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## UNDERSTANDING INSECTICIDE RESISTANCE IN *MUSCA DOMESTICA* L. (DIPTERA: MUSCIDAE), RESPONSIBLE ENZYME AND ITS INTERACTION NETWORK USING PPI STUDIES

Sharat Kumar Pattar<sup>1</sup>, Riaz Mahmood<sup>2\*</sup>, Sushil Kumar Jalali<sup>3</sup>, Santosh Kumar H.S<sup>3</sup>

<sup>1,2</sup> Department of Biotechnology and Bioinformatics, Kuvempu University Jnanasahyadri, Shankaraghatta-577451, Karnataka., India

<sup>3</sup> Department of Entomology, National Bureau of Agricultural Insect Resources, Bangalore-560024, Karnataka., India

<sup>3</sup> Department of Biotechnology and Bioinformatics, Kuvempu University Jnanasahyadri, Shankaraghatta-577451, Karnataka., India

\*Email: [riaz\\_sultan@yahoo.com](mailto:riaz_sultan@yahoo.com)

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### ABSTRACT

The housefly, *Musca domestica*, L. (Diptera: Muscidae) is a genuine danger to human and creature wellbeing. Houseflies are vectors of in excess of 100 human and creature intestinal maladies. They are fit for communicating parasites that cause illnesses, for example, typhoid fever, cholera, bacillary looseness of the bowels, juvenile the runs, tuberculosis, plague, sickness, yaws, salmonellosis, trachoma, and Bacillus anthracis. Creature wellbeing concerns incorporate the transmission of pinkeye. If we want to quell this insect pest the humans using insecticides and repellents but due to chronic use of these chemical compounds will create insecticide resistance in these domestic insect pests. There are numerous proteins/enzymes responsible for degradation of the chemicals used to get rid of these pests, but due to the action of some of the proteins/enzymes namely Ache gene (considering in the current study) will be rigorously involved in degradation of chemical compounds results in expressing the resistance in Houseflies. With the application of network biology the current study dealt efficiently in understanding how the interacting/supporting mechanism helps in expressing the resistance mechanism. With the help of STRING DATABASE in data collection and CYTOSCAPE-3.0 in visualization helps to its best in understanding the mechanism.

**Keywords:** Insecticide resistance, Diptera: Muscidae, Insect pest, *Musca domestica*, Network Biology, STRING DATABASE, Cytoscape.

### INTRODUCTION

The house fly, *Musca domestica* L. (Diptera: Muscidae), is the most well-known and across the board types of fly on the planet. It is said to have begun from the savannahs of Central Asia and spread all through the world, and can be found in both rustic and urban territories of tropical and mild atmospheres. The house fly has a place with a gathering of flies regularly alluded to as “rottenness flies”; different individuals have a place with the families Calliphoridae and Fanniidae. The house fly has been in presence since the source of human life and very much adjusted to life in human homes. *M. domestica* is an eusynanthropic, endophilic species (Montella *et al.*, 2012), for example it lives intently in relationship with people and can finish its whole lifecycle inside homes of people and residential creatures. House flies are frequently found in bounty in territories of human exercises, for example, emergency clinics, food markets, butcher houses, food focuses or eateries, poultry and domesticated animals ranches where they establish an irritation to people, poultry, domesticated animals and other livestock, and furthermore go about as likely vector of sicknesses. The house fly is known to convey microbes that can cause genuine and perilous maladies in people and creatures. More than 100 microbes including microscopic organisms, infections, growths

and parasites (protozoans and metazoans) have been related with the creepy crawly (Qingfeng Li, *et al.*, 2018). Atomic examination uncovered that house flies convey differing gatherings of microorganisms. Proof supporting the job of the house fly in transmission of sicknesses are for the most part incidental, with the most grounded proof highlighting the relationship between the ascent in frequency of looseness of the bowels and an expansion in the fly populace. The qualities of the microbes conveyed by house flies rely upon the region where the bug is gathered; house flies caught from the emergency clinic condition or animal homesteads (where there is broad utilization of anti-infection agents as development advertisers) regularly convey antimicrobial safe microscopic organisms and parasites. All the more along these lines, house flies introducing in the emergency clinic condition may likewise be related with the transmission of nosocomial diseases. House fly causes mechanical transmission of microbes, which is the most generally perceived system (Xu C, Min J. 2011). This happens when microorganisms are sent starting with one vertebrate has then onto the next without enhancement or improvement of the creature inside the vector. House flies generally take care of and duplicate in dung, creature excrement, remains and other rotting natural substances, and subsequently live in personal relationship with different microorganisms including



**Figure-1:** PPI network retrieved from STRING DATABASE for the submitted orthologous Ache Gene.

human microbes, which may adhere to body surfaces of the fly (Khamesipour, F. *et al.*, 2018). The consistent to and fro development of house flies between their reproducing locales and human abodes can prompt the transmission of microorganisms to people and creatures so in order to address this menace the community started using the repellents for which the pest started showing resistance towards it. In order to address this resistance mechanism, we have used the tool of systems Biology to understand how and what are the gene products involving and interacting with the responsible proteins/enzymes to exhibit this mechanism of resistance in this considering insect pest.

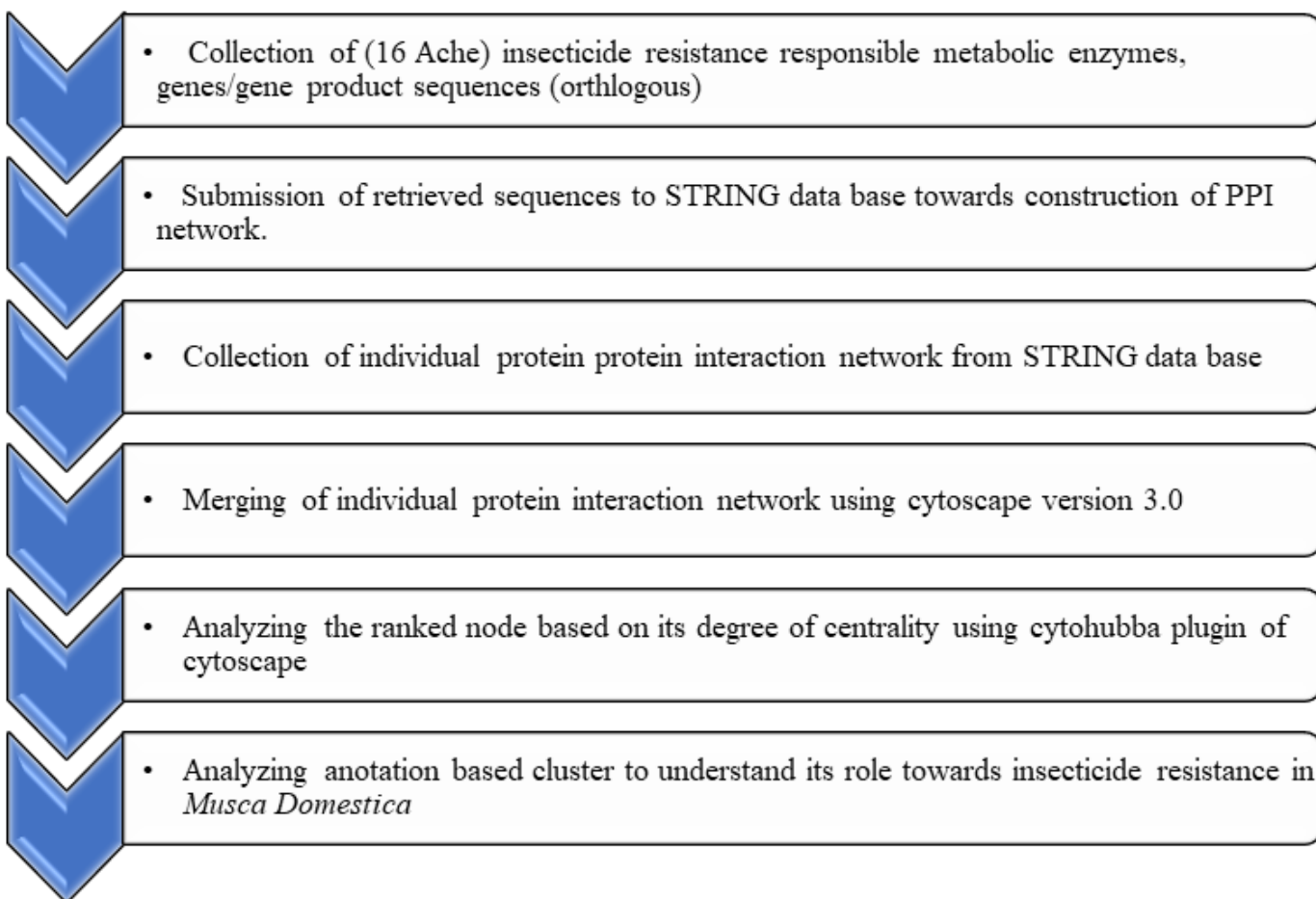
### Network Biology

Biological Networks are frequently spoken to as systems which are intricate arrangements of two fold associations or relations between various substances/mechanisms. Basically, every biological mechanism and its responsible gene/gene product has communications

with other individual or group of the mechanism with its responsible gene/gene products, from the sub-atomic to the biological system level, giving us the chance to demonstrate science utilizing a wide range of sorts of systems, for example, environmental, neurological, metabolic mechanisms. Here in this study we are concentrating on the mechanism of insecticide resistance in *Musca domestica*.

The information blast that began in the -omics period of organic exploration required the improvement of more fundamental ways to deal with information investigation and a move away from the single quality/protein viewpoint. Frameworks science intends to comprehend organic substances at the foundational level, dissecting them as individual segments, yet additionally as collaborating frameworks and their emanant properties. Identified with this is organize science which permits the portrayal and examination of natural frameworks.

## MATERIALS AND METHODS



## RESULTS AND DISCUSSION

Retrieved 16 ache genes from Genbank and in-turn collected its gene products to onward submission to the STRING (Paul Shannon *et al.*,2003) PPI Database. As a result of this submission resultant to see the following PPI network as follows:

The above PPI network consists of the network parameters which will play a pivotal role (Santosh Kumar, *et al.*, 2016) in the considering the bulkiness of the network.

**Table:1-** Details of the STRING PPI network parameter

Details Of The Network Parameter	Values
number of nodes	41
number of edges	98
average node degree	4.78
avg. local clustering coefficient	0.856
expected number of edges	46
PPI enrichment p-value	1.32e-11

The above obtained PPI network has been submitted to network visualisation tool called CYTOSCAPE 3.0 (Xu C, Min J. 2011) and visualized the network followed by manually we have supplied the ontology information as label for each of the Nodes/protein on the PPI network, this will gives a better opportunity to visualize, understand and interpret the Nodes and their functionalities.

### Discussion

with the obtained results of PPI network with 49Nodes (protein) connected with 98 Edges(connecting lines) it is depicting that the considering Ache gene of *Musca domestica* is orthologously similar with the *Drosophila melanogaster* in STRING DATABASE, so we have considered the same as a pre-data set for this study. With this resultant network clearly indicates that the role Ache towards exhibiting resistance mechanism is expression with the involvement of the various other mechanism/ components/ontologies (as shown in the Table:-2). This combinatorial effect of resistance mechanism can be understood with the study of network biology (Batagelj, V. *et al.*, 1998) (Kim.J I *et al.*, 2012) using STRING DATABASE and can be interpreted using Cytoscape V-3.0 and above.

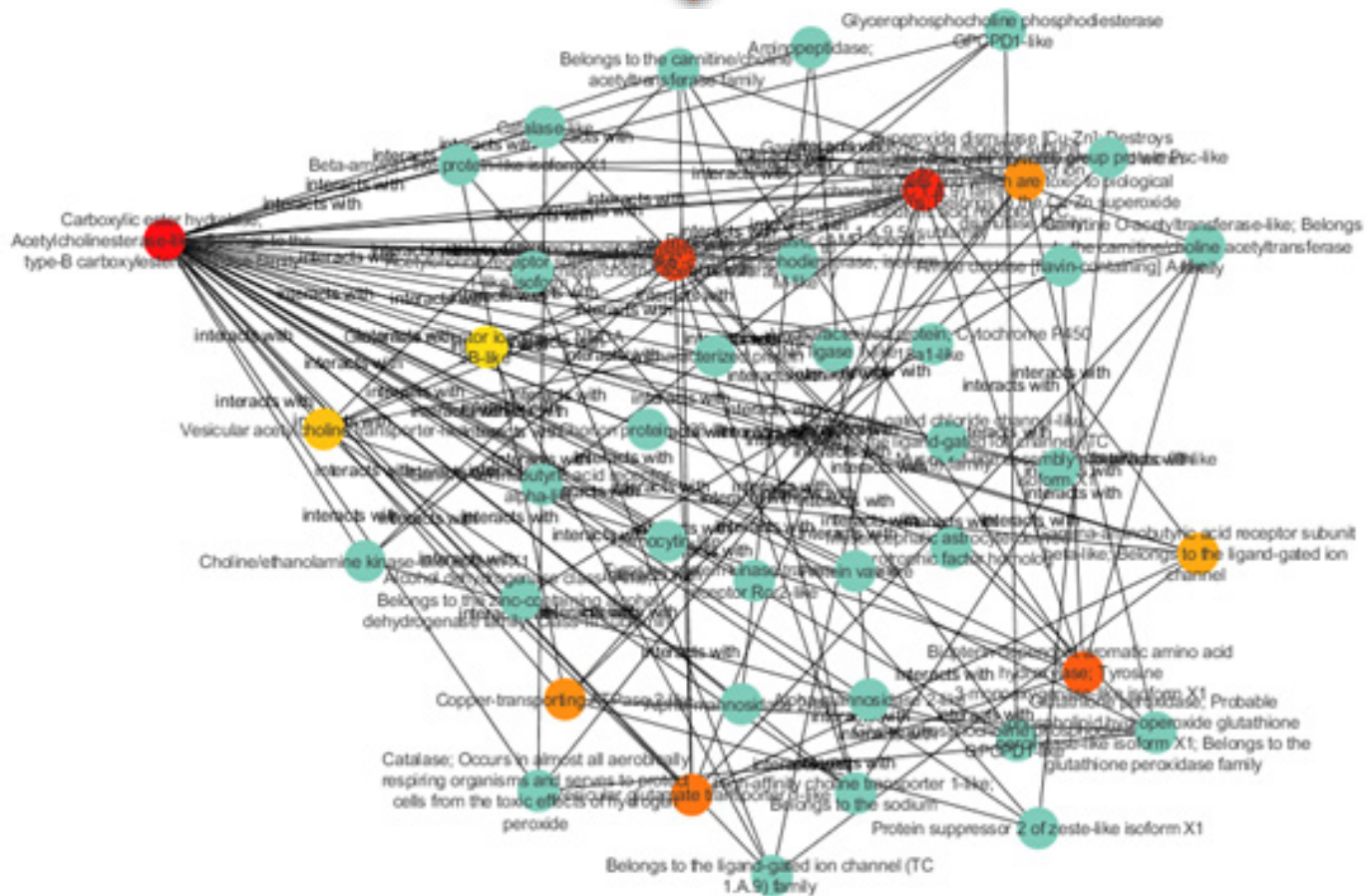
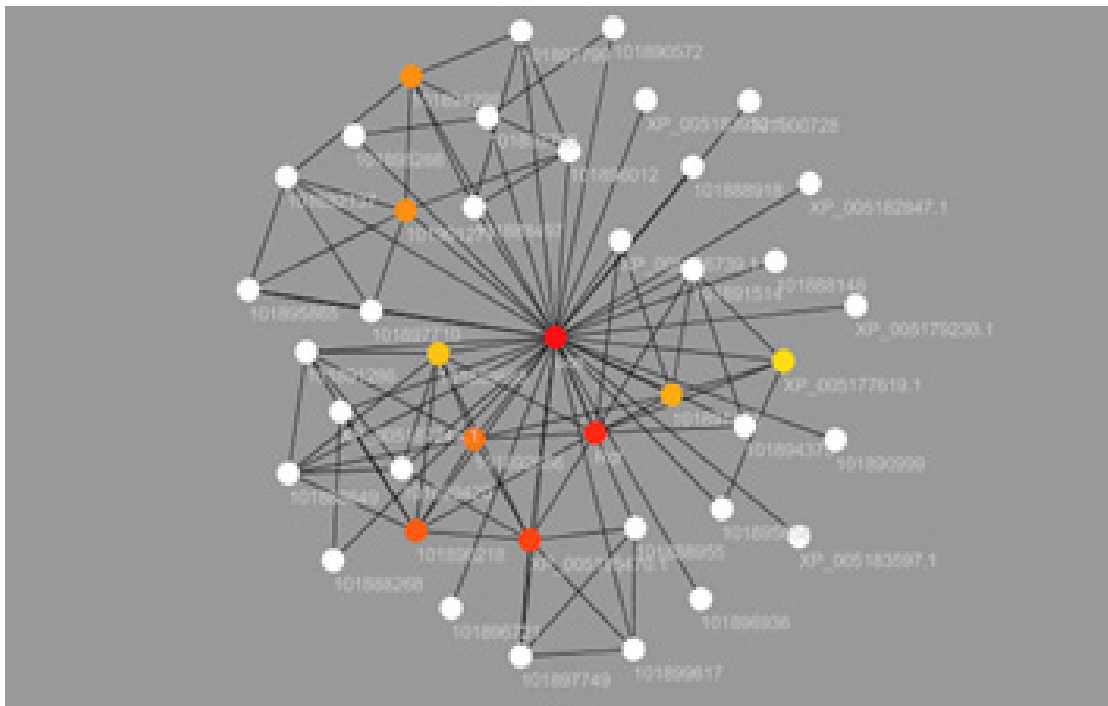


Figure-2: Network visualisation in cytoscape with the labelled Nodes with their respective functionalities

**Table-2:** Protein/Node ID of the PPI Network with their details of Interaction partners

#node ID	Details of the Interacting Partner Proteins
101888918	Tyrosine-protein kinase transmembrane receptor Ror2-like
101890572	Alpha-mannosidase 2-like
101892137	Beta-amyloid-like protein-like isoform X1
XP_005176739.1	Gamma-aminobutyric acid receptor alpha-like
101899617	Choline/ethanolamine kinase-like isoform X1
XP_005177619.1	Glutamate receptor ionotropic, NMDA 2B-like
101892656	Vesicular glutamate transporter 1-like
101891514	Belongs to the ligand-gated ion channel (TC 1.A.9) family
XP_005179230.1	Uncharacterized protein
101894375	Acetylcholine receptor subunit beta-like 1-like isoform X1
101897799	Catalase; Occurs in almost all aerobically respiring organisms and serves to protect cells from the toxic effects of hydrogen peroxide
101896218	Biopterin-dependent aromatic amino acid hydroxylase; Tyrosine 3-monooxygenase-like isoform X1
101890999	DNA ligase 1-like
101893750	Aminopeptidase;
101895658	Muscle M-line assembly protein unc-89-like isoform X1
101888649	Belongs to the carnitine/choline acetyltransferase family
101891286	Carnitine O-acetyltransferase-like; Belongs to the carnitine/choline acetyltransferase family
XP_005182847.1	Chorion protein S38-like
101896012	Glutathione peroxidase; Probable phospholipid hydroperoxide glutathione peroxidase-like isoform X1; Belongs to the glutathione peroxidase family
ace	Carboxylic ester hydrolase; Acetylcholinesterase-like; Belongs to the type-B carboxylesterase/lipase family
101900728	Uncharacterized protein; Cytochrome P450 18a1-like
XP_005183597.1	Phosphodiesterase; cAMP-specific 3',5'-cyclic phosphodiesterase, isoform M-like
101897749	Glycerophosphocholine phosphodiesterase GPCPD1-like
XP_005183932.1	Glutamate-gated chloride channel-like; Belongs to the ligand-gated ion channel (TC 1.A.9) family
101899420	High-affinity choline transporter 1-like; Belongs to the sodium
101896936	Mesencephalic astrocyte-derived neurotrophic factor homolog
101889588	Vesicular acetylcholine transporter-like
XP_005185470.1	Choline O-acetyltransferase-like; Belongs to the carnitine/choline acetyltransferase family
101898268	Alpha-mannosidase 2-like
101891413	Gamma-aminobutyric acid receptor subunit beta-like; Belongs to the ligand-gated ion channel
101888955	Glycerophosphocholine phosphodiesterase GPCPD1-like
XP_005187245.1	Amine oxidase [flavin-containing] A-like
101896721	Protein vav-like
Rdl	Gamma-aminobutyric acid receptor subunit beta; GABA, Belongs to the ligand-gated ion channel (TC 1.A.9) family. Gamma-aminobutyric acid receptor (TC 1.A.9.5) subfamily
101888268	Alcohol dehydrogenase class-3-like; Belongs to the zinc-containing alcohol dehydrogenase family. Class-III subfamily
101888148	Hemocytin-like
101901271	Copper-transporting ATPase 2-like
101888497	Catalase-like

continued...

101894298	Superoxide dismutase [Cu-Zn]; Destroys radicals which are normally produced within the cells and which are toxic to biological systems; Belongs to the Cu-Zn superoxide dismutase family
101895865	Protein suppressor 2 of zeste-like isoform X1
101897710	Polycomb group protein Psc-like

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