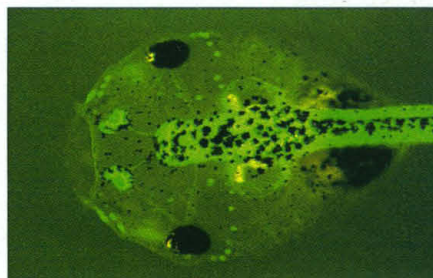
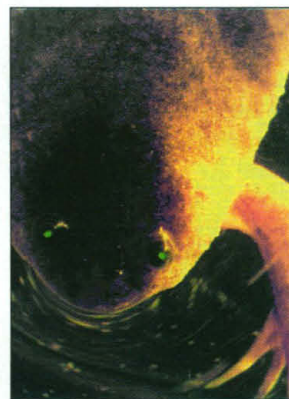


DEVELOPMENTAL BIOLOGY

Frog Is a Prince of a New Model Organism

CHARLOTTESVILLE, VIRGINIA—*Xenopus laevis*, a fist-sized brown frog that is a favorite of developmental biologists, has an embarrassment of genes. For decades, biologists have studied its large, hardy embryos, transplanting bits of tissue to create monster tadpoles with two heads or missing tails—and in the process deciphering some of the key steps that shape a developing vertebrate. But in the age of molecular biology, *X. laevis* has a major drawback: Somewhere in its evolution, the frog's genome doubled, leaving the animals with four copies of most genes instead of the usual two. The extra genes make it nearly impossible for scientists to do the genetic studies that have been so powerful in flies, worms, and mice: interrupting the function of a gene and watching what goes wrong when it is missing.

Now a frog from the damp floor of the West African rainforest, called *Xenopus (Silurana) tropi-*



It's easy when they're green. *Xenopus tropicalis* frogs expressing green fluorescent protein in their eyes (top) and nervous system (bottom) allow researchers to watch the organs develop in live embryos.

calis, may provide the best of both worlds to developmental biologists, who crowded into a recent symposium* here to learn about it. The species is the only close relative of *Xenopus* that has a diploid genome, with just two copies of each gene, like people and most other vertebrates. It is smaller and easier to house than *X. laevis* and also becomes sexually mature in 4 or 5 months instead of 1 to 2 years, so scientists can quickly breed transgenic colonies.

Yet the species are close enough that even minor steps in development are the same,

* "Moving into *Xenopus tropicalis*," University of Virginia, 12 June.

and transcription promoters and other genes cloned from *X. laevis* seem to work just fine in *X. tropicalis*. The two species will be "two parts of the same system," predicts cell biologist Marc Kirschner of Harvard Medical School in Boston. "All of this wonderful work and technology in *laevis* has been directly applicable to *tropicalis*," he says.

Kirschner was the first to import *X. tropicalis* to the United States. But most of the work on the new species has been in the laboratories of the symposium organizers: developmental biologist Enrique Amaya of the Wellcome/CRC Institute in Cambridge, U.K., and Robert Grainger of the University of Virginia in Charlottesville.

Already, these labs are toying with the genetics of their new model. At the meeting, developmental biologist Lyle Zimmerman, a post-doctoral fellow in Grainger's lab, described some of the first transgenic *X. tropicalis*. A few years ago, Amaya and Kristen Kroll, now of Harvard Medical School, developed a technique for extracting nuclei from *Xenopus* sperm, treating the DNA so that it efficiently incorporates new genes, and then injecting the transgenic nuclei into eggs. A transgenic frog, with the new genes in all of its cells, then de-

velops. Zimmerman and his colleagues have now used the technique to create frogs that express green fluorescent protein (gfp) in cells destined to become eye, heart, or the nervous system, allowing the scientists to observe the growing organs in live embryos. Although the gfp doesn't disrupt normal gene function, scientists can design DNA inserts that do interrupt key genes, then breed the frogs to produce offspring in which both gene copies are faulty.

Such mutant frogs should prove a powerful tool for developmental biology. The ability to watch gene regulation without killing the embryo "is really unprecedented in a vertebrate," says molecular biologist Barry Knox of the State University of New York, Syracuse. In mice, scientists can do even more sophisticated knock-out experiments, but they cannot observe the embryo as it grows inside its mother. And zebrafish, praised for their see-through embryos, are not as suitable for tissue transplant experiments as the larger frogs.

To lay the groundwork for studying *X. tropicalis*, Grainger, Amaya, and a number of their colleagues hope to launch a major screen for mutant frogs, similar to the systematic screens done in flies and zebrafish. By causing random mutations and then watching their effects, scientists hope to tease out the genes that control various stages of development—and turn their frog into a prince of a model organism.

—GRETCHEN VOGEL

not supported by the primary data."

Responding to an unknown whistleblower's allegations of scientific misconduct by Liburdy, LBNL in January 1995 appointed a panel of four lab scientists to investigate. After reviewing raw data and interviewing Liburdy and other scientists, the panel concluded in a July 1995 report that Liburdy "deliberately created 'artificial' data where no such data existed" in a figure in *FEBS Letters*. In addition, it found, he fabricated data noise for a figure in the *Annals of the New York Academy of Sciences* "in order to mislead the reader." These actions, the panel stated, "fall within the definition of scientific misconduct." When contacted by *Science*, LBNL officials declined to comment, other than to confirm that Liburdy no longer works at the lab.

Because Liburdy had been awarded more than \$3.3 million in federal grants for his EMF research, ORI launched a formal review of LBNL's report in fall 1997. ORI approved a request by Liburdy for an interview with ORI staff and two outside experts, which took place in March 1998. At the meeting, Liburdy produced original data he had not shared with LBNL investigators, according to the ORI report. But the data failed to exculpate him: In its analysis, ORI accuses Liburdy of having lied to LBNL and ORI investigators, and it "concurs with [LBNL's] findings of scientific misconduct." "Some of the numbers, essentially, he made up," says John Krueger, an ORI investigator involved in the case.

In a May 1999 agreement signed by Liburdy and ORI acting director Chris Pascal, Liburdy agreed to retract the tainted figures in the two papers and not to receive federal funds for 3 years. He "neither admits nor denies ORI's findings of scientific misconduct," the document states. Liburdy did not respond to requests for an interview.

The misconduct findings are unlikely to shift the playing field in EMF research. Since 1992, 20 to 30 scientific papers have looked at EMF exposures and calcium signaling, without settling the issue, says Christopher Portier, associate director of the environmental toxicology program at the National Institute of Environmental Health Sciences (NIEHS). In a report to Congress released on 15 June, NIEHS director Kenneth Olden states the scientific evidence that EMF exposures "pose any health risk is weak" and that mechanistic and toxicology studies "fail to demonstrate any consistent pattern." The day before the report came out, National Institutes of Health officials had asked NIEHS to determine quickly whether any of Liburdy's research had influenced the report's conclusions, Portier says. The truth was simple, he says: "It had no impact whatsoever."

—DAN VERGANO

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