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Article: A zebrafish phenotypic assay for assessing drug-induced hepatotoxicity

Zebrafish as an alternative for confirming drug induced hepatotoxicity, toxicity of the liver, yields promising results. The authors of the article, “A Zebrafish Phenotypic Assay for Assessing Drug-induced Hepatotoxicity,” identified four physical symptoms to diagnose cases of hepatotoxicity in zebrafish. The scientists separated the zebrafish embryos into different treatment groups. The groups included six drugs known to be toxic to humans, two drugs that are not toxic to humans, and one control. After treatment, each of the zebrafish embryos were imaged under a microscope. The first indicator of hepatotoxicity was a liver dark gray or brown in color, contrasting the typically clear liver of healthy zebrafish embryos. From these images the scientists were able to conclude the density of the zebrafish liver, the size of that liver, and the size of the yolk sac. The percent degeneration and reduction of the liver, as well as the percent of the yolk sac that was unabsorbed, was determined by comparing the measurements from the images to the measurements of the control images. A high percentage of degeneration and size reduction indicate the death of the liver cells. A larger yolk sac area after treatment implies that the liver has ceased to function because the yolk sac is metabolized by the liver. To confirm their analysis, the scientist conducted histopathology tests to determine if the zebrafish were actually suffering from toxicity of the liver. The proposed method of diagnosing hepatotoxicity in zebrafish embryos proved to be accurate for all eight drugs.

Liver toxicity is one of the main reason for a drug to be disqualified during both early and late stages of a drug’s development. *In vitro* tests are not sufficiently sensitive, and *in vivo* tests in rodents or monkeys are costly, laborious, and time consuming. Preliminary testing in zebrafish
offers a low cost method of eliminating potentially harmful medicines early on in their
development before a company invests in extensive research. Zebrafish are optimal candidates
for testing because their methods of detoxification are similar to humans, their livers remain
clear for several days post fertilization, and their liver is functional at only three days post
fertilization. Zebrafish offer a viable option for early testing of drugs for hepatotoxic effects.

References
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