Lower Mainland's 9th Nematode Regional Research Review

Wednesday, Jan. 17th, 2007

Hosted by the Leroux/Hawkins Labs
South Science Building
Rm 7172

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Itinerary:

(1) 5:30 pm - Introduction

Update from the NRRR Committee

(2) 5:35 pm – Talks

(A) Andrew Giles - The role of dopamine in mechanosensory habituation in *Caenorhabditis elegans*

(B) Victor Jensen - A DAF-16 target involved in longevity

(C) Dr. Jack Chen - Identification of ciliary and ciliopathy genes in the nematode *Caenorhabditis elegans* through comparative genomics

(3) 6:30 pm - Food/Beverages

Pizza (courtesy of Leroux/Hawkins Labs)

Drinks (courtesy of Invitrogen)

Abstracts:

Presenter: Andrew Giles from the Rankin Lab

The role of dopamine in mechanosensory habituation in *Caenorhabditis elegans*.

Caenorhabditis elegans have been shown to possess both short- and long-term memory for habituation of the tap withdrawal response. Recent evidence suggests that a D1-like dopamine receptor homolog gene is expressed in the mechanosensory neurons of the tap withdrawal circuit. We hypothesized that dopamine might play an important role in modulating this circuit and therefore could play a role in habituation of the tap withdrawal response. Mutant strains of *C. elegans* with deficits at dopaminergic neurotransmission were found to have food-dependent deficits for the modulation of short-term habituation of the frequency but not magnitude of response. Further mutant analysis suggests this effect is mediated by the phospholipase C-_ signaling pathway. *In vivo* calcium imaging of the mechanosensory neurons of the tap withdrawal circuit indicates that the modulation affects the whole cell excitability of the anterior neurons. We have also found that deficits in dopamine signaling completely abolition the formation of long-term memory for habituation. We are currently investigating whether the long-term effects of dopamine are mediated by the same signaling cascade and whether the neural activity in the mechanosensory neurons is altered by this dopamine effect after training for long-term memory.

Presenter: Victor Jensen from the Riddle Lab

A DAF-16 target involved in longevity

Genes differing in steady-state RNA levels between wild-type N2 and *daf-2* adults and N2 dauer larvae were identified using Serial Analysis of Gene Expression (SAGE). One gene (*zip-5*), encoding a basic leucine zipper transcription factor, was identified by screening our candidate longevity genes using RNAi. A knockout strain has extended longevity (~40% increase in mean life span at 25 ºC) compared to N2. A double mutant with *daf-2*(e1370) was shown to have no significant increase in longevity relative to *daf-2* alone, suggesting that the *zip-5* effect on life span is *daf-2* dependent. 1 kb of genomic sequence 5' of the confirmed *zip-5* SL1 splice site contains a possible DAF-16 binding site as well as three GATA motifs. By using a series of truncated promoters to drive GFP expression, in vivo activity for these DAF-16 binding sites was observed. One DBE (DAF-16 Binding Element) consensus site, found only once at -492bp, appears to repress transcription. This is in agreement with the SAGE data showing down-regulation of this transcription factor in an activated DAF-16 background. In addition, RNAi against *daf-16* on a strain expressing a ZIP-5::GFP fusion protein shows increased expression over the control. By contrast, the GATA motifs are required for transcription. RNAi for the GATA transcription factor *elt-2* was shown to reduce reporter gene expression. *zip-5* appears to antagonize long life and its inhibition by DAF-16 may be responsible for a portion of the *daf-2* longevity phenotype.

Abstracts (continued):

Presenter: Dr. Jack Chen

Identification of ciliary and ciliopathy genes in the nematode *Caenorhabditis elegans* through comparative genomics

The recent availability of genome sequences of multiple related *Caenorhabditis* species has made it possible to identify, using comparative genomics, similarly transcribed genes in *Caenorhabditis elegans* and its sister species. Taking this approach, we have identified numerous novel ciliary genes in *C. elegans*, some of which may be orthologs of unidentified human ciliopathy genes.By screening for genes possessing canonical X-box sequences in promoters of three *Caenorhabditis* species, namely *C. elegans*, *C. briggsae* and *C. remanei*, we identified 93 genes (including known X-box regulated genes) that encode putative components of ciliated neurons in *C. elegans* and are subject to the same regulatory control. For many of these genes, restricted anatomical expression in ciliated cells was confirmed, and control of transcription by the ciliogenic DAF-19 RFX transcription factor was demonstrated by comparative transcriptional profiling of *daf-19(+)* and *daf_9(-)* animals. Finally, we demonstrate that the dye-filling defect of *dyf-5* (*mn400*) animals, which is indicative of compromised exposure of cilia to the environment, is caused by a nonsense mutation in the serine/threonine protein kinase gene M04C9.5. Our comparative genomics-based predictions may be useful for identifying genes involved in human ciliopathies, including Bardet-Biedl Syndrome (BBS), since the *C. elegans* orthologs of known human *BBS* genes contain X-box motifs and are required for normal dye filling in *C. elegans* ciliated neurons.

The Lower Mainland Collective of *Caenorhabditis elegans* Researchers

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NRRR organizing committee

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Special Thanks to **our volunteer presenters** and all those who helped organize this event

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