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Intimate look at the typhus organism

LEAD STORY 1244

Cancerkilling viruses





1 2 4 7 Dinomania gives research a charge

York Times earlier this year.

Holt didn't dwell on his scientific credentials during the campaign, and as a freshman from the minority party he is unlikely to have a significant impact on national science policy. But he did claim "technical expertise that is so rare in Congress and political expertise that is so rare in science." He promises to be a "strong advocate for R&D" but declines to say whether he is seeking a seat with direct responsibility for science policies or spending. He also knows that his narrow win marks him as vulnerable in the 2000 campaign. "There are a dozen Republicans already thinking about running against me," he says. "I say, bring 'em on." -DAVID MALAKOFF

## DEVELOPMENTAL BIOLOGY

## Understanding of Ears, Bristles Jumps a Notch

The arrangement of cells in the inner ear, which allows a music lover to sense harmonies, is itself as complex as a Bach fugue. It is orchestrated during development when precursor cells in the inner ear organize into a mosaic of sensory patches made of hair cells, which sense vibrations, neurons, which send messages to the brain, and supporting cells. In the December issue of *Development*, researchers describe part of the system of molecules that creates this intricate pattern. In an example of evolution's tendency to reuse basic mechanisms, it turns out to be the same system that guides the development of a much simpler sense organ in the fruit fly.

Developmental biologist Julian Lewis of the Imperial Cancer Research Fund in London and his colleagues demonstrate that proteins called Delta and Notch, already known to help pattern the vibration-sensing bristles on a fly, control the development of the hair cell mosaic in the inner ear of zebrafish and chicks. Other evidence from mice, which developmental biologist Matthew Kelley of Georgetown University has presented at several meetings, suggests that the same proteins are at work in mammalian ears as well.

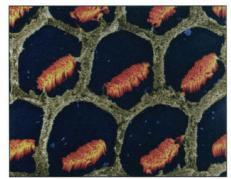
Lewis's work "begins to give us an idea of the molecular pathways that govern the development of the mosaic," Kelley says. And it may eventually have clinical applications: In mammals, including humans, damaged hair cells are lost for good, but birds can regenerate them. Understanding how the cells develop in the first place "begins to

give us insight into the pathways that prevent regeneration," Kelley says.

Delta and Notch are powerful determinants of cell fate in both the fly and in vertebrates. For example, as a group of vertebrate pre–neuronal cells matures, one cell gets slightly ahead of its cousins. Delta, which is lodged in the cell's membrane, interacts with the Notch receptor on neighboring cells, preventing them from becoming neurons. In the developing fly bristle—a miniature sense organ on the fly's head and body,

which is made of a neuron and accessory cells—Delta-Notch signaling seems to work in a similar fashion to determine which precursor cells become neurons, bristle shafts, and supporting cells.

Because of the similarities between bristle and hair cell structure and function, scientists had suspected that the inner ear might also use Delta-Notch signaling in development. To find out, Lewis, Julie



**Hearing aid.** During development, chick inner ears (*above*) and fly bristles (*top*) are both patterned by the Notch protein.

Adam, Anna Myat, and their colleagues looked for expression of the *Delta* gene in the ears of chick embryos. A few hours before the first neurons appear, the scientists found *Delta* expressed in scattered cells. Several days later, *Delta* was expressed again at just the site where the mature hair cells appeared a few hours later. By the time the hair cells were recognizable, Delta had nearly disappeared, but the two bouts of *Delta* expression are "strong evidence" that *Delta* guides neuron and hair cell development, says developmental neurobiologist Jeffrey Corwin at the University of Virginia, Charlottesville.

In a second paper in the same issue, Lewis, Catherine Haddon, and their colleagues suggest that a similar process also controls ear development in the zebrafish. They examined the embryonic ears of a mutant zebrafish called *mind bomb*, so named for its excess of neurons. No one has yet pinpointed the gene responsible for the fish's bumper crop of neurons but researchers think that the mutation somehow blocks Delta-Notch signaling. Sensory patches in the inner ears of *mind bomb* fish become "wall-to-wall hair cells," says Lewis, with no visible supporting cells—every cell becomes a hair cell.

Given that fly bristles and ear hair cells do basically the same thing and use the same developmental genes, Lewis and his colleagues propose that they may have evolved from a common ancestral sensory structure. But Corwin isn't so sure.

Delta-Notch signaling is so common that "it may be like a subroutine in computer programming that evolution uses over and over," he says. So it's possible, says Corwin, that evolution reused the system in unrelated organs.

However the system evolved, understanding it may be useful. After chick inner ear cells are damaged, they express Delta as they regenerate, according to developmental neurobiologists Edwin Rubel and Jennifer Stone at the University of Washington, Seattle. These findings, under review at *Development*, may bring scientists a little closer to the day when "we will be able to restore hair cells in the human ear," says Rubel—an achievement that may allow today's headbangers to enjoy Bach in their old age.

-GRETCHEN VOGEL

## COMPUTER SCIENCE

## Microsoft Picks Beijing For New R&D Lab

**BEIJING**—Microsoft Corp. is making a major research investment to help it capture and retain a large chunk of China's fast-growing computer business. Last week, the software giant announced that it will open a research center in Beijing, and it pledged to spend \$80 million over 6 years to make computers more user friendly for speakers