AQUATIC ZEBRAFISH CORE

Zebrafish Information

Why would you want to model a disease in a fish? Read about the remarkable fast development of zebrafish (it only takes 5 days), the ability to image whole organs in vivo, drug screens, behavioral analysis, and the ease with which we can create knockouts and transgenic lines. These qualities make it straightforward to analyze disease phenotypes.

Zebrafish Development

Watching the external zebrafish development is fascinating, since the whole embryo is clear. You can watch the development form the first cell and see the formation of all organs under the microscope. It only takes little patience; fish develop from a single cell to an embryo with all organ precursors in 24 hours. https://youtu.be/ahJjLzyioWM

Following the very early steps of development allows us to study developmental disease models.

Zebrafish Imaging

Imaging is an essential part of zebrafish research. The larvae are clear and all organs are visible without preparation. The size of 5-day-old larvae is ideal for microscopy; it is thin enough to focus through a whole larvae, and organs are small enough so an entire organ can be imaged with a confocal microscope and a 20x lens.

Zebrafish researchers have created fluorescent lines labeling nearly all organs and specific tissues within organs. Time-lapse analysis is another hallmark of zebrafish research, as fish can be followed under a microscope for hours or days, allowing researchers to observe organ development, nerve growth, interaction of tissues during tumor formation, or whole animal development in mutants.

Genetic Manipulation

Genetic manipulation is straightforward in fish. Most agents can be injected in the first forming cell with a fine glass needle and then passed along to the dividing cells. CRISPR/Cas9 knockouts are efficient and we can create a direct, complete knockout of a locus in the injected generation for most genes. Transgenic expression and integration is also very efficient due to special tools.

Most zebrafish researchers use the gateway cloning system that relies on 3 fragments (e.g. promoter, gene, fluorescent tag) that is cloned in a transgenesis vector; the fragments are interchangeable and a large toolbox of different promoters, genes, and labels is available. Most of the GFP and the transgenic expression constructs described here were made with this system.

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The Aquatic Zebrafish Core has developed an efficient protocol for CRISPR/Cas9 knockouts. 75% of gRNA the core designs cause a complete bi-allelic knockout.

Drug screening

The fast, efficient creation of gene knockouts and transgenes makes the zebrafish an excellent disease model to screen for drugs, the results of which can then be translated into the clinic. Fish can be grown in small groups in 6-96 well plates. Drugs can be added to the water and most are taken up through the skin, intestine, or the thin gill epithelium. Due to the clarity and size of larvae drug rescue is easily detectable.

Behavioral analysis

Zebrafish have a set of well-described and defined behavioral patterns. The Core can monitor activity (speed, velocity, frequency) and response to startle stimuli.