VanWoRM

Vancouver-area Worm Research Meeting

Wednesday, October 1st, 2008

4:30 pm

Academic Quadrangle

Room 3003

Simon Fraser University

Sponsored by:

MACROGEN

and

Fisher Scientific

Itinerary:

4:30 pm - Introduction

4:35 pm – Talks

(1) **Victor Jensen** - A screen of putative DAF-16/FOXO target genes for novel SynDaf genes reveals a connection between dauer formation and innate immunity

(2) Adam Warner - An update on the role of paxillin in *C. elegans* muscle, and an introduction to high throughput RNAi screening for muscle affecting genes

(3) Nick Inglis - Piecing together the mechanism of IFT via analysis of distinct modules

6:00 pm - Food/Beverages

Pizza (courtesy of Macrogen)

Drinks (courtesy of Fisher Scientific)

Abstracts:

(1) A screen of putative DAF-16/FOXO target genes for novel SynDaf genes reveals a connection between dauer formation and innate immunity

Victor Jensen (Riddle Lab)

The DAF-16/FOXO transcription factor is the major downstream output of the insulin/IGF1R signaling pathway in *C. elegans* for lifespan and dauer formation. To determine the effects of DAF-16 target genes on dauer formation, we tested previously identified candidate genes putatively regulated by DAF-16. We used RNAi in a sensitized background [*eri-1(mg366); sdf-9(m708)*], which enhances RNAi and constitutive dauer formation (Daf-c). Among 515 genes tested, 22 have a synthetic Daf-c (SynDaf) phenotype with *sdf-9*. Two of these genes are previously identified SynDaf genes. Five other genes are involved in processes known to affect dauer formation. Two of the 22 genes are known to participate in innate immunity, and six more are predicted to be involved. The latter result suggests that disrupting the immune response may contribute to dauer formation. When grown on bacteria that are pathogenic to *C. elegans*, *daf-8* and *sdf-9* show a stronger Daf-c phenotype. This indicates that dauer formation is a response to pathogen exposure, in addition to the well-known environmental cues of population density, food supply and temperature.

(2) An update on the role of paxillin in *C. elegans* muscle, and an introduction to high throughput RNAi screening for muscle affecting genes

Adam Warner (Moerman Lab)

Attachment of actin and myosin filaments to dense bodies and M-lines respectively is necessary to convert the force generated by sliding myofilaments into movement of the worm. Not surprisingly, worm muscle attachment complexes contain many of the same protein components as vertebrate focal adhesion complexes, which rely on anchoring of actin filaments for movement of migrating cells over the extracellular matrix. One of the major focal adhesion components, paxillin, had not previously been identified in the worm. I will describe work that demonstrates such a protein is present in the worm, plays an important role in muscle, and is homologous to full length paxillin in humans and other species.

The paralyzed and arrested at two-fold stage of embryogenesis (Pat) phenotype is observed when genes essential for the initial assembly of the sarcomere, or involved in the attachment of muscle cells to the basement membrane are disrupted (Williams and Waterston, 1994). Notable Pat genes include the beta-integrin homolog *pat-3* (Gettner et al. 1995), the perlecan homolog *unc-52* (Rogalski et al. 1993), and the vinculin homolog *deb-1* (Barstead et al. 1991), among others. In order to identify novel Pat genes, our lab is screening over 3000 genes found to be expressed in body wall muscle in both SAGE and microarray experiments (Moerman lab, unpublished; Fox et al. 2007). Wild type worms, along with hypomorphic mutant strains of *unc-97* and *unc-95* are being screened. Our results to date, and methodology will be discussed.

Abstracts:

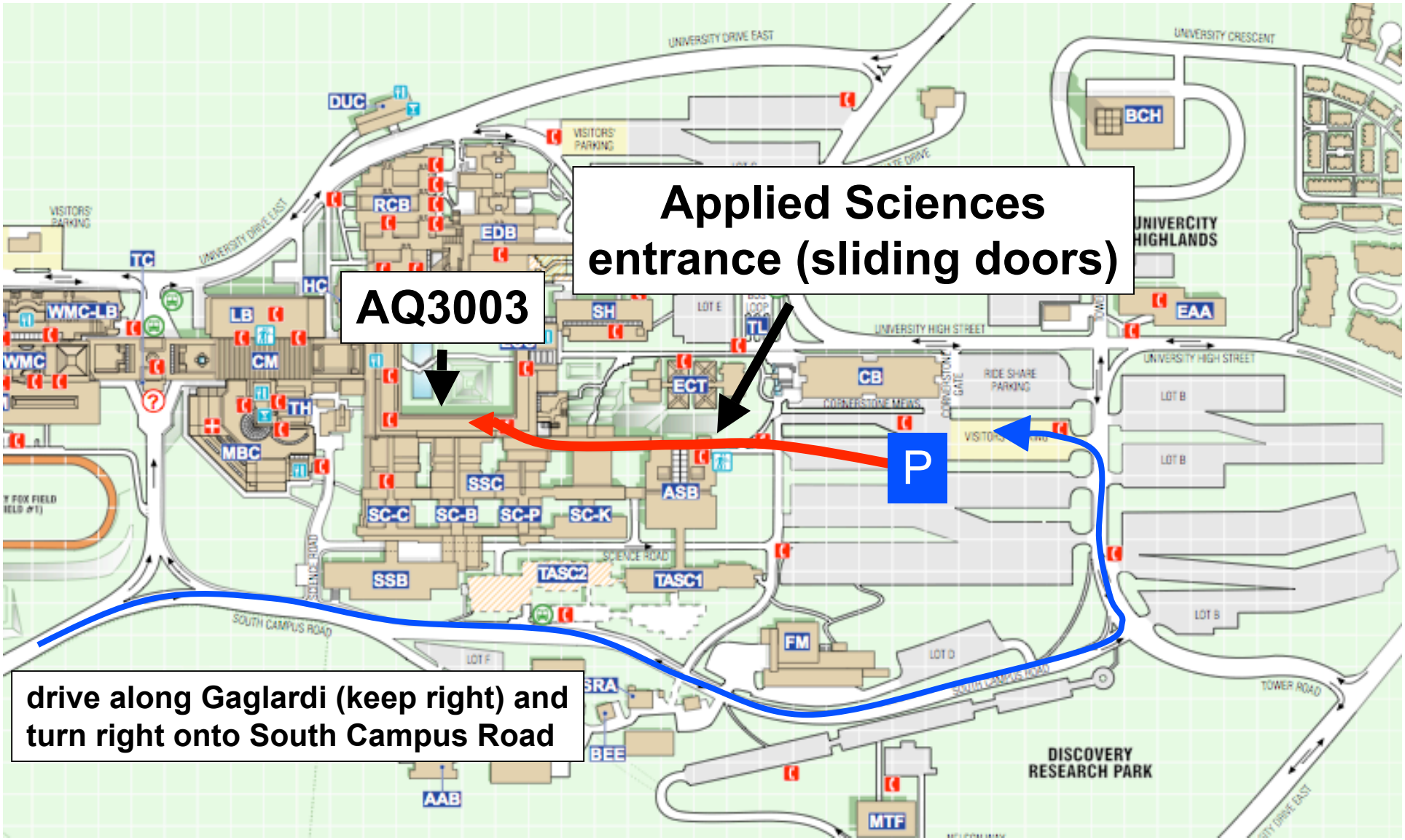
(3) Piecing together the mechanism of IFT via analysis of distinct modules

Nick Inglis (Leroux Lab)

Intraflagellar transport (IFT) is the bidirectional process required for the building and maintenance of eukaryotic cilia. The core IFT machinery, consisting of microtubule motors and a complex of highly conserved proteins, carries structural and membrane proteins to and from their presumptive sites of action. Mechanistically, IFT can be divided into several modules: (1) the assembly of the IFT particle at the basal body (the centriolar structure nucleating the cilium), (2) the Kinesin-2-driven anterograde IFT, which carries IFT particles to the distal tip of the structure, (3) the Dynein-driven retrograde IFT, in which the remainder of the IFT particle and older ciliary proteins are returned to the basal body, and (4) the disassembly of the IFT particle at the base of the cilium. The nematode *Caenorhabditis elegans* has rapidly emerged as an excellent model system in the study of cilia and IFT. Its cilia are non-motile, and are restricted to a subset of sensory neurons in the head and tail. Nematode cilia are more complex than the canonical ciliary structures found in mammalian sperm or *Chlamydomonas* cells, and are reminiscent of vertebrate sensory cell types, including photoreceptors.

For the most part, ciliary research in *C. elegans* has been focused on the process and regulation of anterograde IFT. My presentation will address two of the other primary IFT modules. First, we have identified a new class of genes that appear to be regulating the 'docking' of membrane proteins onto the IFT particle at the base of cilia, and are thus required for specific sensory/signalling processes. These genes, which have previously been associated with diseases such as Meckel-Gruber Syndrome, are found exclusively in ciliated organisms, and are strictly associated with basal bodies. In the second part of my presentation, I will discuss new experimental approaches we are employing to examine the mechanism of retrograde IFT, including a genetic screen for retrograde IFT-specific mutants, as well as a brief overview of the challenges of, and approaches to, piecing together the retrograde-IFT 'jigsaw puzzle.'

Please see attached map to AQ3003 on the next page



-Try to park in the visitor parking lot close to the ‘blue/white P’ on the map.
-AQ3003 is located in the centre of the Southern Concourse of the Academic Quadrangle opposite of the vending machines.
-The meeting starts at 4:30 pm.