# nabr National Association *for* Biomedical Research

# Aquatic Models

## Introduction

While mice, rats, and other small mammals are generally thought of as the typical model system used by researchers in biomedical studies, aquatic models including both freshwater and marine organism have long proved to be invaluable in the study of basic biological processes. Through the understanding gained in aquatic models of mechanisms of biology scientists have elucidated their role in human health and disease. The value of aquatic models for disease research is rooted in the fact that across species numerous general cellular properties are common in all organisms. In addition to shared biological properties, many species exhibit unique features or disease syndromes that make them particularly suitable as animal models of specific disease processes. Research on aquatic animals occupies a broad variety of disciplines such as immunology, physiology, microbiology, molecular biology, pathology, toxicology, microbiology, embryology, and genetics(*1*).

## Daphnia

Daphnia (water flea) are microcrustaceans that have served as a model organism in biological research for over a century. Phenotypically diverse, Daphnia have been vital in both ecological and toxicological studies due to their extensive distribution, minute size, and essentially effortless growth conditions.  Daphnia have been used as a model in functional genomic based studies (*2*) such as metabolic profiling and transciptomics, which is a branch of chemistry used to study messenger RNA molecules. Increasingly, Daphnia have served as an indicator species that has added to our understanding of genomic responses to environmental stressors that are important to both environmental and human health and well-being.

The versatility of Daphnia as a biological model is so great that they have even been used as a model in studies on antioxidants to determine whether or not they can slow down aging. A newly synthesized antioxidant, called SkQ, was observed to decelerate the three types of accelerated aging (progeria) and also of normal aging (*3*) in Daphnia. This data translated to studies in mammals where it was observed that in, SkQ inhibits the development of diseases such as osteoporosis, cataract, and retinopathy.

## Horseshoe Crab

The horseshoe crab, *Limulus pluphemus*, has played an essential role in biomedical research due to its large size, durable body, easily accessible retinal neurons, and compact visual system. Not only does their blood contain special cells that scientists use to detect bacteriotoxins in our medicines, but their eyes also contain a neural network that has provided much insight about physiological processes operating in the human visual system, such as light adaptation (*4*). Due to their unique visual system, horseshoe crabs are studied to determine how visual messages are communicated from eyes to the brain and as well as how circadian-clock messages are transmitted.

In light of the fact that they have the best-characterized immune-system of any invertebrate, Horseshoe crabs also play an important role in immune system studies  (*5*). Recent studies show that a biosensor that detects bacterial endotoxin (a toxin that is an essential part of the cell wall of certain bacteria and is only released when the cell dies) was created using a protein derived from the horseshoe crab (*6*)(*5*).

## Hydra

Hydra, a freshwater cnidarian, was first described in 1700s and has been used in research for over 300 years!  Hydra has been used as a model in numerous studies, including those of axial patterning, stem cell biology, and regeneration (*7*). of Hydra extends to it ability to exhibit an almost limitless generation potential and immortality. Scientists have proposed that the basic properties of stem cells in animals are connected to the Hydra's archaic method of reproduction. Studies of stem cells in Hydra continue to be important and add to our understanding of the basic mechanisms of stem cell biology.

The Hydra is a simple organism, inexpensive, and easy to manipulate in the lab, which makes it an attractive model to investigate the mechanisms of basic biological processes that are linked to human disease such as Huntington's disease and Alzheimer's. Researchers have discovered that Hydra have comparable genes to the human genes that mutate and cause particular neurodegenerative disorders including the two mentioned above.

## Octopus

Octopi are cephalopods, and are recognized to be some of the most intelligent invertebrates due to their relatively large brain size and learning and memory abilities. However, since they are an invertebrate, the octopus brain has a smaller number of nerve cells and is anatomically less complex which lends it to serving as a good model of neurological function. Researchers have determined that the vertical lobe (VL) of the Octopus is an essential brain location for learning and memory. Studies suggest that mainly in the mammalian hippocampus a convergent evolutionary process has resulted in similar neural organization as that seen in octopi  (*8*).

The octopus has also served as an important model for understanding biological systems and hormones. Recently researchers isolated a homologue of the GnRH (gonadotropin-releasing hormone) that plays a major role in regulating reproduction in humans. The homologue found in the octopus, called oct-GnRH, was isolated from *Octopus vulgaris* and was shown to behave similarly to the invertebrate homologue, thus showing that both the structure and functions of the GnRH family are evolutionarily conserved between octopuses and chordates. (*9*).

## Planarians

Planarians are free living flatworms that are used as a model for the study of regeneration, development, and effects of drug interactions. Because planarians can regenerate their entire body, they are an ideal model for analyzing events such as morphogenesis, restoration of pattern and polarity, control of tissue proportions and tissue homeostasis (*10*). In addition, adult planarians contain pluripotent stem cells that can give rise to differentiated cell types and germ cells. These characteristics allow for planarians to be used in study of maintenance and differentiation of cell populations in intact and regenerating animals and adds to our understanding of stem cell function (*10*).

The planarian model's versatility has allowed for it to serve as model in studies on the inhibitory effects of anti-Parkinson's drugs and the effects of polydrug use with cocaine and cannabis. The result of the antiparkinson's study suggested the effects induced by certain mitochondrial complexes associated with Parkinson's disease can be inhibited by the drugs that were tested in the planarian model (*11*) The planarian model has also made it feasible for researchers to determine the biological interactions between drugs used in polydrug abuse (*12*). As a result, for the first time, biomedical researchers have been able to study and quantify the withdrawal effects of cocaine and a cannabinoid receptor called agonist WIN 55212-2, a powerful painkilling for neuropathic pain. (*12*).

## Sea Snails

Sea snails, especially those from the genus Conus, are vital to the advancement of potential therapeutics. Cone shells contain toxic venom called conotoxin that is made up of at least 50 different peptides. These peptides "selectively inhibit the function of the ion channels" that are involved in nerve signaling in animals (*13*). As researchers continue to study the properties of conopeptides, the development of new therapeutics for various neurological conditions is largely becoming an actuality.

Today, there are numerous conopeptides used in clinical trials, and some of them have even received approval to be used as analgesics for neuropathic pain in humans (*14*). These compounds are unique in their ability to target pain receptors, and certain families of conopeptides, like the alpha-conotoxins, exclusively target particular isoforms of a receptor. Due to their highly selective action, alpha-conotoxins have also been utilized to regulate neurotransmitter and the pathophisiology of Parkinson's disease (*15*).

## Sea Urchin

Sea urchins are model organisms in developmental biology research, and sea urchin embryos have even been used by researchers as a model for mammalian developmental toxicity (*16*). This is possible due to the fact that the same neurotransmitters used in embryonic development are conserved between sea urchins and the mammalian brain. The results of these embryonic studies suggest that during development, the sea urchin contains a high-affinity choline transporter that is similar to the one found in the brains of mammals, and which is important in the development of proper neurological function. Due to its evolutionary similarities, the sea urchin model has proven to be useful in screening developmental neurotoxicants in mammals.

In addition, "85% of cases of autosomal dominant polycystic kidney disease, the most frequent human monogenic disease (an inherited disease controlled by a single pair of genes), are caused by mutations in the human polycystic kidney disease-1 (hPKD1) gene" (*17*). Sea urchins have ten hPKD1 proteins, whereas humans have five. The study of the sea urchin proteins can allow researchers to determine their exact function and better translate this understanding to human polycystic kidney disease.

Utilizing information gained in the lab, s, sea urchins also serve as an indicator species and biological tool to assess the ecology of coastal water quality. The sea-urchin embryo test (SET) is cited to be frequently used as a rapid, sensitive, and cost-effective biological tool for marine monitoring worldwide (*18*).

## Squid

In squid, the giant axons, eye, blood, ink, olfactory system, and oculomotor/equilibrium system each serve as an important model in biomedical research. Due to the important role that squid play in neurological research,their sustainable has even been taken into account and today providing squids--especially their giant axons--for biomedical research has now been achieved in 10 mariculture trials (*19*).

Squid have played in important role as a model organism in the study of neurodegenerative disorders that can cause dementia and memory loss. In neurodegenerative disorders, such as hereditary spastic paraplegia (HSP), neuronal loss occurs due to build-up of proteins in the form of plaque (*20*). These accumulations of plaque occur due a deregulation of a normal protein. Despite the decades of research, studying mammalian systems is hard because their neurons are too small to study in separate parts. However, studies on the squid's giant fiber system have allowed researchers to directly observe the factors that are involved in neuron function and the regulation of proteins involved in neurodegenerative disorders.

Through the use of internally perfused squid giant axons, pioneering studies of local anesthesia led to the conclusion that these anesthetics block the sodium channel from inside the nerve membrane in the cationic form (*21*). Through biomedical research using squid as a model of neurological function researchers can continue to build our understanding of neurotoxicology and neuropharmacology thereby elucidating the mechanism of disease and developing future therapies.

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