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NIH to build zebrafish lab

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The National Institutes of Health (NIH) will break ground in October for a new facility to breed and house zebrafish (*Danio rerio*) for intramural research. When completed in 2005, the $10 million, 5000-square-foot facility will house more than half a million zebrafish in some 25,000 tanks. The facility will be built as an addition to Building 6, an existing animal lab on NIH's main campus in Bethesda, Md.

Demand for zebrafish at NIH has been fast growing as word spreads that the tiny, black-striped creature makes an excellent supplement and, in some cases, alternative to lab mice for research. "We feel the need for a centralized and more expanded facility to serve the needs of the NIH community," said Paul Liu, a senior investigator with the Genetics and Molecular Biology Branch of the National Human Genome Research Institute (NHGRI).

Liu, a leukemia researcher, uses both mice and zebrafish in parallel studies. He has generated zebrafish mutants defective in myelopoiesis and screens fish embryos for the loss of expression of myeloid-specific markers.

Zebrafish have many advantagesover mice. To study embryo development, pregnant mice have to be cut open and are frequently killed. But zebrafish embryos, which are relatively large, develop outside the mother's body in Petri dishes, making them readily observable. "For the first 2 days, the embryos are transparent and you can even see the circulating blood cells," Liu said. "It's very, very neat."

Zebrafish are also prolific: each female can lay 100 to 200 eggs every 4 to 5 days. Zebrafish grow to maturity in about 3 months, allowing many generations to be produced quickly. Sequencing the zebrafish genome, which is roughly half the size of the mouse or human, began in 2001 at the Sanger Institute and should be finished by the end of 2005. While genetically more distant from humans, the vertebrate zebrafish nevertheless has comparable organs and tissues, such as heart, kidney, pancreas, bones, and cartilage. Zebrafish are also far less expensive to raise and to maintain than mice.

"The bubbling water is also pleasant to look at," noted Shawn Burgess, an investigator in NHGRI's Genome Technology Branch. He uses zebrafish to identify and functionally characterize novel developmental genes, focusing on human ear development. "I'm a classical geneticist, and zebrafish provide a great opportunity to do this on a large scale with relatively little resources."

Burgess has about 10,000 zebrafish in a 200-square-foot section of his lab, one of five such labs at NIH that exclusively use the fish in research. Maintaining that many fish is almost a full-time job. "But it's easier to care for that many fish than to care for one tenth the number of mice," Burgess said. At least eight NIH labs are using zebrafish alone or in tandem with mice, twice as many as a year ago.

The new NIH zebrafish facility is being built with funds supplied by NHGRI and the National Institute of Child Health and Human Development. Other institutes will "rent" space from the facility as intramural researchers request the fish for research.

But the zebrafish is already making its mark. In June, NIH scientists reported using transgenic zebrafish with fluorescent blood vessels to search for new genes involved in artery development. A zebrafish model of T-cell leukemia has also been reported, highlighting the potential of using the fish to find cures for cancer.

Burgess's lab is one of many around the world racing to develop a line of zebrafish with knocked-out genes. Paul Collodi, professor of animal sciences at Purdue University, this month received a $1-million, 3-year NIH grant to develop zebrafish knockouts. Collodi and his team are exploring ways to introduce specific alterations into zebrafish embryonic stem cells and keep them alive long enough to pass on the genetic traits.

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