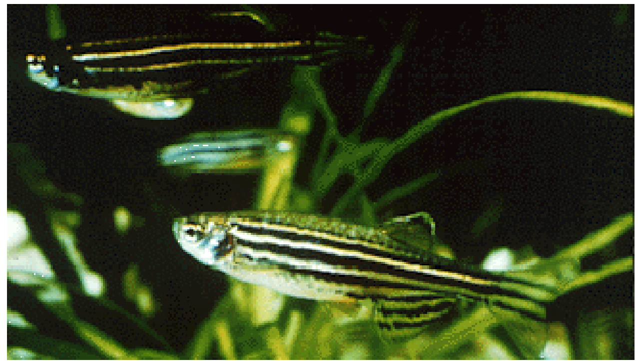
Why are zebrafish ideal models for development and disease research?

The new lab rat – almost every disease and condition known to mankind is being studied on zebrafish.

Zebrafish (*Danio rerio*) are one-inch-long freshwater animals that originate in south and southeast Asia.



- **Zebrafish are vertebrates. Like humans, they have a backbone. This means that they are more closely related to humans than commonly used invertebrate models such as insects and worms (*Drosophilia* - fruit flies and *Caenorhabditis elegans* - nematodes) which do not have backbones. Because zebrafish are more closely related to humans, they are more likely to be similar to them in many biological traits than a more distantly related organism. These biological traits would include genes, developmental processes, anatomy, physiology, and behaviors. This is an advantage that invertebrate lab animals do not share with humans. The invertebrates are more appropriately used in comparisons at the cellular or biochemical level of organization where they share many features with humans.**

- **No single model is perfect, but zebrafish have features that make them easy to maintain, manipulate, and observe in the lab. They do well in many environments, and their small size, their ability to be kept together in large numbers, and the ease with which they can be bred makes them a favored model. Breeding and getting eggs from the zebrafish is relatively easy. Their eggs are externally fertilized, produced regularly in large numbers, and are non-adhesive. Their embryos develop rapidly, and are clear throughout their development. Their embryos are also smaller than many vertebrate embryos and contain smaller numbers of cells. It is easier to trace the development of individual cells.**

- **Females lay large quantities of eggs. For many types of genetic analysis you need to look at many different embryos at many different stages to understand what the problem is with a given mutation. Zebrafish offer three major advantages over rodents. First, they quickly make more zebrafish. A female spawns hundreds of embryos three days after fertilization; mice take three weeks to produce just 10 pups. They are also inexpensive to maintain—about 6.5 cents a day for a tank of a few dozen fish, compared with 90 cents for five mice in a cage. Finally, because larval fish are transparent, researchers can literally watch their organs grow, which makes them especially good for studying problems with organ development.**

- **The embryos develop outside the mother's body, so you can have easy access to them. In contrast, mouse embryos develop inside the mother, and you have to kill the mother to get at them. This would have to be done at each of the stages of development you want to look at. Once you do this, of course, the embryos die as well as the mother, so you are very limited in the types of experiments you can do.**

- **Zebrafish embryos are transparent. This means you can watch development as it happens in living embryos. You can see internal organs, such as the brain, heart, blood, muscles, etc. In addition, you can monitor the behavior of single cells in live embryos and watch the cells divide and through dyes, trace where each cell's "daughters" go in making up the complete organism. It is not possible to achieve this resolution with other systems.**

- **The embryos develop quickly. They go from a single cell to something that is recognizable as a tiny fish within 24 hours. Mice take 21 days.**

- **You can physically manipulate the embryos. By this I mean you can transplant single cells or groups of cells into host embryos. This kind of experiment is performed frequently to analyze the behavior of cells at different stages, or to ask how mutant cells behave in wild type embryos. This can give us a lot of information about how certain gene products act. In addition, fertilization of the egg can be manipulated so that the embryo contains only it's mother's genes. This is done by exposing the sperm to ultraviolet light which destroys the genes it contains from the male. This allows scientists to study recessive mutations since the characteristics and defects are inherited from only one parent.**

- **There is a large community of researchers willing to share their knowledge of the more specific areas of zebrafish research. Since scientists learned to selectively mutate zebrafish DNA in 1988—giving them the ability to turn the species into models of human diseases—the number of biomedical zebra-fish papers has skyrocketed, from 26 to 2,100 last year.**

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