VanWoRM

Vancouver Worm Research Meeting

Wednesday, February 27th, 2008

5:00 pm

South Science Building

Room 7172

8888 University Drive, SFU

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Itinerary:

5:00 pm - Introduction

Update from the NRRR Committee

5:10 pm – Talks

Andreas Steimel - The non-classical cadherin FMI-1 is involved in pioneer-follower axon guidance in the ventral cord of *C. elegans*

Yang Zhao - DOG-1's role in genome stability in *Caenorhabditis elegans*

6:00 pm - Food/Beverages

Pizza (courtesy of Macrogen)

Drinks (courtesy of Invitrogen)

Abstracts:

The non-classical cadherin FMI-1 is involved in pioneer-follower axon guidance in the ventral cord of *C. elegans*

Andreas Steimel (Hutter Lab)

The ventral cord of *C. elegans* is the main nerve connection along the anterior-posterior body axis. The two ventral cord axon tracks are established through the sequential outgrowth of pioneer and follower axons. The PVP axon pioneers the left axon track closely followed by the PVQ axon. PVP and PVQ axons are characterized by a tight pioneer-follower relationship. In an EMS screen for animals with defects in ventral cord axon guidance we isolated the *fmi-1* allele *rh308* (1). *fmi-1(rh308)* animals display strong PVP and PVQ axon guidance defects. Interestingly the pioneer-follower relationship between PVP and PVQ axons is disrupted in *fmi-1(rh308)* animals. Independent of the PVP axons the PVQ axons cross the ventral midline, leave the ventral cord or stop prematurely in 98 % of *fmi-1(rh308)* animals. HSN axons as PVP- followers are similarly affected. In a separate EMS screen for defects in HSN axon guidance performed by the Garriga Lab two *fmi-1* alleles were isolated. In 68% of *fmi-1(rh308)* animals HSN axons fail to join the ventral cord axon tracks and circle around the vulva. Moreover HSN axons stop outgrowth before reaching the head region in nearly all *fmi-1(rh308)* animals. Interneuron axons that extend along pioneers in the right axon track are affected in 31 % of *fmi-1(rh308)* animals.

The non-classical cadherin FMI-1 is the *C. elegans* homologue of *Drosophila* Flamingo and vertebrate CELSR1,2 and 3. FMI-1 is characterized by a unique domain composition with eight cadherin repeats, laminin G and EGF modules and a G-protein coupled receptor domain. *Drosophila* Flamingo functions in the planar cell polarity (PCP) pathway, axon target selection in the eye and establishment and maintenance of dendrites. Similarly CELSR2 and 3 mediate maintenance of dendrites and establishment of axonal tracks in mouse respectively (2).

To characterize the expression pattern of *fmi-1* we generated a 2.6 kb *fmi-1*-promoter GFP reporter construct. This construct is mainly expressed in neurons among them PVP, PVQ and HSN. Expression starts shortly after gastrulation before axons grow out, persists throughout all larval stages and decreases noticeably in adults. To determine the subcellular localization of FMI-1 we fused the *fmi-1* transcript to GFP. FMI-1::GFP is predominantly localized to axons and is able to rescue PVQ defects in *fmi-1(rh308)* animals.

Currently we are investigating the function of *fmi-1* in pioneer-follower axon guidance via mosaic analysis and targeted gene expression. We are performing a domain analysis and are searching for downstream effectors of *fmi-1*.

DOG-1's role in genome stability in Caenorhabditis elegans

Yang Zhao (Rose Lab)

The dog-1 strain of C. elegans causes mutations at poly-G/poly-C tracts, most likely as a consequence of unresolved replication blocks during S phase. Previous work has described short deletions associated with these tracts; however the full range of mutational consequences has not been explored. I have used the eT1 balancer system in a dog-1 mutant background to screen for lethal mutations. Mutation frequency in dog-1 mutants was 10 fold higher than the spontaneous mutation rate observed in wild-type worms. Mutations recovered from this system were analyzed by a variety of genetic and molecular mapping approaches, including genetic complementation, SNP, and the powerful array comparative genome hybridization (aCGH) technique. Several types of mutations were observed. In addition to the small deletions reported previously, I observed and characterized large chromosome rearrangements, demonstrating that loss of DOG-1 function results in chromosome instability (CIN), which is a hallmark of many types of human tumors. Most of these mutations are associated with G/C tracts. Recently, Youds, et al showed that the dog-1 gene is a homolog of the human Fanconi anemia gene FancJ. Fanconi anemia is a cancer susceptibility syndrome characterized by sensitivity to interstrand crosslinks (ICL). While many of the components of the FA pathway have been identified, little is known about how these proteins maintain genomic stability. Characterization of the mutational spectrum of the dog-1 strain will provide insights into repair defects associated with Fanconi anemia. The existence of the G/C tracts in C. elegans creates a fortuitous but perplexing problem. In the genome of C. elegans, G/C tracts exist at high frequency and they are distributed along every chromosome in a non-random pattern. Most G/C tracts are within introns or are close to genes and analysis of SAGE data showed that G/C tracts correlate with the levels of regional gene expression in C. elegans. G/C tracts are over-represented and dispersed across all chromosomes in another Caenorhabditis species, C. briggsae. However, the positions and distribution of G/C tracts in C. briggsae differ from those in C. elegans. The abundance and genomic distribution of G/C tracts in C. elegans, the effect of G/C tracts on regional transcription levels, and the lack of positional conservation of G/C tracts in C. briggsae suggest an intriguing role for G/C tracts in the functional organization of chromosomes. .