might also enable researchers to determine the structures of important but uncooperative biological molecules, says Janos Hajdu, an x-ray crystallographer at Uppsala University in Sweden. To determine a molecule's structure, researchers usually shine x-rays on a crystal; the multiple copies of the molecule produce a scatter pattern that reveals its shape. Some molecules, however, refuse to form large crystals. But a single blast from an X-FEL could shower a tiny sample—perhaps just a single molecule—with enough x-rays to reveal the molecular structure, just before it blows the sample to bits, Hajdu says. "It could allow you to use tiny samples because it is so intense," he says, "and because it is so short, the atoms don't have time to move."

X-rays from an X-FEL could also produce a state of matter similar to that found in centers of planets, called "warm condensed matter." Such matter has the density of a solid but is heated to temperatures of about 10,000 kelvin, which are more typical of an ionized gas or plasma. The x-rays from an X-FEL could produce this type of matter by heating a sample so rapidly that it doesn't have time to expand. X-FEL studies of warm condensed matter should provide new data for astrophysicists studying planet formation and for engineers and physicists developing laser-induced nuclear fusion, says physicist Dick Lee of Lawrence Livermore National Laboratory in California.

For the moment, though, all these studies remain thought experiments, as researchers await the political and financial decisions that will determine when the first X-FELs shine. DESY's X-FEL, for example, is currently tied to the fate of TESLA, Europe's bid for the next international particle physics experiment after the Large Hadron Collider now under construction at CERN in Switzerland. Japanese and U.S. researchers are working on rival linac designs, and particle physicists worldwide will have to pick one before any money arrives (*Science*, 27 July 2001, p. 582).

But SLAC's Linac Coherent Light Source already has DOE's backing, says Patricia Dehmer, DOE's director of basic energy science. SLAC researchers should receive $6 million in 2003 to plan the construction of the machine, she says, but "it's premature to say when it's going to be commissioned."

Some researchers worry that in some regards the scientific potential of X-FELs is being oversold. For example, Richard Henderson, a structural biologist at Cambridge University, U.K., says that the first X-FELs won't be able to determine the structures of single molecules any better than an electron microscope can when a sample is frozen to slow radiation damage. Henderson says that, overall, X-FELs have great potential and that one should be built. "But," he says, "what you mustn't do when you're asking for a lot of money is overstate your case."

And even x-ray physicists say there are still challenges to be met in building the machines. For example, to make an X-FEL work at wavelengths of a tenth of a nanometer, researchers must be able to control the position of the electron beam to within 20 micrometers over the entire length of the undulator, says DESY's Joerg Rossbach. They will also have to double the current in their beams while reducing the beams' size and tendency to spread by a factor of 2. "We know how to do this," Rossbach says, "because we understand the underlying mechanism and we understand the technology."

Despite the scientific and political challenges, physicists are confident that their turbo-charged x-ray sources will be well worth the money and years of effort. "I personally believe it will be a revolution," Rossbach says. And just maybe that will be enough to satisfy the physicists—at least until they come up with an even brighter idea.

–ADRIAN CHO

Adrian Cho is a freelance writer in Boone, North Carolina.

MEETING EVOLUTION OF DEVELOPMENTAL DIVERSITY

Evo-Devo Devotees Eye Ocular Origins and More

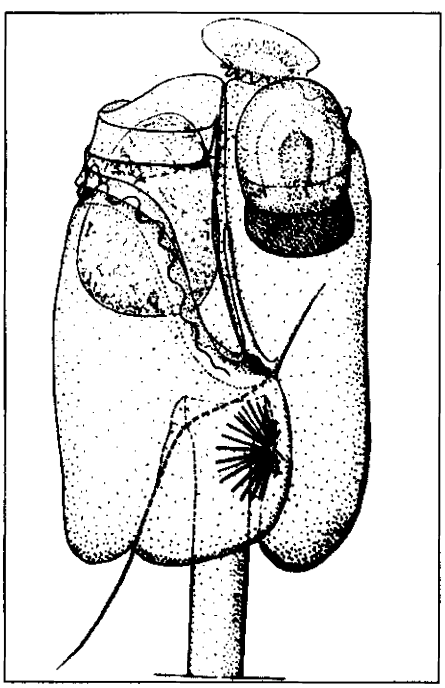
COLD SPRING HARBOR LABORATORY, NEW YORK—From 17 to 21 April, evo-devo researchers met here for the Evolution of Developmental Diversity meeting to discuss how environment and quirks in development prompted the branching of the tree of life.

Did Eyes Come From Microbes?

In the mid-1990s, developmental biologist Walter Gehring came up with a heretical proposition: Eyes evolved only once. The idea was a hard sell. Because eyes are ubiquitous and come in vastly different varieties, most evolutionary biologists assumed that they arose independently many times. Now, Gehring has come up with an even more eye-popping suggestion: The original eye belonged to a microbe that later became a chloroplast, a subcellular center of photosynthesis best known for fueling growth in plants.

"It's a wild idea," says Richard Behringer, a developmental biologist at the University of Texas M. D. Anderson Cancer Center in Houston. If true, "it would be fantastic," adds Nipam Patel, an evo-devo researcher at the University of Chicago. But he and others have their doubts.

At the meeting, Gehring of the University of Basel, Switzerland, described the thinking behind his new view of eye evolution. His proposal that eyes evolved only once rests on his 1995 discovery of a gene called *Pax-6* that is involved in eye formation in fruit flies, mice, and humans. Since then, he and others have been shaking the tree of life in search of more versions of this gene.



Eye to eye. This schematic of the eye of an obscure species of dinoflagellate reveals a complexity akin to that of our own eyes.

CREDIT: MARIE-ODILE SOYER

It has turned up in some 20 species; even primitive ones, such as sponges, have precursor versions of the gene. Each new find has convinced him that his proposition is correct. However, the notion remains controversial—indeed, it met with

some opposition at the meeting—in part because it's hard to imagine how a primitive eye from a common ancestor could lead to the great diversity seen today. So Gehring has been looking at the simpler animals for clues to support his theory.

He has found *Pax-6* in *Planaria*, primitive flatworms that can regenerate their bodies. And he has used a technique called RNA interference (RNAi) to demonstrate that the gene is involved in the animal's eye formation. He reported at the meeting that if he interferes with *Pax-6* function when a planarian is growing back a severed head, "it can regenerate the brain, but it can't regenerate the eyes." Once the RNAi effect wore off, eyes appeared. The same proved true in eye regeneration in ribbonworms.

Gehring hadn't really considered an even more primitive origin for eyes until a French colleague sent him a 40-year-old Ph.D. thesis that described an obscure dinoflagellate—a single-cell plankton—that has an eye "basically like a human eye and could focus light," Gehring said. This eyespot, which is presumably derived from the dinoflagellate's chloroplast, has a lens, protective pigments, and a stacked layer of membranes akin to a retina.

Over the past decade, many evolutionary biologists have become convinced that, like mitochondria, chloroplasts were once independent microbes. According to one scenario, early in life's history, these productive bugs were engulfed by a larger microbe and subsequently became part of that microbe's cellular machinery. Gehring suggests that the independent microbes may have developed a light-sensing mechanism: "There's a great selective advantage," he explained, "as sensing light could have enabled these early organisms to avoid damaging UV light and track down light for photosynthesis." These proto-chloroplasts, he suggests, were engulfed by dinoflagellates, which in turn became symbionts of more complex organisms. "It could be that eyes are coming from a symbiont within a symbiont," he says.

Some colleagues are skeptical, however. "It's hard to understand how you would take [a subcellular component] and have it become a multicellular structure" such as a modern eye, Patel notes. But others find the theory intriguing. "It's a neat idea, and [he] can really check into it," says Ronald Ellis, a developmental biologist at the University of Michigan, Ann Arbor.

To do that, Gehring wants to isolate DNA from the species of dinoflagellate with the eyespot to check for *Pax-6* and other genes related to vision. "The dinoflagellate is very difficult to find," he notes. At the same time, he's planning to scour the genomes of other animals for chloroplast genes. "If my prediction is right, we should be able to find some chloroplast genes in multicellular animals and dinoflagellates." If so, that would be a real eye-opener.

Good Diet Hides Genetic Mutations

After Claudia Kappen moved from the University of Arizona in Tucson to the University of Nebraska Medical Center in Omaha 2 years ago, she couldn't figure out why the mice she was studying were suddenly much healthier. A developmental biologist, she was interested in skeletal diseases and had bred a strain of transgenic mice whose bones were so fragile that the rib cage couldn't withstand breathing and the animals died soon after birth. But in Nebraska, their skeletons were much stronger.

In her quest to understand the animals' newfound vigor, Kappen and her colleagues have demonstrated again that diet can protect against some genetic diseases: She reported at the meeting that folate, part of the vitamin B complex, compensates for an overactive gene involved in cartilage formation.

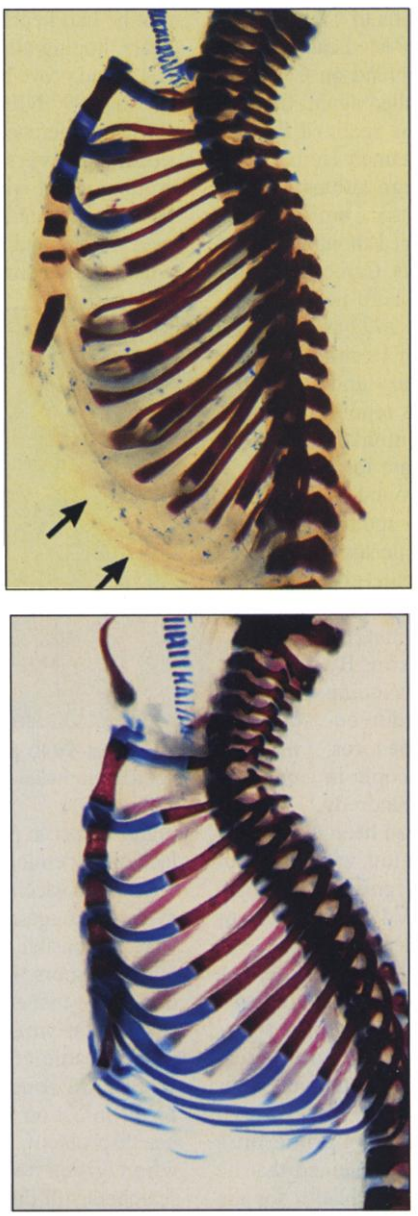
The study suggests a way that mutations could build up in a population, says Nipam Patel, an evo-devo researcher at the University of Chicago. If good nutrition can mask harmful genetic changes, mutations might accumulate unnoticed. Should diet then change, the mutations would exert their influence, possibly changing the animals' physical or behavioral traits. Then evolution could take its course, selecting against some of these traits while favoring others.

"I don't know of anyone in the field who had thought about folate in this regard," says Richard Behringer, a developmental biologist at the University of Texas M. D. Anderson Cancer Center in Houston. He and others have shown that folate can prevent neural tube defects such as those that cause spina bifida in humans, but he had not suspected that the same nutrient could affect skeletal growth.

Kappen and her colleagues realized that the mice were chewing on their bedding—corncobs—a nutrient source they didn't have in the Arizona lab. On a hunch, Kappen decided to see if folate was the secret ingredient that compensated for an aberrant *Hox* gene she had introduced into the mice. The gene helps control the maturation of cartilage precursor cells. The overactive form prevents the formation of intact cartilage in the animals, although the researchers aren't sure why. They found that cartilage cells from the defective mice matured as well as those from healthy embryos if grown in a folate-rich environment. Without folate, "the cells shriveled up and died," she reported. Transgenic mice given extra folate also fared well: Their skeletons stayed intact rather than shattering. "The faulty *Hox* gene can be modified by an environmental substance," she concluded.

It's still unclear how folate makes up for the bad gene. Kappen suspects that folate might speed up cell growth and differentiation, thereby compensating for the defective *Hox*, she explained. At this time, no one knows how important folate in the mother's diet is to cartilage development in human fetuses, she says.

–ELIZABETH PENNISI



Mutation masker. Folate can help mutant mice with defective ribs (*top*) develop more normal ones (*bottom*). Immature cartilage in the defective ribs makes them too weak to support breathing.

CREDIT: Y. G. YUEH, D. P. GARDNER, C. KAPPEN, *PNAS* 95, 9956 (1998)