Name and Title: Dr. Thomas Hurd, Assistant Professor
Department: Molecular Genetics

TITLE OF RESEARCH PROJECT: Determining How Deleterious Mitochondrial DNA Mutations Are Eliminated

Number of 299Y Spots: 1  Number of 399Y Spots: 1

OBJECTIVES AND METHODOLOGY:

Background
Unusual among organelles, mitochondria have their own genomes, which encode a small number of essential genes. Unlike nuclear genes, we inherit these mitochondrial genes only from our mothers. Given the importance of these genes, mothers have evolved mechanisms to ensure they pass on good, mutant-free copies to their progeny. Without such mechanisms deleterious mutations would accumulate from one generation to the next ultimately causing the collapse of the species. Exactly what the molecular nature of these selection mechanisms is remains obscure, despite their fundamental importance. In this proposal we seek to understand how these selection mechanisms work on a molecular level.

The medical importance of these mechanisms is demonstrated by the damage caused later in life by mutations in the mitochondrial genome. While a mother may succeed in ensuring we start life with good mitochondrial genes, mutations nonetheless inevitably arise in those genes as we age. This causes disease in people, most often neurological, affecting on the order of 1 in 4,300. By understanding how mothers prevent deleterious mitochondrial genes from being inherited, we aim to develop strategies to eliminate these bad mutations and the diseases they cause as we age.

Objectives
The goal of this research project is to identify genes and pathways necessary for the elimination of deleterious mitochondrial DNA mutations.

Methodology
The students will assist in the development of a high-throughput quantitative PCR (qPCR) assay to measure wildtype and mutant mitochondrial DNA in a Drosophila melanogaster model. The students will then use this assay and RNAi to knockdown genes one by one to determine which are necessary for the elimination of deleterious mitochondrial DNA mutations. Lastly, if time-permits, the students will validate the ‘hits’ from the above RNAi screen by generating null mutations in candidate genes using CRISPR/Cas9.
**Suggested Reading**

**DESCRIPTION OF STUDENT PARTICIPATION:**
This project is ideally suited to motivated students interested in gaining research experience for graduate school. The students will work under the direct supervision of Dr. Hurd and a graduate student in the lab. The students will be expected to participate in all aspects of the research process including: reading appropriate background literature; helping to design and plan experiments; conducting experiments on a semi-independent basis, with the expectation of increased independence as the project progresses; keeping accurate and thorough records of their experimental work; and participating in regular (bi-weekly) lab meetings.

The students will be exposed to a variety of genetic, biochemical and molecular biology methods that are widely applicable to a range of experimental disciplines. These include:

1. Quantitative PCR  
2. Gene knockdown using RNAi  
3. Molecular cloning  
4. Drosophila genetics/husbandry  
5. CRISPR/Cas9

Additionally, students should expect to learn how to present their data as publication-quality figures, and to improve their ability to communicate their research clearly and concisely, both orally and in writing.

**MARKING SCHEME (assignments with weight and due date):**

1. **Research Proposal (10%; due 2 weeks after project start):**  
   Students will prepare a 2-4 page written summary of their research project, which will include background, hypothesis, aims, methods, predicted outcomes and significance.

2. **Attendance, work ethic and participation in the lab and in meetings (20%; throughout)**

3. **Experimental lab work (20%; throughout)**  
   Students will be evaluated on their ability to conduct experiments, and to analyze and interpret the data generated.

4. **Lab notes and organization (20%; throughout)**  
   Students will be evaluated on their ability to keep organized and detailed experimental records, which will include aims, methods, results and interpretation.

5. **Final Project Presentation (15%; due mid-July or mid-October)**  
   Students will present their research objectives, results and future directions to the lab (20 minutes), followed by a questions discussion period. Students will be evaluated on their presentation skills and ability to answer questions related to their research project.

6. **Final Research Report (15%; due at noon on the last day of term)**  
   Students will provide a 5-10 page written report describing the background and rationale for the research project, experimental methods, results and interpretation, conclusions and future directions.
Name and Title: Derek van der Kooy
Department: Molecular Genetics

TITLE OF RESEARCH PROJECT: Learning and Memory in C. elegans.

Number of 299Y Spots: 1 Number of 399Y Spots: 1

OBJECTIVES AND METHODOLOGY:
Our goal is to use the power and specificity of modern molecular genetics to reveal the component processes of learning and memory. In undertaking a mutational screening approach to learning and memory, we have taken advantage of the best-known multicellular organism, the nematode C. elegans. C. elegans has proven to be an excellent molecular model for mammalian (including human) biochemical functions. We will use the C. elegans learning and memory genes discovered to find their relevant mammalian homologues. Most important, the C. elegans mutants should allow us to ask if we can separate associative from non-associative learning, short from long-term memory, and learning and memory in one sensory modality from that in another sensory modality.

DESCRIPTION OF STUDENT PARTICIPATION:
10 hours per week: The students will participate in the initial screens for new learning mutant worms, as well as all of the behavioural testing to determine if the deficits are in learning, memory storage of the recall of memories. ROP students can expect to learn such skills as standard lab operating procedures, including: sterile techniques, biosafety-level 1, and how to collect and analyze data. In many cases, students will also learn academic collaboration protocols, including how to work with their peers and with other labs.

Technical skills will include: autoclaving, microscopy, screening, preparing solutions and running behavioural assays, pipetting, pouring plates, DNA analysis, breeding worms, and how to critically analyze data. The application of these skills will be relevant in all laboratory settings and especially important to understanding how to analyze, interpret and present data. ROP students will also be asked to present their data at our weekly lab chalk-talk and to participate in weekly journal club meetings.

MARKING SCHEME (assignments with weight and due date):

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<thead>
<tr>
<th>Assignment</th>
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<tbody>
<tr>
<td>Journal and/or documentation of research process</td>
<td>10%</td>
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<tr>
<td>Attendance at weekly Breakfast Club Meeting</td>
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<tr>
<td>Attendance at weekly Wormies group journal club</td>
<td>10%</td>
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<td>Activity</td>
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<tr>
<td>Oral presentation of results at weekly Wormies meeting</td>
<td>10%</td>
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<tr>
<td>2 page written summary near the end of the course, Aug 15, 2019</td>
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<tr>
<td>Final oral presentation of results to entire lab on Aug 26, 2019</td>
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<tr>
<td>ROP FORUM Presentation</td>
<td>10%</td>
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RESEARCH OPPORTUNITY PROGRAM
299Y/399Y PROJECT DESCRIPTIONS 2019-2020
SUMMER

Name and Title: Mei Zhen
Department: Molecular Genetics

TITLE OF RESEARCH PROJECT: EM Reconstruction of the C. elegans Developing Connectomes

Number of 299Y Spots: 2

OBJECTIVES AND METHODOLOGY:
How do neuronal circuits develop and remodel as animals progress from birth to adulthood? How do they function robustly to help an animal respond appropriately to complex cues? These are challenging questions to answer in humans, with 80-100 billion neurons in the adult brain. In order to fully understand how neuronal circuits work to regulate behaviours we need to know how the circuits are wired, and how circuit activity is modulated. The fundamental processes and the rules that govern neuronal circuit formation and function are well conserved between humans and the small nematode worm, Caenorhabditis elegans. C. elegans larvae are born with 220 neurons, increasing to 302 neurons by the time the worm reaches adulthood. We have been using serial-section electron microscopy (EM) and computational approaches to map the entire nervous system of young larval animals at synaptic resolution. This work has resulted in a dataset consisting of full reconstruction of the nervous systems of multiple animals, at multiple developmental stages, which we are using to extract principles about nervous system development. The insights from this project are being used to further our understanding of how a nervous system forms and remodels across development, and how neuronal circuits work together to mediate complex behaviours.

DESCRIPTION OF STUDENT PARTICIPATION:
The successful students will have the opportunity to:
1. Assist with using the electron microscope to take high-resolution images of the nervous system
2. Assist tracing neurons and identifying, and processing electron microscopy data
3. Participate in the lab research environment and lab meeting schedule

MARKING SCHEME (assignments with weight and due date):
• 20% - 4-8 page report due Aug. 25th 2019 (double spaced, including Introduction, aim/hypothesis, methods, results, discussion, references (standard journal format).
• 20% Oral presentation before Aug. 25th 2019 for the project
• 10% participation in weekly lab meetings (duration of project)
• 30% lab competency
• 20% good recording of data