INTERNATIONAL RESEARCH JOURNAL OF PHARMACY ISSN 2230 – 8407
Available online www.irjponline.com Review Article

MODEL ORGANISMS USED IN MOLECULAR BIOLOGY OR MEDICAL RESEARCH

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Article Received on: 02/09/11 Revised on: 23/10/11 Approved for publication: 11/11/11

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ABSTRACT
A model organism is a non-human species that is studied to understand specific biological phenomena with the expectation that investigations made in the organism model will provide insight into the workings of other organisms. The model organisms are widely used to explore potential causes and treatments for human as well as animal diseases when experiments on animals or humans would be unfeasible or considered less ethical. Studying model organisms may be informative, but care must be taken when generalizing from one organism to another. Often, model organisms are chosen on the basis that they are amenable to experimental manipulation. When researchers look for an organism to use in their studies, they look for several traits. Among these are size, generation time, accessibility, manipulation, genetics, conservation of mechanisms and potential economic benefit. As comparative molecular biology has become more common, some researchers have sought model organisms from a wider assortment of lineages on the tree of life. There are many model organisms, such as viruses (e.g., Phage lambda virus, Tobacco mosaic virus, etc.), bacteria (e.g., *Bacillus subtilis, Escherichia coli, Pseudomonas fluorescens, Vibrio fischeri*, etc.), algae (e.g., *Chlamydomonas reinhardtii, Emiliania huxleyi,* etc.), molds (e.g., *Aspergillus nidulans*, *Neurospora crassa,* etc.), yeasts (e.g., *Saccharomyces cerevisiae, Ustilago maydis,* etc.), higher plants (e.g., *Arabidopsis thaliana, Lemna gibba, Lotus japonicus, Nicotiana tabaccum, Oryza sativa*, *Physcomitrella patens, Zea mays,* etc.) and animals (e.g., *Caenorhabditis elegans,* guinea pig, hamster, mouse, rat, cat, chicken, dog, frog, *Hydra, Drosophila melanogaster fruit fly,* fish, etc.).
KEYWORDS: Biomedical researches, experiments, model organisms (animals and plants).

INTRODUCTION

Models are those organisms with a wealth of biological data that make them attractive to study as examples for other species and/or natural phenomena that are more difficult to study directly. Continuous research on these organisms focus on a wide variety of experimental techniques and goals from many different levels of biology- from ecology, behaviour and biomechanics, down to the tiny functional scale of individual tissues, organelles and proteins. Inquiries about the DNA of organisms are classed as genetic models (with short generation times, such as the fruit fly and nematode worm), experimental models and genomic models, investigating pivotal position in the evolution. Historically, model organisms include a handful of species with extensive genomic research data. Hence, a model organism is a non-human species that is studied to understand particular biological phenomena with the expectation that discoveries made in the organism model will provide insight into the workings of other organisms[1]. Model organisms are widely used to explore potential causes and treatments for human disease when human experimentation would be unfeasible or considered less ethical. This strategy is made possible by the common descent of all living organisms, and the conservation of metabolic and developmental pathways and genetic material over the course of evolution[2].

Studying model organisms can be informative, but care must be taken when generalizing from one organism to another. Often, model organisms (animals and plants) are chosen on the basis that they are amenable to experimental manipulation. This usually will include characteristics such as short life-cycle, techniques for genetic manipulation (inbred strains, stem cell lines, and methods of transformation) and non-specialist living requirements. Sometimes, the genome arrangement facilitates the sequencing of the model organism's genome, such as by being very compact or having a low proportion of junk DNA (e.g., yeast, *Arabidopsis*, or puffer fish). When researchers look for an organism to use in their studies in Molecular Biology or biomedical researches, they look for several traits. Among these are size, generation time, accessibility, manipulation, genetics, conservation of mechanisms and potential economic benefit. As Comparative Molecular Biology has become more common, some researchers have sought model organisms from a wider assortment of lineages on the tree of life.

There are many model organisms. One of the first model systems for Molecular Biology was the bacterium *Escherichia coli* (a Gram negative prokaryotic model organism), which is a common constituent of the human digestive system. Several of the bacterial viruses (bacteriophage) that infect *E. coli* have also been very useful for the study of gene structure and gene regulation (e.g., phages Lambda and T4). However, bacteriophages are not organisms because they lack metabolism and depend on functions of the host cells for propagation. In eukaryotes, several yeasts, particularly *Saccharomyces cerevisiae* (baker's or budding yeast), have been widely used in Genetics and Cell Biology, largely because they are quick and easy to grow. The cell cycle in simple yeast is very similar to the cell cycle in humans, and is regulated by homologous proteins. The fruit fly, e.g., *Drosophila melanogaster* (one of the most famous subjects for experiments) is studied again, because it is easy to grow for an animal, and has various visible congenital traits and has a polytene (giant) chromosome in its salivary glands that can be examined under a light microscope. A roundworm (nematode), *Caenorhabditis elegans* is studied because it has very defined development patterns involving fixed numbers of cells, and it can be rapidly assayed for abnormalities. Considering the above facts in view, the present article explore out the different model organisms (plants or animals) and their usefulness in Molecular Biology or biomedical researches/experiments.

IMPORTANT MODEL ORGANISMS

Viruses

Viruses include: Phage Lambda, Tobacco mosaic virus (TMV) and Phi X 174. The genome of Phi X 174 was the first ever to be sequenced. The genome is a circle of 11 genes, 5386 base pairs in length.

Prokaryotes

Prokaryotes include: *E. coli* (most widely used organism in Molecular Genetics), *Bacillus subtilis* (an endospore forming Gram positive bacterium), *Caulobacter crescentus* (a bacterium that divides into two distinct cells used to study cellular differentiation), *Mycoplasma genitalium* (a minimal organism), *Vibrio fischeri* (quorum sensing, bioluminescence and animal-bacterial symbiosis with Hawaiian bobtail squid), *Synechocystis* (a photosynthetic *Cyanobacterium* widely used in photosynthesis research) and

Pseudomonas fluorescens (a soil bacterium that readily diversifies into different strains in the laboratory).

Eukaryotes

Eukaryotes include: protists, fungi, higher plants and animals (invertebrates and vertebrates).

Some of the protists are *Chlamydomonas reinhardtii, Dictyostelium discoideum, Emiliania huxleyi, Tetrahymena thermophila* and *Thalassiosira pseudonana. C. reinhardtii* is a unicellular green alga used to study photosynthesis, flagella and motility, regulation of metabolism, cell-cell recognition and adhesion, response to nutrient deprivation, and many others. *C. reinhardtii* has a well-studied genetics with many known and mapped mutants and expressed sequence tags, and there are advanced methods for genetic transformation and selection of genes. Sequencing of the *C. reinhardtii* genome was reported in October, 2007. *Chlamydomonas* is easy to grow on an inexpensive defined medium. *D. discoideum* is used in Molecular Biology and Genetics (its genome has been sequenced), and is studied as an example of cell communication, differentiation and programmed cell death. *E. huxleyi* is a unicellular marine coccolithophore alga, extensively studied as a model phytoplankton species. *Te. thermophila* is a free living freshwater ciliate protozoan. *Th. pseudonana* is a unicellular marine diatom alga, extensively studied as a model marine diatom since its genome was published in 2004.

Important fungi are *Ashbya gossypii* (a cotton pathogen, subject of genetic studies like polarity and cell cycle), *Aspergillus nidulans* (a mold subject of genetic studies), *Coprinus cinereus*, mushroom (genetic studies of mushroom development and genetic studies of meiosis)[3], *Neurospora crassa* (an orange bread mold for genetic studies of meiosis, metabolic regulation and circadian rhythm)[4], *S. cerevisiae* (baker's yeast or budding yeast used in brewing and baking), *Schizophyllum commune* (model for mushroom formation)[5], *Schizosaccharomyces pombe* (a fission yeast used to study the cell cycle, cell polarity, RNAi, centromere structure and function, and transcription) and *Ustilago maydis* (a dimorphic yeast and plant pathogen of maize used to study the dimorphism, plant pathogen and transcription).

There are many plants (higher plants) which are selected as model organisms. *Arabidopsis thaliana* is currently the most popular model plant. This herbaceous dicot is a brassica, a member of the mustard family. Its small stature and short generation time facilitates rapid genetic studies, and many phenotypic and biochemical mutants have been mapped. *Arabidopsis* was the first plant to have its genome sequenced. So, this plant is used for the experiments of Plant Physiology, Developmental Biology, Molecular Genetics, Population Genetics, Cytology and Molecular Biology. *Selaginella moellendorffii* is a remnant of an ancient lineage of vascular plants and key to understanding the evolution of land plants. It has a small genome size and its sequence was released by the Joint Genome Institute in early 2008 for Evolutionary Biology and Molecular Biology. *Brachypodium distachyon* is an emerging experimental model grass that has many attributes that make it an excellent model for temperate cereals in Agronomy, Molecular Biology and Genetics. *Lotus japonicus* is a model legume used to study the symbiosis responsible for nitrogen fixation in Agronomy and Molecular Biology. *Lemna gibba* is a rapidly-growing aquatic monocot, one of the smallest flowering plants. *Lemna* growth assays are used to evaluate the toxicity of chemicals to plants in ecotoxicology. Because it can be grown in pure culture, microbial action can be excluded. *Lemna* is being used as a recombinant expression system for economical production of complex biopharmaceuticals. It is also used in education to demonstrate population growth curves. *Zea mays* (Maize) is a cereal grain. It is a diploid monocot with 10 large chromosome pairs, easily studied with the microscope. Its genetic features, including many known and mapped phenotypic mutants, and a large number of progeny per cross (typically 100-200) facilitated the discovery of transposons (jumping genes). Many DNA markers have been mapped and the genome has been sequenced in the field of Genetics, Molecular Biology and Agronomy. *Medicago truncatula* is a model legume, closely related to the common alfalfa. Its rather small genome is currently being sequenced. It is used to study the symbiosis responsible for nitrogen fixation in Agronomy and Molecular Biology subjects. *Mimulus* (Phrymaceae family) is a model organism used in evolutionary and functional genomes studies. Tobacco BY-2 cell is suspension cell line from tobacco *(Nicotiana tabaccum)*. It is useful for Cytology, Plant Physiology and Biotechnology studies. Its genome will not be sequenced (at least in near future). *Oryza sativa* (Rice) is used as a model for cereal Biology or Agronomy and Molecular Biology. It has one of the smallest genomes of any cereal species, and sequencing of its genome is finished. *Physcomitrella patens* is a moss, increasingly used for studies on development and molecular evolution of plants. It is so far the only non-vascular plant (and so the only 'primitive' plant) with its genome completely sequenced[6]. Moreover, it is currently the only land plant with efficient gene targeting that enables gene knockout[7]. The resulting knockout mosses are stored and distributed by the International Moss Stock Centre for experiments/researches of Plant Physiology, Evolutionary Biology, Molecular Genetics and Molecular Biology. *Populus* is a genus used as a model in forest Genetics and woody plant studies. It has a small genome size, grows very rapidly, and is easily transformed. The genome sequence of *P. trichocarpa* sequence is available.

Many invertebrate animals are also being used as model organisms in Molecular Biology or biomedical researches/experiments. *Amphimedon queenslandica*, a demosponge from the phylum Porifera used as a model for Evolutionary Developmental Biology and Comparative Genomics[8]. *Arbacia punctulata,* the purple-spined sea urchin, is used for classical subject of embryological studies. *Aplysia* is a sea slug, whose ink release response serves as a model in Neurobiology and the growth cones serve as a model of cytoskeletal rearrangements. *Branchiostoma floridae,* a species commonly known as amphioxus or lancelet from the subphylum Cephalochordata of the phylum Chordata, is used as a model for understanding the evolution of nonchordate deuterostomes, invertebrate chordates, and vertebrates[9]. *C. elegans,* a nematode, is an excellent model for understanding the genetic control of development and Physiology. It was the first multicellular organism whose genome was completely sequenced[10]. *Ciona intestinalis* is a sea squirt. *Drosophila,* usually the species *D. melanogaster* is a kind of fruit fly, famous as the subject of Genetics experiments by Thomas Hunt Morgan and others. It is easily raised in lab, has rapid generations and its mutations are easily induced, having many observable mutations. Recently, *Drosophila* has been used for neuropharmacological research[11]. So, *Drosophila* is useful in Molecular Genetics, Population Genetics and Developmental Biology. *Euprymna scolopes,* the Hawaiian bobtail squid, is a model for animal-bacterial symbiosis, bioluminescent vibrios. *Hydra* genus, a Cnidarian, is the model organism to understand the processes of regeneration and morphogenesis, as well as the evolution of bilaterian body plans[12]. *Loligo pealei,* a squid, is used to study the nerve function because of its giant axon (nearly 1 mm diameter, roughly a thousand times larger than typical mammalian axons). *Macrostomum lignano,* a free-living, marine flatworm, is a model organism for the study of stem cells, regeneration, ageing, gene function and the evolution of sex. It is easily raised in lab, having short generation time, undetermined growth and complex behaviour[13]. *Mnemiopsis leidyi,* from the phylum Ctenophora (comb jelly) is used as a model for Evolutionary Developmental Biology and Comparative Genomics[14]. *Nematostella vectensis,* a sea

anemone from the phylum Cnidaria, is used as a model for Evolutionary Developmental Biology and Comparative Genomics[15]. *Oikopleura dioica,* an appendicularia is a free-swimming tunicate (or urochordate). *Oscarella carmela,* a homoscleromorph sponge (phylum Porifera), is used as a model in Evolutionary Developmental Biology[16]. *Parhyale hawaiensis,* an amphipod crustacean, is used in evolutionary developmental studies, with an extensive toolbox for genetic manipulation. *Pristionchus pacificus,* a roundworm used in Evolutionary Developmental Biology in comparative analyses with *C. elegans. Schmidtea mediterranea,* a freshwater planarian, is a model for regeneration and development of tissues such as brain and germline. Stomatogastric ganglion of various arthropod species is a model for motor pattern generation seen in all repetitive motions. *Strongylocentrotus purpuratus,* the purple sea urchin, is widely used in developmental Biology. *Symsagittifera roscoffensis,* a flatworm, is a subject of studies of bilaterian body plan development. *Tribolium castaneum,* the flour beetle- a small, easily kept darkling beetle, is used especially in Behavioural Ecology experiments. *Trichoplax adhaerens*, a very simple free-living animal from the phylum Placozoa, is used as a model in Evolutionary Developmental Biology and Comparative Genomics[17].

Similar to the invertebrate, many vertebrate animals are also used as model organisms for researches/experiments. *Cavia porcellus* (Guinea pig) has been used by Robert Koch and other early bacteriologists as a host for bacterial infections; hence a byword for "laboratory animal" even though less commonly used today. *Cricetus cricetus* (Hamster) was first used to study kala-azar (Leishmaniasis). *Mus musculus* (Mouse) is the classic model vertebrate. Its many inbred strains exist, as well as lines selected for particular traits, often in biomedical researches, e.g., body size, obesity, muscularity, etc.; so useful in Quantitative Genetics, Molecular Evolution and Genomics. *Rattus norvegicus* or *Rattus rattus* (Rat) is particularly useful as a Pharmacology and Toxicology model; also useful as a neurological model and source of primary cell cultures, owing to the larger size of organs and suborganellar structures relative to the mouse; so useful in Molecular Evolution and Genomics. *Canis lupus familiaris* (Dog) is an important respiratory and cardiovascular model, also contributed to the discovery of classical conditioning. *Lepus cuniculus* or *Oryctolagus cuniculus* (Rabbit) and *Rana tigrina* (Frog) are also used in various biological or biomedical experiments. The standard experimental hepatotoxic models have been produced in mouse[18-19], rat[19-20], rabbit[19] and dog[21]. Similarly, the cancer model has been induced experimentally in rat[22]. *Sigmodon hispidus* (Cotton rat) was formerly used in polio research. *Xenopus laevis* (African clawed frog) is used in Developmental Biology because of its large embryos and high tolerance for physical and pharmacological manipulation. *Felis sylvestris catus* or *Felis domesticus* (Cat) is used in neurophysiological research. *Macaca mulatta* or *Rhesus macaque* (Monkey or rhesus monkey) is used for studies on infectious disease and cognition. *Gallus gallus domesticus* (Chicken) is used for developmental studies, as it is an amniote and excellent for micromanipulation (e.g., tissue grafting) and over-expression of gene products. *Taeniopygia guttata* (Zebra finch or chestnut-eared finch, a bird) is used in the study of song system of songbirds and non-mammalian auditory systems.

A wide variety of experiments such as antibacterial, antiparasitic and anaesthetic drugs, besides the pharmacokinetic and pharmacodynamic researches have been done on different species of fish. Several groups of drugs, such as tetracyclines, penicillins, macrolides, quinolones, sulfonamides, immunostimulants, anticancer agents, herbal drugs and vaccines, have been successfully experimented on fish. Hence, fish is also used as an important model organism for different biological or biomedical researches. *Danio rerio* (Zebrafish, a freshwater tropical fish) has emerged as a major model organism in the Developmental Genetics, Neurophysiology or biomedical researches[23]. This fish has a nearly transparent body during early development, which provides unique visual access to the animal's internal anatomy. Zebrafish are used to study development, toxicology and toxico-pathology[24], specific gene function and roles of signaling pathways. In the 1960s to mid-1970s, the fish species used as models for carcinogenesis studies were primarily the zebrafish and the guppy (*Poecilia reticulata*). Species that have predominated in later years are rainbow trout, rivulus (*Rivulus marmoratus*), guppy, sheepshead minnow (*Cyprinodon variegatus*) and medaka (*Oryzias latipes*). The contaminations associated neoplasia, including aflatoxin-induced hepatocellular carcinoma in rainbow trout (*Onchorynchus mykiss*) fish, have also led to the study of fish as alternative models in carcinogenesis and toxicity bioassays[23]. The zebrafish models for liver cancers have been successfully established which are now increasingly used as a promising animal model for cancer research. Hence, these models will be characterized in order to understand the molecular and genetic mechanisms of liver carcinogenesis as well as for anticancer drug discovery[25]. Therefore, the zebrafish has been recognized as a suitable model for different experimental studies[23]. Teleost fish cell lines have been developed from a broad range of tissues such as ovary, fin, swim bladder, heart, spleen, liver, eye muscle, vertebrae, brain and skin. One hundred and twenty-four new fish cell lines from different fish species ranging from grouper to eel have been reported. Presently, about 283 cell lines have been established from finfish around the world[26]. *O. latipes* (Medaka, the Japanese rice fish) is an important model in Developmental Biology and has the advantage of being much sturdier than the traditional Zebrafish. *Takifugu rubripes* (Takifugu, a puffer fish) has a small genome with little junk DNA. Lamprey eels (predator family of jawless fish) have been used in spinal cord research. Other fishes which have been used in biomedical researches include: *Carassius auratus* (goldfish), *Catla catla*, *Catostomus commersoni* (teleost fish), *Channa punctatus* (spotted snakehead), *Clarias gariepinus, Labeo rohita* (freshwater fish), *Myoxocephalus scorpius* (short-horned sculpin marine fish), *Oncorhynchus mykiss* (rainbow trout), *Oreochromis mossambicus* and *O. niloticus* (tilapia fishes), and *Salmo trutta* and *S. iredius* (trouts)[23].

MODEL ORGANISMS IN SPECIFIC RESEARCH

Callosobruchus maculatus (Bruchid beetle), *Chorthippus parallelus* (Meadow grasshopper), Coelopidae (Seaweed flies), Diopsidae (Stalk-eyed flies), *Drosophila* spp. (Fruit flies), *Macrostomum lignano* (Sand flatworm), *Gryllus bimaculatus* (Field cricket) and *Scathophaga stercoraria* (Yellow dung fly) are used for research on sexual selection and sexual conflict. *Bombina bombina* and *variegate, Podisma* spp. (in the Alps) and *Caledia captiva* (in eastern Australia) are used for experiments/researches pertaining to hybrid zones; while, *Daphnia pulex* (an environmental indicator model organism) is used for research on Ecological Genomics.

CONCLUSION

Several experiments/researches of Life Sciences or biomedical areas have been performed in different plant and animal species, which are now called the "model organisms". These model organisms are widely used to explore potential causes and treatments against human and animal diseases. Therefore, the model organisms are a wealth of biological data that make them attractive to study as examples for other species and/or natural phenomena that are more difficult to study directly. There have been investigated many model organisms of viruses, bacteria, algae, molds, yeasts, higher plants and animals (including fish).

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