NON-MAMMALIAN ANIMALS AS EXPERIMENTAL MODELS FOR MODERN SCIENTIFIC RESEARCH

Pramod Kumar Gautam*

Sanjay Kumar*

Arbind Acharya*

Abstract: *Model organisms refer to the animals used for executing research for particular objectives or to understand particular biological phenomena includes metabolic, developmental, immunological, genetical, evolutionary etc. Currently, different animals of both mammalian and non-mammalian origin are being used as a model organism for modem scientific research. Though, use of mammalian animals for modem scientific research is very popular. History reveals that a number of major scientific achievement has been brought about by using non-mammalian animals such as Drosophila melanogaster, Caenorhabditis elegans etc. This review deals with the use and future prospects of use of non mammalian model organisms for modem scientific research to develop scrutinized result related to human welfare.*

Key words: *Non-mammalian animals; Model organisms; Scientific research*

*Department of zoology, Faculty of Science, Banaras Hindu University, Varanasi, U.P., India

INTRODUCTION

Several approaches can be used to study how biological systems function. Over the last century, research on a small number of organisms has played a pivotal role in advancing our understanding of numerous biological processes due to similarities in many aspects of biological consequences in most or all organisms, but it is frequently much easier to study a particular aspect in one organism than in others. These much studied organisms are commonly referred to as model organisms. Each has one or more characteristics that make it suitable for laboratory study. A modem organism must also be utilitarian. To select a good model organism, several characteristics such as rapid development with short life cycles, small adult size, ready availability and reasonable cost of maintenance is essential parameters. Non-mammalian organism includes all these qualities to use as a model organism for research work. This review explains about non-mammalian model organism being used modem scientific research.

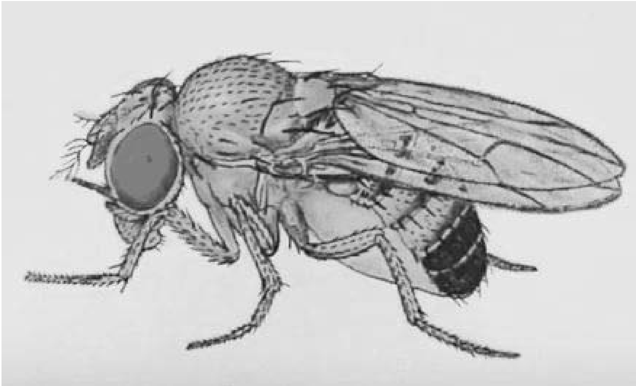
NEMATODES: CAENORHABDITIS ELEGANS

The nematode Caenorhabditis elegans (C. elegans) was first introduced as a model organism by Dr. Sydney Brenner at the Laboratory of Molecular Biology, Medicinal research Council at Cambridge about 40 year ago. It is a close descendent of the organism evolved from unicellular organism and is the simplest multicellular model animal (1). C. elegans is a small (about I mm long as an adult), free living (as opposed to parasitic) round worm (Fig 1.). The normal habitat of the animal is soil, where it feeds on bacteria and fungi. In the lab, it can be easily cultivated on agar plates fed with E .Coli as a food. It grows to adulthood in 2 days at 25°C and its brood size is 200-300, allowing fast proliferation. It can be stored for years in deep freezers or liquid nitrogen(2, 3). The C. elegans genome size is relatively small (9.7 x 10^7 base pairs or 97 megabases) and is first organism whose genome have been completely sequenced (4). Its genome has 43% homology with the genome of human(5). Conversely, many C. elegans genes can function similarly to mammalian genes. Because of ease of its handling and maintenance, it has been used for such diverse aspects of animal

physiology and behavior as embryonic development, chemoreception, and the genetic control of lifespan, systematic and cornpfieransive analysis, such as the description of phenotype by RNA interference etc (6-7).

THE INSECTS: DROSOPHILA MELANOGASTER (FRUIT FLY)

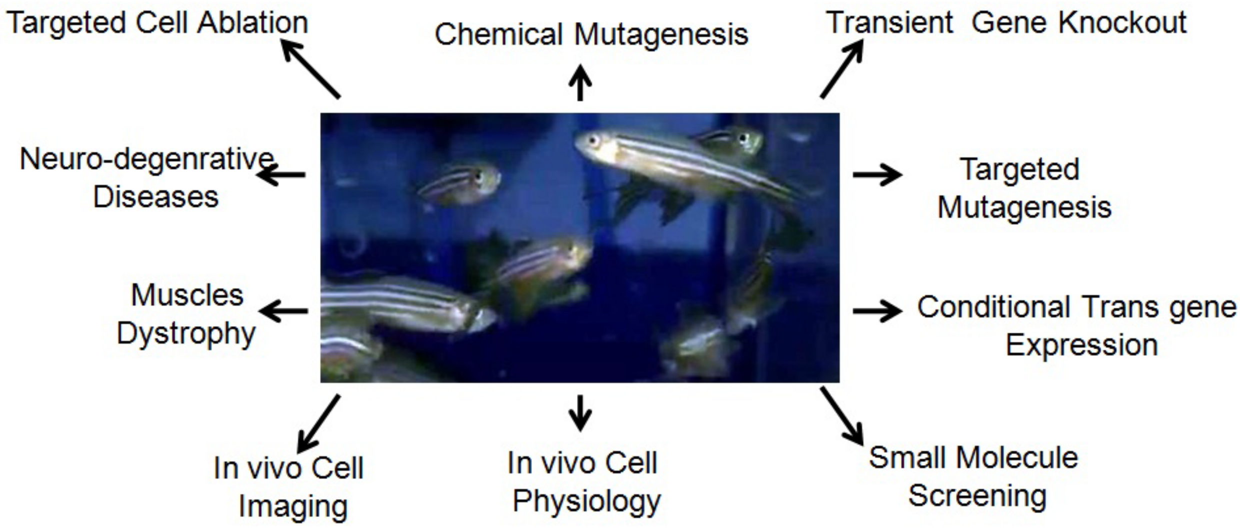
Drosophila melanogaster is commonly known as fruit fly, a little insect about 3mm long of the kind that accumulates around spoiled fruit (Fig 2.). It is also one of the most valuable of organisms in biological research, particularly in genetics and developmental biology. Drosophila has been used as a model organism for research for almost a century. It has four pairs of chromosomes: the X!Y sex chromosomes and the autosomes 2,3, and 4. The fourth chromosome is quite tiny and rarely heard from. The size of the genome is about 165 million bases and contains approx 14,000 gene(8). Its genome has been completely sequenced in 2000, and analysis of the data is now mostly complete. It has been considered as an attractive system for scientific research due to a number of reasons including its easy- to-manipulate genetic system, relatively low cost, and biological complexity comparable to that of a mammal. Many organ systems in mammals have well-conserved homologs in Drosophila and Drosophila research has already led the way in providing new insights into forms of cancer, neurodegenerative diseases, behavior, immunity, aging, multi genic inheritance and development. The study of speciation was brought into the modern age and onto a firmer, more genetic basis by drosophilists such as Sturtevant, Dobzhansky and others in T.H. Morgan's lab during the 1930s and 1940s. Dobzhansky's reproductive isolation species concept, later incorporated into Mayr's biological species concept, is based in large part on the discovery of pairs of sibling species of Drosophila: genetically close and morphologically almost identical, but showing strong reproductive isolation in the form of hybrid sterility, hybrid inviability and assortative mating. More interesting, it has been used in the study of various neurodegenerative disorders such as Huntington Disease, Parkinson Disease, ALS (amyotrophic lateral sclerosis) and Alzheimer Disease(9-13). These neurological degenerative diseases are largely heritable



and affect well over 100 million people worldwide, with an incidence of greater than 15% in those over sixty-five years of age.

THE FISH: DANIA RERIO (ZEBRA FISH)

Zebra fish (Danio rerio) are small about 3 em long. They are native to streams in India and are commonly kept as pets. The males are slender and torpedo shaped, with black longitudinal stripes and usually a gold colouration on the belly and fins. Females are fat when laden with eggs and have little, if any, gold on their undersides. Zebra fish are easy to raise with a short generation time of 3 months. Females can lay



hundreds of eggs at weekly intervals. Fertilization is external, allowing easy access to embryos for observation and manipulation. Developing embryos can be easily studied under a dissecting microscope since they are transparent. Zebra fish embryos develop rapidly (in 2 ± 4 days), with a beating heart and visible erythrocytes by 24 h. Another advantage of studying the Zebra fish is that, it maintains the diploid state, in contrast to other fish, which are triploid or tetraploid making makes genetic analysis difficult(14). The Zebra fish has been shown to be a useful model for the development of several complex tissues such as the kidney(15) the olfactory system" and the visual system(16, 17). In the study of haem- atopoiesis, Zebra fish mutants have been demonstrated strikingly similar to those in human diseases (18). The use of Zebra fish in various scientific research has been demonstrated as a web in Fig .3.

THE AMPHABIAN: XENOPUS LAEVIS

It has been introduced as a model organism in 1950s. Amongst amphibians, most of the work has been focused on African clawed frog Xenopus laevis. It can grow up to a length of

5 in (12 ern) with a flattened head and body (Fig 4.), but no external ear or tongue. Its name is derived from the three short claws on each of its hind feet, which it probably uses to stir up mud to generation time and genetic simplicity generally desired in gene tic model organisms, it is an important model organism in deve lopmental biology. X. laevis takes 1 to 2 years to reach sexual maturity and, like most of its genus, it is tetraploid. However, it does have a large and easily manipulatable embryo (20). The ease of manipulation in amphibian embryos has given them an important place in historical and modem developmental biology.

Oocytes, eggs and embryos from the frog Xenopus laevis have been an important model system for studying cell-cycle regulation for several decades (21). A related species, Xenopus torpicles, is now being promoted as a more viable model for genetics. Roger Wolcott Sperry used X. laevis for his famous experiments describing the development of the visual system. These experiments led to the formulation of the Chemoaffinity hypothesis. Xenopus oocytes provide an important expression system for n0lccular biology. By injecting DNA or mRNA into the oocyte or developing embryo, scientists have been studying the protein products in a controlled system. It allows rapid functional expression of manipulated DNAs (or mRNA). It is particularly useful in electrophysiology, where the ease of recording from the oocyte makes expression of membrane channels attractive. One challenge of oocyte work is eliminating native proteins that might confound results, such as membrane channels native to the oocyte (22). Translation of proteins can be blocked or splicing of pre-mRNA can be modified by injection of morpholino antisense oligos into the oocyte (for distribution throughout the embryo) or early embryo (for distribution only into daughter cells of the injected cell). Extracts from the eggs of X. laevis frogs are also commonly used bfor biochemical studies of DNA replication and repair (23) as these extracts fully support DNA replication and other related processes in a cell-free environment which allows easier manipulation. X. laevis is also notable for its use as the first well documented method of pregnancy testing when it was bdiscovered that the urine from pregnant women induced X. laevis oocyte production.

THE REPTILE: CALOTES VERSICOLOR

The origin of the reptiles lies about 320--310 million years ago. Squamate reptiles (lizards, snakes, amphisbaenians) number approximately 8200 living species and are a major component of the world's terrestrial vertebrate diversity. Calotes versicolor is a garden lizard and body size up to 6-13 inch long flattened (Fig 5.). Adult lizards weighing 35-65 g were housed in wooden cages and fed on live termites and water ad libitum (24). Calotes versicolor is used as a model organism in the field of immunology, sex determination, cancer, many metabolic detection, pheromones and evolutionary study (25). Calotes versicolor is recognized as one of the best model organism in scientific research in immunology. Calotes versicolor is cold blooded animal and having much similarity with the human blood. Detection of cell-mediated immunity in lizard, binding pattern of antigen with T cell and B cell have been studied in lizard. Calotes versicolor is best studied in sex determination (TDMs) etc.

THE AVES: GALLUS GALLUS (CHICKEN)

The chicken genome has a haploid content of 1.2 x 109 base pairs (bp) of DNA; approximately 40% have homology with either mouse or human. The chicken is the premier non-mammalian vertebrate model organism (Fig 6.). It is one of the primary models for embryology and development as its embryonic development occurs in ovo rather than in utero. The chicken is a major model organism for the study of viruses and cancer. The first tumor virus (Rous sarcoma virus) and oncogene (src) were identified in the chicken, and the avian leukosis viruses (AL V) remain among the most intensively studied retroviruses. The chicken immune system provided the first indications of the distinctions between T and B cells.

Moreover, the B cell omenclature is based on the avian bursa of Fabricius. The chicken has also provided an important model system for studies of gene regulation(26).

The chicken as a model for human eye defects is used as an example of its use in medical research. Five chicken mutants have been used as models of retinal degeneration. A candidate gene study defined the defect in retinal degeneration as a null mutation in the photoreceptor guanylate cyclase (27). Other blind defects include blindness enlarged globe (28) sex-linked retinal dysplasia and degeneration, delayed amelanotic strain DAM8, and retinopathy globe enlarged.

The chicken has been used as a model in developmental biology for over 100 yr. Classic grafting experiments of posterior regions of the limb bid to the anterior region generated mirror duplications of the digit pattern. Further studies over many decades defined many aspects of this polarizing region. In particular, a molecule sonic hedgehog (SHH) homologous to a gene found in Drosophila was identified as a major component of the polarizing region. The SHH pathway has a role to play in the development of many organs, including" the limb, nervous system, face, gut, lung, teeth, hair or feathers, and biological processes: hematopoiesis, vasculogenesis, angiogenesis, etc. So it is not surprising that genetic defects in this pathway causes many disorders and syndromes, including holoprosencephaly, gut and lung malformations, as well as many cancers such as medulloblastoma, basal cell carcinoma, glioblastoma and a form of prostate cancer. In addition to pure sequence comparisons, the chicken genome provides an excellent model with which to understand the evolution of gene order and arrangement. Studies from several labs have demonstrated a remarkable level of conservation in gene order between mammalian and chicken genomes. Indeed, although the evidence remains far from complete, the number of genome rearrangements separating the chicken and human genomes (on a gross level) appear to be similar to, if not fewer than, those separating the mouse and human genomes. Overall gene order is often conserved over segments of many tens of cM between chicken and human (average conserved segment length is about 30-40 cM) with the evidence clea"rly suggesting a higher rate of inversions vs. translocations having occurred in the 600 M years separating the two genomes (300 My from each present day genome back to the last common ancestor). The chicken has been extensively used as model organism for human health research. Vaccine against the Marek's Disease has been first administered in the chicken before going to its clinical trial. Marek's Disease virus is an oncogenic herpesvirus of fowl,the only tumor virus in any species for which an effective vaccine presently exists. The enormous commercial populations of chickens (far exceeding those of any other captive model species) means that large scale breeding studies can be done in the chicken. In many cases the traits that are of interest (nutrition, growth, disease resistance, reproductive success) to the poultry industry who possess the largest flocks are traits that are of similar importance to human health, so studies of chicken genetics and human medicine are often complementary.

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