eyes. Because vision was of little use in lightless caves, there was no evolutionary pressure to keep eyes.

That's an extremely interesting idea, says Hall. He cautions that one "can't make much of an evolutionary story out of one species" and suggests that additional research in other eyeless animals may be necessary. Even so, he says, the cave fish model "begins to provide a way of tackling how such coordinated evolutionary changes happen."

Insights Into Cellular Travel

The intricately choreographed movements of cells during development have long posed fascinating riddles for biologists: How do cells know where to go, and how do they manage to get there? Now, researchers are learning how one group of specialized cells in the fruit fly moves during egg development—and in the process, they have uncovered new clues about how cancer cells might spread to form new tumors.

At the meeting, developmental biologist Denise Montell of Johns Hopkins University School of Medicine in Baltimore reported that she and her colleagues had identified a new gene needed for the movement of the so-called border cells in the reproductive tract of female fruit flies. During oocyte development, the six to 10 border cells migrate from the tip of the egg chamber to its center, where they eventually help form the shell that surrounds the mature egg. The gene that the researchers linked to these movements resembles one previously identified as involved in the spread of human breast cancer and may even work in a similar way: by cooperating with a steroid hormone, ecdysone in the case of the fruit fly, to regulate gene expression. If so, then the work may not only provide clues about how hormones influence development, but it may also help cancer biologists understand why exposure to hormones such as estrogen makes some cancers more aggressive.



Moving on. Specialized border cells (dark cluster) travel from the tip of the fruit fly egg chamber to the edge of the immature oocyte. Inset shows close-up of border cells, with nuclei stained blue.

Montell, with graduate student Jianwu Bai and postdoc Yoshi Uehara, found the gene by searching for mutations that cause border cells to move abnormally. Among the handful of mutants they identified was one in which the cells seemed to form properly, but migrated at a slower than normal pace. Bai named the mutant *taiman*, Chinese for "too slow."

Thanks to the then partly finished fly genome project, the team was able to identify and clone the gene at fault in a matter of days. They found that it closely resembles a human gene called *amplified in breast cancer–1 (AIB1)*, which takes its name from the fact that particularly aggressive tumors frequently contain extra copies of the gene, leading to overproduction of the AIB1 protein (*Science,* 15 August 1997, p. 965). Scientists think that excess AIB1 may help tumor cells spread, although they don't know exactly how. They do know that the protein works with activated estrogen receptors to help turn on genes in the nucleus, but have not yet identified the target genes. The evidence in flies suggests that *taiman* works in a similar way: When the team tested the interactions of *taiman* and the fruit fly's only known steroid hormone, ecdysone, in a cell culture assay, they found that adding more of the *taiman* gene increased the hormone's effects on gene expression.

Many cancer biologists had assumed that AIB1 and estrogen primarily promote growth, and that additional tumors were a side effect. But *taiman*'s role in cell movement suggests that the human version might have a more direct effect on cell motility, Montell says. To find out more about how *taiman* influences cell movement, the team stained mutant border cells for e-cadherin, a protein required for border cell movements. The researchers thought that the slow-moving cells might be missing that protein, but found instead that they had higher than normal levels of e-cadherin on their leading edge.

That may not be completely surprising, as e-cadherin, which sticks out from the cell membrane and hooks onto cadherins on other cells, seems to play a dual role in movement. It can hold cells in place, but cells can also use it to pull themselves forward, which requires that they periodically break their links with one cadherin to move to the next. Montell and her colleagues suspect that *taiman* might be part of a pathway that breaks down cadherins, allowing a cell to let go of its current partner. "Clearly the *taiman* gene affects the invasive behavior of the border cells," says developmental biologist Ruth Lehmann of New York University, although she cautions that the steps between *taiman*'s cooperation with ecdysone, the reorganization of cadherin, and cell mobility are still unknown.

Another big question concerns whether AIB1 and estrogen might have similar effects on cadherin in cancer cells, enabling them to move throughout the body. In that case, Montell says, it might be useful to design antimetastasis drugs that work by blocking the effects of AIB1. Lehmann agrees. Indeed, she suggests, the fruit fly border cells might even be a useful assay for such drugs. If so, a gene named "too slow" may speed up progress in finding better ways to block cancer.

–GRETCHEN VOGEL

CREDITS: (LEFT TO RIGHT) DENISE MONTELL/JOHNS HOPKINS UNIVERSITY SCHOOL OF MEDICINE; JIANWU BAI/JOHNS HOPKINS UNIVERSITY SCHOOL OF MEDICINE