Curriculum Vitae

Anuradha Singh

Research Scholar, IISER Mohali

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Educational Qualifications:

- **January 2016 – Present: Completed PhD.** in Neuroscience under the supervision of Dr. Kavita Babu from **Indian Institute of Science Education and Research**. Mohali, India. The Topic of my research is "Understanding the role of DOP-2, a dopamine autoreceptor, in ethanol dependent locomotion of Caenorhabditis elegans", **Thesis submitted**. Currently holding the position of S.R.F. in the same lab.
- **2013-2015: First Class (89%)** in Masters of Science (Molecular and Human Genetics), Banaras Hindu University, Varanasi, Uttar Pradesh, India.
- **2009-2012: First Class (72%)** in Bachelor of Science from C.S.J.M. Kanpur University, Kanpur, Uttar Pradesh, India.

Research Experience:

- **January 2016 – Present.** PhD. Research Scholar at IISER Mohali under the guidance of Dr. Kavita Babu. Received UGC-JRF. Pursuing my research on project entitled "**DOP-2 modulates Acetylcholine and GABA signaling in *Caenorhabditis elegans.***" During these studies we found a very interesting behaviour and utilized it for the delineation of synaptic dopamine signalling through dopamine receptor, DOP-2 and showed that EIS behaviour is the direct outcome of increased dopamine levels. We showed that PDE neuron synapses onto DVA interneuron where NLP-12 (a neuropeptide) and DOP-1 (Dopamine receptor) are the two molecules important for movement regulation through motor neuron. Interestingly, it is quite distinct from the anterior dopamine circuitry that functions extra-synaptically to control various behaviours. Moreover, EIS behaviour can be used to screen for array of chemicals/conditions those can enhance the dopamine signalling. Our manuscript creates a paradigm for future studies where post withdrawal effects of this chronic ethanol exposure will be understood. Furthermore, transgenerational effects of chronic ethanol exposure will be studied by performing genome wide transcriptome analysis and the knowledge generated can be utilized to overcome AUDs in humans.

Publications from the above work:

Pandey, P., **Singh, A**., Kaur, H., Ghosh-Roy, A. and Babu, K. (2021). Increased dopaminergic neurotransmission results in ethanol dependent sedative behaviors in Caenorhabditis elegans. PLoS GENETICS (in press).

Ethanol Induced Sedative (EIS) Behavior Assay, to determine increased Dopamine and Acetylcholine defects in *C. elegans*. Protocol Under Revision in Bio Protocol.

January – May 2015. Dissertation under the guidance of Dr. Ashim Mukharjee, Department of Molecular and Human Genetics, Banaras Hindu University on the project entitled "Structural and Functional Study of Notch Binding Protein in *Drosophila Melanogaster*."

May – July 2014. Summer Training under the guidance of Dr. Debasmita Upadhyay, Biological Sciences, National Institute of Science Education and Research (NISER) on the project entitled "Genetic Association Studies of Factor V Leiden and G6PD With Recurrent Spontaneous Abortion in North Indian Population".

May - June 2011. Summer Training on the project entitled "Electrophoresis for Varietal Identification of Pisum Sativum", from C.S.A. University of Agriculture and Technology.

Research Expertise:

C. elegans forward and reverse genetics**,** molecular biology**,** neurobiology, fluorescence microscopy, confocal microscopy, calcium imaging, worm transformation, other basic worm techniques.

Molecular Techniques: Protein Extraction, SDS PAGE, Western Blotting, RNA Extraction, cDNA Preparation, RT PCR, Real time PCR, Denaturing PAGE, Immunoprecipitation.

Basic Techniques used in Drosophila, Immunostaining, In-situ Hybridization, FISH, Cloning, Mass Spectroscopy.

Conferences And Workshops Attended:

- EMBO Conference on Molecular Neuroscience: From genes to circuits in health and disease Feb 2019 NCBS, presented poster on "DOP-2, Dopamine autoreceptor affects the locomotor behavior of C. elegans in an ethanol dependent manner".
- DOP-2, Dopamine autoreceptor affects the locomotor behavior of *C. elegans* in an ethanol dependent manner. Poster presentation at the 2nd Indian *C. elegans* Meeting and Workshop held in NII, New Delhi, India from Feb 2018.
- GIAN Couse and Workshop on "Conservation and Evolution of Developmental Gene Regulatory Networks: A Systemic View", held at IISER Mohali, November 2017.
- GIAN Couse and Workshop on "Cognition: an interdisciplinary perspective", held at IISER Mohali, August 2016.
- AISSQ 2014, Banaras Hindu University.
- Seminar on Emerging Frontiers And Challenges In Biotechnology, presented poster on Genetically Modified Crops, Feb 2012.
- National workshop on studies in Environmental Analysis – Feb 2012.

Fellowships:

- UGC-CSIR-NET-2015 qualified (National level test) conducted by Council of Scientific and Industrial Research, Delhi, India.
- Obtained Department of Biotechnology fellowship given by the Government of India for pursuing studies leading to Masters of Science degree in Molecular and Human Genetics Department, B.H.U.

Publications:

Anuradha Singh, Pratima Pandey and Kavita Babu. Ethanol Induced Sedative (EIS) Behavior Assay, to determine increased Dopamine and Acetylcholine defects in *C. elegans*. Protocol Accepted in Bio protocol, April 2021.

PLOS GENETICS

RESEARCH ARTICLE

Increased dopaminergic neurotransmission results in ethanol dependent sedative behaviors in *Caenorhabditis elegans*

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Data Availability Statement: All relevant data are within the manuscript and its Supporting Information files. The underlying numerical data for the graphs is attached as a supporting excel file.

Abstract

Ethanol is a widely used drug, excessive consumption of which could lead to medical conditions with diverse symptoms. Ethanol abuse causes dysfunction of memory, attention, speech and locomotion across species. Dopamine signaling plays an essential role in ethanol dependent behaviors in animals ranging from *C. elegans* to humans. We devised an ethanol dependent assay in which mutants in the dopamine autoreceptor, *dop-2*, displayed a unique sedative locomotory behavior causing the animals to move in circles while dragging the posterior half of their body. Here, we identify the posterior dopaminergic sensory neuron as being essential to modulate this behavior. We further demonstrate that in *dop-2* mutants, ethanol exposure increases dopamine secretion and functions in a DVA interneuron dependent manner. DVA releases the neuropeptide NLP-12 that is known to function through cholinergic motor neurons and affect movement. Thus, DOP-2 modulates dopamine levels at the synapse and regulates alcohol induced movement through NLP-12.

Author summary

We show that in the presence of ethanol, mutants in the D2-like dopamine autoreceptor, DOP-2 in *C. elegans* show a sedative phenotype. Our work goes on to reveal the mechanism of DOP-2 function in the presence of ethanol. Our initial analyses indicate that DOP-2 functions in the posterior PDE dopaminergic neuron to allow for normal locomotion in ethanol. We have also unearthed the mechanism of DOP-2 functioning and demonstrate that mutants in the *dop-2* autoreceptor show increased dopamine release, which in turn causes increased signaling from the neuron postsynaptic to the dopaminergic neuron PDE. This could in turn cause increased signaling at the cholinergic motor neurons, which results in increased body wall muscle contraction and leads to the locomotory defects seen in *dop-2* mutants treated with ethanol.

eNeuro

Research Article: New Research

Cognition and Behavior

Dauer Formation in *C. elegans* Is Modulated through AWC and ASI-Dependent Chemosensation

Pratima Pandey,[1] Umer S. Bhat,[1] Anuradha Singh,[1] Aiswarya Joy,[1] Varun Birari,[1] Nagesh Y. Kadam,[1] and Kavita Babu[1,2]

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Abstract

The perception of our surrounding environment is an amalgamation of stimuli detected by sensory neurons. In *Caenorhabditis elegans*, olfaction is an essential behavior that determines various behavioral functions such as locomotion, feeding and development. Sensory olfactory cues also initiate downstream neuroendocrine signaling that controls aging, learning, development and reproduction. Innate sensory preferences toward odors (food, pathogens) and reproductive pheromones are modulated by 11 pairs of amphid chemosensory neurons in the head region of *C. elegans*. Amongst these sensory neurons, the ASI neuron has neuroendocrine functions and secretes neuropeptides, insulin-like peptide (DAF-28) and the TGF-β protein, DAF-7. Its expression levels are modulated by the presence of food (increased levels) and population density (decreased levels). A recent study has shown that EXP-1, an excitatory GABA receptor regulates DAF-7/TGF-β levels and participates in DAF-7/TGF-β-mediated behaviors such as aggregation and bordering. Here, we show that *exp-1* mutants show defective responses toward AWC-sensed attractive odors in a non-autonomous manner through ASI neurons. Our dauer experiments reveal that in *daf-7* mutants, ASI expressed EXP-1 and STR-2 (a G-protein-coupled receptor; GPCR) that partially maintained reproductive growth of animals. Further, studies suggest that neuronal connections between ASI and AWC neurons are allowed at least partially through ASI secreted DAF-7 or through alternate TGF- β pathway/s regulated by EXP-1 and STR-2. Together, our behavioral, genetic and imaging experiments propose that EXP-1 and STR-2 integrate food cues and allow the animals to display DAF-7/TGF-β neuroendocrine dependent or independent behavioral responses contributing to chemosensensory and developmental plasticity.

Key words: ASI neuron; *C. elegans*; chemotaxis; dauer; EXP-1; STR-2

Significance Statement

This work sheds light on a possible developmental and postdevelopmental function for the excitatory GABA receptor, EXP-1. We show that mutants of *exp-1* are defective in their response toward AWC-sensed odors. Our genetic, behavioral and expression studies reveal that EXP-1 functions in the ASI neuron to modulate chemosensation and to regulate the behavioral switch between dauer and the reproductive state. EXP-1 has been shown to function in a DAF-7/TGF-β-dependent manner. However, in the absence of DAF-7/TGF-β, EXP-1, and a G-protein-coupled receptor (GPCR), STR-2 integrate sensory information to maintain the reproductive state of the animal through an ASI-dependent alternate pathway.

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The authors declare no competing financial interests.

Author contributions: P.P. designed research; P.P., U.S.B., A.S., A.J., and V.B. performed research; P.P. and N.Y.K. contributed unpublished reagents/analytic tools; P.P. and K.B. analyzed data; P.P. and K.B. wrote the paper.

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Ethanol Induced Sedative Behavior: An assay to investigate increased dopamine signaling in *C. elegans*

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[Abstract] Dopamine signalling affects locomotion, feeding, learning and memory in *C. elegans*. Various assays have been developed to study the proteins involved in these behaviours. However, these assays show behavioural output only when there is major change in the dopamine levels. Thus, we decided to design an assay where we could observe behavioural output even with low levels of alteration in dopamine levels. To achieve this, we combined movement assay with ethanol that is also known to function through dopamine pathway. We successfully utilized this assay to assign function for a dopamine autoreceptor, DOP-2. This assay correlates the increase in dopamine levels due to ethanol and movement obstruction due to dry surface into a circular sedative behaviour that we designated as Ethanol Induced Sedative (EIS) behaviour.

Keywords: EtOH (Ethanol), *C. elegans*, Dopamine, sedative behavior

[Background] Alcohol is widely used abusive drug with a plethora of associated diseases and societal devastations. Multiple studies have focused on unravelling the mode of action and effect of this drug. However, the behavioural response to alcohol and susceptibility to alcohol use disorders (AUDs) varies, since they are dependent upon environmental as well as physiological and genetic differences amongst individuals. Studies across various species have demonstrated that alcohol intake increases the release of the neurotransmitter dopamine that induces the reward pathway (Baik, 2013; Imperato and Di Chiara, 1986; Weiss *et al.*, 1993). The dopamine system in *C. elegans* is involved in feeding, movement, learning and memory. Dopamine functions through two types of receptor subfamilies D1-like and D2-like receptors. The D2-like receptor, DOP-2, was found to have a weak phenotypes when analysed for dopamine dependent behaviours (Chase *et.al.*, 2004). Hence, DOP-2 dependent functions were largely unknown. We devised an ethanol dependent movement assay to investigate the neuronal circuitry that might play a role in regulating locomotory behaviour under the influence of ethanol (Pandey *et. al.*, 2021). *C. elegans* has already been used to study the important aspects of ethanol abuse, such as acute tolerance, withdrawal behaviour, neuronal effect and there is a dose dependent decline in the locomotor activity upon acute exposure to the depressive effect of ethanol and it corresponds with the (Davies *et. al.*, 2003) mammalian internal dose of ethanol (Lee J *et. al.*, 2009). Although *C. elegans* can't mimic all the complexities of the mammalian system, it has been modelled for studying some A lot of other