

Research Project for which
“Raman Research Fellowship”

was Awarded by CSIR (2015)

Expression of Class-III histone deacetylase in alpha synuclein expressing *C.*

***elegans* model: Studies on Dopaminergic neurodegeneration in context of**
Parkinson's disease.

The phenomenon of aging is known to modulate many disease conditions including neurodegenerative ailments like Parkinson's disease (PD) which is characterized by selective loss of dopaminergic neurons. Recent studies have reported on such effects, as calorie restriction, in modulating aging in living systems. We reason that PD, being an age-associated neurodegenerative disease might be modulated by interventions like calorie restriction. In the present study we employed the transgenic *Caenorhabditis elegans* model (P(dat-1)::GFP) expressing green fluorescence protein (GFP) specifically in eight dopaminergic (DA) neurons. Selective degeneration of dopaminergic neurons was induced by treatment of worms with 6-hydroxy dopamine (6-OHDA), a selective catecholaminergic neurotoxin, followed by studies on effect of calorie restriction on the neurodegeneration. Employing confocal microscopy of the dopaminergic neurons and HPLC analysis of dopamine levels in the nematodes, we found that calorie restriction has a preventive effect on dopaminergic neurodegeneration in the worm model. We further studied the role of sirtuin, sir-2.1 (a class-III histone deacetylase), in modulating such an effect. Studies employing RNAi induced gene silencing of nematode sir-2.1, revealed that presence of Sir-2.1 is necessary for achieving the protective effect of calorie restriction on dopaminergic neurodegeneration. Our studies provide evidence that calorie restriction affords, an sir-2.1 mediated, protection against the dopaminergic neurodegeneration, that might have implications for neurodegenerative Parkinson's disease.

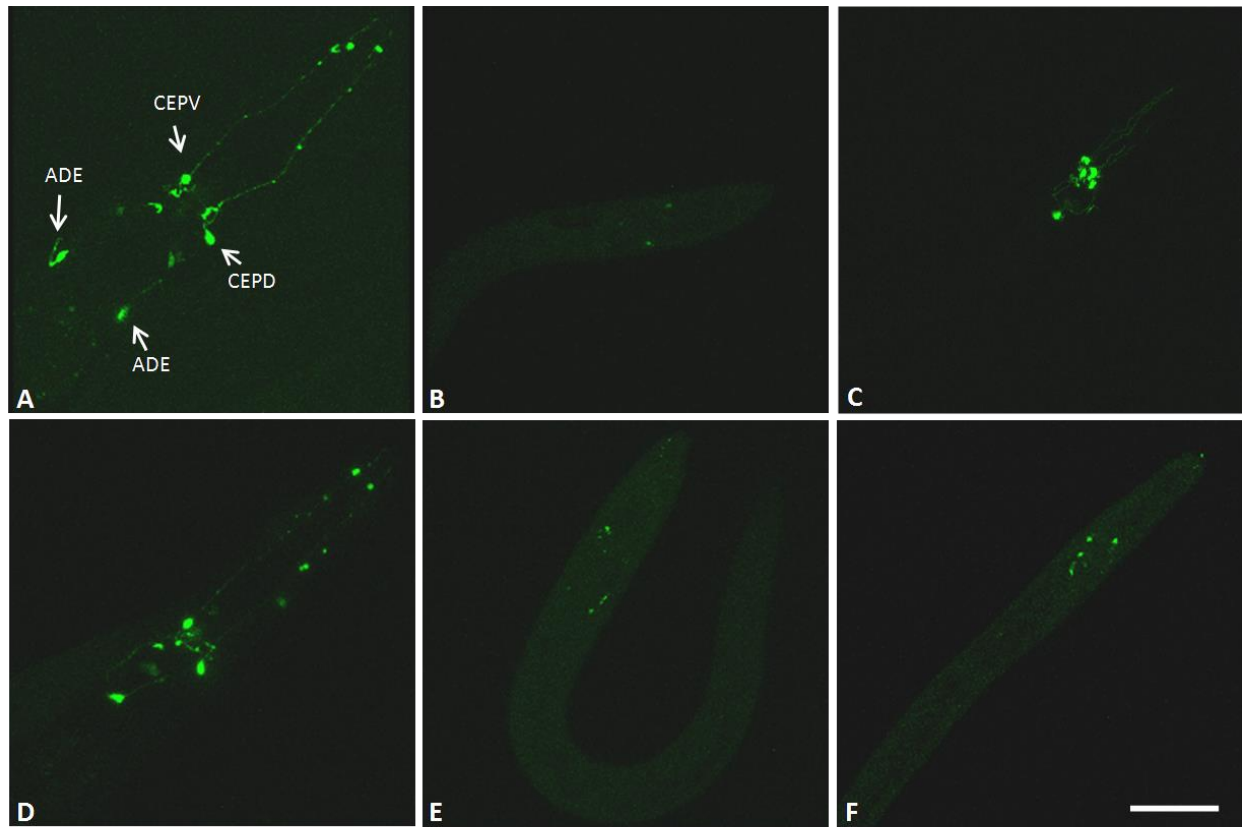


Figure: GFP expression pattern in dopaminergic neurons of transgenic *C. elegans* strain ($P_{dat-1}::GFP$). Control (A), 6-OHDA treated (B), 6-OHDA treated worms raised on reduced calorie diet (C), Worms with RNAi induced gene silencing of sir-2.1 (D) sir-2.1 silenced worms exposed to 6-OHDA (E) and sir-2.1 silenced worms exposed to 6-OHDA, raised on reduced calorie diet (F). Scale bar, 50 μ m.

Highlight of the findings:

Expression of Sirtuin (sir-2.1, the *C. elegans* orthologue of mammalian Sirt1) via calorie restriction, exerts neuroprotective effects.