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Selecting Optimal Animal Models to Investigate Environmental Toxicology

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Within the broad area of toxicology, investigation of environmental toxicology continues to bear great importance to both human and animal populations. The focus of environmental toxicology is assessment of the effects of agents (including physical, chemical and biological agents) on the plants and wild life around us. [http://www.usgs.gov/ecosystems/genetics_genomics/\\afs\usgs.gov\www\www\htdocs\ecosystems\genetics_genomics\environmental_toxicology.html]We then use this information to assess the health of our environment and ecosystems, and determine how natural catastrophes such as hurricanes and earthquakes as well as industrial production around the world affect ourenvironment. There is ever greater need to assess how acute events as well as chronic situations contributed to environmental pollution and how we can carry out and document remediation efforts.

In the past, toxicologists relied on exposures of chemicals and biological agents to rodents, primarily rats, to determine LD50 (lethal dose 50%), dose response curves and to a lesser extent, reproductive and embryonic toxicities. This research provided a great deal of information, but that information is somewhat limited in its applicability to non-mammalian species as well as the ability of these data to address questions concerning the effects of contamination of aquatic ecosystems. To this end, more recent research has emphasized use of various fish species to carry out investigations of environmental toxicology.

Three-fourths of the earth's surface covered by water and there are 31,000 species of fishes compared to 5,500 species of mammals. [http://www.currentresults.com/Environment-Facts/Plants-Animals/number-species.php] given these facts, it appears logical to look to fish species to assess our aquatic environmental health. Saltwater fish are harder to maintain in laboratory situations, so it is no surprise that less experimental research is conducted using saltwater fish compared to freshwater fish. However, Atlantic salmon (*Salmo salar*) is one marine fish that has been studied intensively with respect to environmental toxicology [1-3]. Common wild or native freshwater fish species that are used in toxicology research include rainbow trout (*Oncorhynchus mykiss*), fathead minnows (*Pimephales promelas*) and blue gill sunfish (*Lepomis macrochirus*) [4] and to a lesser extent, largemouth bass [5]. It has been noted that there can be considerable difference in how individual species of fish respond to various toxicants, which may be due to differences in metabolism and / or excretion. Thus, due to observed differences in species-specific sensitivity, it sometimes can be difficult to make broad conclusions from data obtained from some of these wild fish species.

On the other hand, two freshwater fish that have become widely used for toxicology research in the laboratory are the Japanese medaka (*Oryzias latipes*) and zebrafish (*Danio rerio*). Japanese medaka, alsoknown as Japanese rice fish and Japanese killifish, are native to rice fields in Southeast Asia, hence the name. It is interesting that these fish, which belong to the family of Cyprinodontidae, are amphidromous, meaning that they tolerate both fresh water and saltwater during different parts of their life cycle [6]. Japanese medaka and zebrafish have many important characteristics in common that make them excellent vertebrate models for laboratory research, but zebrafish are currently the more widely used model.

Zebrafish are members of the Cyprinidae family, which has the largest number of species of any extant vertebrate family [7,8]. Zebrafish have been studied for many years as a model organism for developmental biology and for developmental genetics. More recently they are beginning to the used as a vertebrate system to study mechanisms of toxicity. Not only can the adults be used for toxicity research but the zebrafish embryo also isan excellent vertebrate model that can be used to assess developmental toxicity. The many advantages to using zebrafish embryos in research include: external fertilization; a transparent "shell" or chorion over the developing zebrafish embryos; embryos that are transparent themselves early in development; and rapid *ex utero* development. In addition, much is known about normal zebrafish development and zebrafish genetics also are well documented [9-12]. Also adding to the importance of this model for toxicology research is the ability to directly deliver chemicals to zebrafish embryos as they develop [9,13,14]. Zebrafish also can be used as a model for behavioral studies, where they can model some aspects of more complex behavior such as learning and memory and anxiety [15]. Zebrafish have even been developed to model mechanisms associated with neurological disorders that may have important environmental components in their etiology, such as autism [16] and Parkinson's disease [17]. Thus the vast amount of information that already exists for zebrafish concerning their genetics, developmental biology and behavior make them an excellent research animal model. In addition, the efficiency they bring to the research arena due to their ability to be used in high-throughput experiments and the ease with which they can be genetically manipulated make them a powerful vertebrate model system to assess mechanisms underlying many aspects of environmental toxicology [18].

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