

## MODEL ORGANISM USED IN BIOLOGICAL RESEARCH: DROSOPHILA MELANOGASTER

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### ABSTRACT

*Drosophila melanogaster*, (species of Fly; order Diptera; family *Drosophilidae*) used as model organism and is widely used for various immunobiologically studies especially genetics, animal physiology along with microbial pathogenesis etc. It is one of the most typically used organism in invertebrates that is easy to care, breeds quickly and lays many eggs. In this study, our group collected literature about drosophila (invertebrates) related to the prevalence of disorders which effects metabolism and other cellular functions. In view of this, this organism is used as model organism for various biological studies.

**KEYWORDS:** *Drosophila Melanogaster*, Biological Studies, Model, Organism.

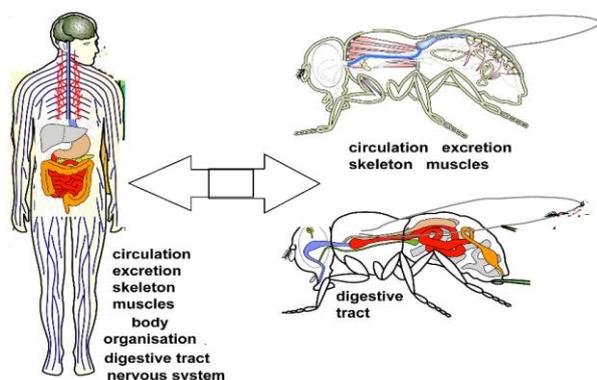
### INTRODUCTION

**Drosophila** (fruit flies" or vinegar fly) belongs to the family *Drosophilidae* and is widely studied in various biological model based studies e.g. Microbial pathogenesis, genetics etc.<sup>[1-4]</sup> This organism used as a versatile model organism because its entire genome (168736537 base pairs in length) has already been sequenced. As per the literature, nearly 13,937 genes in genome of drosophila were reported and contained 4 homologous pairs of chromosomes i.e. 3 pairs of autosomes and one pair of sex chromosomes.<sup>[1-7]</sup> In addition, this organism is not so much expensive and easily to maintained in the laboratory and normally require simple diet i.e. carbohydrates and proteins. The identification of male and female on the basis of sex chromosomes i.e. XX female; XY male and XO sterile males. In contrast, more than 75% of the genes are responsible for causing disease in humans and this is also reported in drosophila as well.<sup>[4-8]</sup> The most striking feature in drosophila is the presence of polytene chromosomes and researchers could easily identified chromosomal rearrangements and deletions under the microscope.<sup>[5-9]</sup>

In general, most of the animal testing is observed in invertebrates e.g. *Drosophila melanogaster*<sup>[1-9]</sup> and *Caenorhabditis elegans*, nematode.<sup>[10]</sup> These invertebrates given so many advantages over vertebrates as suggested by various researchers with respect to its short life cycle, simple anatomical features etc. In comparison with developmental stages of other invertebrates, this organism undergoes complete metamorphosis (i.e. egg, larvae, pupae and flying adult)

and its natural life span is 40 to 50 days.<sup>[4-7]</sup> According to the literature, researchers identified this organism and claimed the concept of genetic information which is carried on chromosomes. In short, this organism is widely used in genetics and developmental biological research for almost a century and today also several thousand scientists are working on many different aspects of its biology.<sup>[11,12]</sup> In this regard, our group collected some information from various sources regarding immunobiologically applications using drosophila.

**Examples of immunobiologically reactions using drosophila as model organism:** The importance of *Drosophila* used as an animal model organism was firstly realized by Thomas Hunt Morgan and got Nobel Prize for physiology or medicine in 1933 and later on got second Nobel Prize in year 1995 for working on the genetic control of early embryonic development.<sup>[13-15]</sup> All these achievements as well as studies related to drosophila were conducted by various researchers (Fig.1). Most importantly are mentioning as below.



**Fig. 1. Human and drosophila model based studies.**

### Cancer

In recent years, *Drosophila* is considered to be one of the highly well-developed powerful genetic techniques that will allow for the rapid identification as well as characterization of genes which involved in tumor formation and development. Various studies were conducted with respect to cancer models in animal based studies especially in *Drosophila*. Number of drug screening efforts were taken by various researchers and considered that *Drosophila* is one of the most valuable animal model for studying as well as exploring cancer issues.<sup>[16,17]</sup> Several examples for these studies are.

- *Drosophila* tracheal system, branched tubular network that supplies oxygen to the fly. The most common feature is observed in vertebrate lung and *Drosophila* tracheal systems i.e. both of them are highly dependent on fibroblast growth factor signalling.<sup>[18-20]</sup> This tracheal system is formed through interconnected tubular hierarchy that begin in large primary tubes and branch into several diminishing diameter segments that ultimately ends in terminal branches. One of the studies related to lung cancer model by targeting Ras1<sup>G12V</sup> (tracheal targeted expression of oncogenic isoform) alone or in combination with PTEN knockdown in *drosophila* tracheal system.<sup>[20-22]</sup> Activated Ras isoforms represent the most common genetic mutations associated with NSCLC, and are typically associated with activated PI3K pathway signalling.<sup>[20-23]</sup> For these studies, use two FDA approved compounds i.e. MEK inhibitor trametinib and HMG-CoA reductase inhibitors fluvastatin taken as standard. Oral administration of these drugs as mentioned in literature inhibited both the pathways i.e. Ras and PI3K respectively whereas fluvastatin inhibited protein prenylation, downstream of HMG-CoA reductase in order to increase or promote survival. In contrast, these two drugs act synergistically to reduce the effects of Ras/PI3K pathway activation and tried to improve tracheal development along with reduction in proliferation rate and whole animal toxicity and also these drugs acted synergistically to suppress growth in a standard human lung cancer cell line.<sup>[20-24]</sup>

- One of the highly deleterious disease i.e. Cachexia which leads to the irreparable loss of adipose (fat) and

muscle tissue in humans. With reference to cancer induced Cachexia used as model in *drosophila* larvae was developed which represents one of the most novel technique in cancer model studies. In *drosophila*, pathway function is almost easier because of the presence of two core components i.e. Janus Kinase protein and the Signal Transducer and Activator of Transcription (JAK/STAT) and analysing communication analysis between stem cells, their niches and offspring.<sup>[26-28]</sup>

- Local cell-cell interactions in *drosophila* is observed in transformed cells and their epithelial neighbours along with hematopoietic system. So, all these factors played an important role in regulating tumorigenesis and provide some information about factors that will determine the nature of thyroid tumor progression. In addition, use of *drosophila* as model in human cervical cancer on the based on a homology of the *Drosophila* tumor suppressor protein to human tumor suppressor protein.<sup>[1-8]</sup>

**Cardiovascular disease:** This disease is one of the leading cause of death in all over the world and therefore it is urgently needed as well as highly desirable area in terms of synthesis and development of highly effective therapeutics. In view of this, number of studies were conducted but all these studies were conducted in cell lines and somehow studies were conducted in animal model studies i.e. mice but these studies were very expensive. In this regard, researchers focused on invertebrates especially *drosophila* used as best model for conducting these cardiovascular based studies. According to the literature, complex nature of the cardiovascular system in humans which showed some limitations in the fruit fly (depending on set of genes) for accurate modelling i.e. fly heart has only one cardiac chamber and has no coronary arteries.<sup>[29-32]</sup> In view of this, various cardiovascular based studies were conducted as shown below.

- Fly heart beating (visualization, dissection and electrophysiological recording of larva heart) can be observed through traditional dissection microscope for analysis.

- Several forms of dysfunction i.e. structural defects, arrhythmias, cardiomyopathies etc are reported in natural populations of flies. These dysfunction could arise because of age and sometimes cardiac failure.

In short, fruit fly is considered as a valid proof model based studies for studying as well as conducting various experiment with respect to cardiovascular disease and also understanding the physiology of human cardiovascular system as well.<sup>[29-32]</sup> So, this study is one of the important tool in the biological process to discover new therapeutics e.g. identified components genetically and imaging tools available to examine fly heart function.

**Inflammation (Infectious disease):** *Drosophila* is one of the most highly effective and primitive type of blood system with three types of haemocytes and its function throughout different developmental stages and environmental stimuli. In addition, these haemocytes played an important role in tissue modelling (embryogenesis and morphogenesis) and also regulated innate immunity (e.g. Toll like receptors) as well. Recently, researchers focused on type of inflammation i.e. acute or chronic with respect to *drosophila*.<sup>[33-35]</sup>

Numerous studies were conducted by various researchers pertaining to the mechanism of inflammation using *Drosophila* as a model. As per the literature, studies clearly showed the mechanism of immunodeficiency (IMD) pathway and characterized several components at the molecular as well as biochemical level.<sup>[36,37]</sup> In addition, stress response including protein homeostasis also explored in Alzheimer disease fly models with respect to accumulation of polyglutamine-containing protein. Apart from these studies, *Drosophila* embryos also provide a model for wound healing process and is highly associated with various inflammatory response.<sup>[33-37]</sup> These studies were conducted due to the combination of genetics and live imaging that proved to be one of the most powerful technique for uncovering the mechanisms that underpin repair and is not available in other model organisms.

#### Microbial studies

*Drosophila melanogaster* is generally feeds on various microorganism-enriched matter especially bacteria. This organism is developed as a study model and also able to understand its correlation along with mechanism in several strains of bacteria. Various examples were mentioned in the literature i.e.

- Infection of the *Drosophila melanogaster* with *Staphylococcus aureus* results in systemic infection followed by death.<sup>[38]</sup> This study is claimed as high throughput analysis of disease model and these studies should be able to determine the effect of antibiotic using variable concentration on these flies.
- *Drosophila melanogaster* is used to study the effect of microbiota on invertebrates and its beneficial role is extensively described i.e. growth to metabolism, immunity and even behaviour.<sup>[3-6]</sup>
- This model organism is used for genetic research as well but also played an important role in the field of metabolic, neuronal, behavioural, microbial and immunological related disorders.
- Growth promoting activity of different strains of probiotic bacteria were studied as well as investigated in *Drosophila*.<sup>[1-5]</sup>
- With sudden increase in carbohydrate to protein ratio especially in the fly food which augments the proportion of *Acetobacter* versus *Lactobacillus* in adult.<sup>[38,39]</sup>

#### CONCLUSION

In short, *Drosophila melanogaster* is considered to be one of the most ideal organism to use for various immunobiologically studies. Recently, this organism is used by various researchers for easy and reliable comparison with its mammalian counterparts. In contrast, there is no adaptive system in this organism but there is extremely and more accessible innate type of immune system. Therefore, this organism is an excellent model organism to use for immune studies.

#### AUTHORS CONTRIBUTION

This work was carried out in collaboration i.e. Dr Amit Gupta anchored the field study whereas Ketu G Gajera, Henali J Patel and Vidhi N. Pansuriya, students of B.Sc. Microbiology and Supriya B Bhosale (research assistant) managed the literature searches. Finally, all these authors finalized and approved the final draft of this manuscript.

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