Zebrafish genetics used in cancer research

Thousands of tiny zebrafish dart about their tanks, flashes of silver and black against the blue-green walls of water. Thousands of eyes on Dr. James Amatruda as he shifts his gaze from tank to tank, searching for subtle changes in the bodies of the zebrafish: swelling, lumps, protrusions. Every day, each tank, each fish, holds a flash of hope and promise for the future of cancer treatment.

Dr. Amatruda, a doctor on the medical staff at Children's and a pediatric cancer researcher at UT Southwestern, heads the Amatruda Lab, one of a growing number of groups worldwide who are using zebrafish as a model organism for research. Specifically, Dr. Amatruda is using a "forward genetics" approach to screen zebrafish for the genetic mutations that cause cancer.

Dr. James Amatruda in front of several of his zebrafish tanks.

Preventing or curing cancer in humans first requires an understanding of the genetic factors underlying the development of cancer. Zebrafish are susceptible to the same tumors as humans, and zebrafish that predictably develop certain cancers can be used as test subjects for observing cancer growth and testing cancer treatments.

"We use the zebrafish as biological machines and introduce random mutations into their genes," Dr. Amatruda said. "We then watch the fish and let the biology tell us which genes to focus on. When we find fish that develop cancer, we go back and start looking at which genes were altered to see how different cancers arise from alterations to the genetic blueprint."

Zebrafish, mice and humans have similar genetic complexity, with about 35,000 genes each. The genomes of other common model organisms, like yeast, worms and fruitflies, are significantly less complex.

"Each of our experiments requires that we view approximately 50,000 individual organisms," Dr. Amatruda said. "Zebrafish are small, easy to care for and reproduce very quickly."

Zebrafish embryos also are large, transparent and are developed outside the bodies of the fish where the embryos are easy to monitor and manipulate. Adult zebrafish are semi-transparent, making it easy to observe tumors as they grow. The Amatruda Lab has produced a variety of interesting mutations, among them a strain of zebrafish that consistently develop testicular cancer, the most common tumor in people ages 15 to 40.

"We are able to watch each embryo from the time it is a single cell to when it fully expresses cancer," he said. "We want to very directly see the earliest stages of cancer, because if we know what the earliest phases look like, we might be able to detect it earlier in humans."

Pediatric cancers — like leukemia, brain tumors and bone tumors — usually have only one or two mutated genes, as opposed to many adult cancers — lung, breast, prostate and colon cancers — whose cells can easily have a dozen different genetic mutations. The relative simplicity of pediatric cancers makes it much more realistic to develop reproducible models in zebrafish than for adult tumors. n