Molecular Genetics
UNIVERSITY OF TORONTO

# MoGeNews

Issue 13 - Apr 2019

## Editor's message

First and foremost, we are highlighting the upcoming **50th Anniversary Symposium on May 31, 2019**. We are extremely excited to reunite the members of our community and share in the history and accomplishments of the Department. **We have extended the registration deadline to May 15! Please join us and register here.**

In addition to an exceptional lineup of invited speakers, the symposium will feature a career development workshop during lunch and exciting entertainment during the dinner reception, organized by our graduate student community. We also invite all alumni and current members of Molecular Genetics to contribute memories about your time and experience in the Department, which we are collecting and sharing on

the MoGen website. Please read below and visit our 50th Anniversary website.

As always, please keep us posted on discoveries, awards and achievements. Your input is crucial as we continue to build an engaged community.

Barbara Funnell

***



## Table of Contents

**1. 50th MoGen Anniversary Party!** Program, career workshop lunch, dinner reception, and entertainment
**2. Career Development in Molecular Genetics**
**3. Community News and Events:** M.H.Sc. program update, MoGen holiday bash, March recruitment day, St. Patrick's Day pub night, Arcade night, Future GSA events

\*\*\*

**Department of Molecular Genetics
50th Anniversary**

**50th Anniversary Symposium**
**May 31, 2019**
**The Carlu**
444 Yonge St.
Toronto, ON M5B 2H4

Please join us! All current and former members of Molecular Genetics are invited. Come and visit old friends and make new ones. Program registration includes an exceptional lineup of talks, a career development workshop and lunch, and a dinner reception that includes exciting entertainment organized by the graduate students. It is not to be missed! Please register here; the deadline has been extended to May 15.

**Program:**
8:00 a.m. — Registration (Badge pick-up)
8:30 a.m. to 5:30 p.m. — Scientific Symposium and
Career Development Lunch
5:30 p.m. — Dinner Reception & Entertainment

**Speakers:**
*Keynote presentations:*
**Dr. Lap-Chee Tsui**, President, The Academy of Sciences of Hong Kong; Director, Qiushi Academy for Advanced Studies, Zhejiang University
**Dr. Roderick McInnes**, Director, Lady Davis Institute; Professor of Human Genetics and Biochemistry, McGill University

*PhD alumni speakers:*
**Dr. Angela Andersen**, Life Science Editors
**Dr. Anastasia Baryshnikova**, Calico Labs
**Dr. Cheryl Birmingham**, Sanofi Pasteur
**Dr. Joseph Bondy-Denomy**, University of California-San Francisco
**Dr. Arvin Dar**, Icahn School of Medicine at Mount Sinai, NY
**Dr. Scott Dixon**, Stanford University
**Dr. Kristin Hope**, McMaster University
**Dr. Christopher Koth**, Genentech
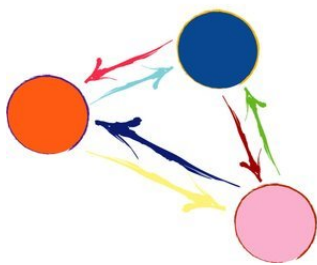**Dr. Tina McDivitt**, Spindle Strategy
**Dr. Pleasantine Mill**, University of Edinburgh
**Dr. E. Elizabeth Patton**, University of Edinburgh

**Please visit the 50th Anniversary website for a full program and more details about the day.**

With thanks to our sponsors: Lunenfeld-Tanenbaum Research Institute, Sinai Health System; Donnelly Centre for Cellular + Biomolecular Research; SickKids Research Institute; LALLEMAND; McLAUGHLIN CENTRE; OICR Ontario Institute for Cancer Research

\*\*\*



**Career Development Workshop and Lunch**
As part of our day of science and celebrations, we will be holding a **Trainee-Alumni Mentorship** session over the lunch period. This event is organized by MoGen students, and is a wonderful networking opportunity for members of the department.

The goal of this session is to connect current trainees with alumni who have gone on to pursue exciting careers in a wide variety of fields. We hope this casual setting will facilitate discussion including personal anecdotes about career choices, struggles, and successes.

**We invite all alumni to participate as mentors for current trainees.** To manage the event, alumni will be categorized into six distinct career fields including:

- Policy, Government, and Law
- Science Communication and Writing
- Academic Research
- Science Education
- Biotechnology and Industry
- Medical Professional Programs

Please click here to read more.

***

## MoGen Stories

**Please share MoGen memories with our friends, colleagues and alumni:**
To commemorate our 50th year, we are looking for short commentaries on your time in the Department, on any aspect that you think would be nice to share with the rest of our community. We will post as many as possible on the MoGen website. Please

[submit your story and read our collection here](#).

\*\*\*

## Career Development in Molecular Genetics

**Looking back on five years of MoGen Career Development.**
Five years ago MoGen students and faculty members came together to fill a vacancy in the expansive MoGen programming, to provide initiatives to educate

graduate students on the many facets of career development. Although there were organizations on campus such as the Life Sciences Career Development Society (LSCDS) that provided considerable resources in this area, there was a dearth of specialized programming focused on careers for which a MoGen degree would prepare students.

This sparked the start of the MoGen Career Development Workshop Series, student-led monthly workshops that educate trainees about the multitude of career options available to them and provide opportunities for skill building and networking to help trainees achieve their career goals. Now in their fifth year, these workshops have showcased the plethora of careers that MoGen alumni pursue including academia, industry, consulting, non-profit, government, law, science communication, medical writing and more. These workshops are designed by trainees for trainees, and provide students with the invaluable experience of hosting or planning workshops in career areas.

These monthly workshops culminate each year in a faculty-led, MoGen Career Development Symposium. The annual event connects MoGen trainees directly with illustrious MoGen alumni, through panel discussions, round table mentoring and networking sessions. Over the past four years, the MoGen Career Development Symposia have provided insightful career education, and created and fostered countless meaningful connections among students and alumni.

Recently, these initiatives have been complemented by co-curricular topic courses geared towards career development. "Graduate Professional Development for Scientists" and "The Ins and Outs of Life Sciences Entrepreneurship" are taught by MoGen alumni Dr. Bruce Seet and Dr. Fredrick Sweeney, respectively, and have given MoGen students the chance to build their career skills in a classroom setting, while being guided by professionals.

Together, the MoGen career development initiatives provide invaluable opportunities for students to explore the careers that they want to pursue upon graduation and provide them with the skills and network to be competitive candidates for these careers. It has been a productive first five years of MoGen Career Development that we hope to build upon even more in the future, as these programs constantly evolve to provide better, more effective career training opportunities to help MoGen trainees achieve their goals.

***

## Community News and Events

**One Year in, The M.H.Sc. in Medical Genomics Program is Thriving**
In September of 2018, the Department of Molecular Genetics launched a new two-year course-based M.H.Sc. in Medical Genomics, accepting 15 high-caliber students into the inaugural cohort. Having now completed two academic terms of the program, which teaches

practical and theoretical aspects of modern genetics and genomics with a strong focus on clinical applications, we're thrilled with the professional, academic, and extracurricular successes of this first group of students. They've exceeded expectations in their coursework, and many have secured interesting and relevant co-curricular positions for themselves, working on a breadth of clinical, industry, and systems biology projects. The group is contributing to a program-specific blog, and they are currently writing and illustrating a book entitled "*100 Things You Didn't Know About Your Genome,*" an entirely student-lead initiative that will be targeted to young teenagers.

The program has also been enthusiastically welcomed into the Department, the Faculty of Medicine, and the UHN and Discovery District. It has received overwhelmingly positive responses and much appreciated support from many academic, clinical, and industry partners. Many of our program partners have elected to support the program by hosting one or more of our second-year students during their capstone placement projects, and we are always welcoming new partnerships for these student placement opportunities – see the description of the practicum course here or reach out directly for details.

The MedGen class of 2021 is being recruited now! Visit the MHSc program website to learn more.

**Annual MoGen Holiday Bash**
MoGen students and faculty ended off the calendar year with our Annual Holiday party, where we all get to celebrate a year's hard work, on Dec 7, 2018 at the Faculty Club. The night started off with plenty of food and a jazz trio to set the mood and ended in classic MoGen style

with a huge dance party until the DJ played that last note. The night was not complete without gathering around the MoGen photo booth to capture memorable moments with their lab mates and friends with many holiday-themed props to help look our best. Every year the holiday party provides MoGen students and faculty the chance to relax and have a great time, and this year was no exception.



**MoGen Opens its Doors at the March Recruitment Day**
MoGen welcomed a new generation of potential graduate students for our recruitment day on March 8th, where we got to show off all the things our department has to offer. Over 40 recruits travelled from across Canada, as well as internationally, to get a taste of the research and culture here in Molecular Genetics.

Dr. Leah Cowen gave the opening remarks, followed by talks from Dr. Jeehye Park, Dr. Will Navarre, and Dr. Stephanie Protze. Next up, the graduate coordinators provided an overview of the department and answered any questions from the potential students. The GSA organized a pizza lunch and provided the opportunity for recruits to chat with real live graduate students about their day-to-day lives in the department. After lunch, the students were sent off across the different nodes throughout Toronto's Discovery District to have individual meetings with PIs whose research interested them and to sample the diverse areas of research in our department. The learning continued into the poster session at PGCRL where students could talk to graduate students about their research projects over drinks and appetizers. The poster session was followed by dinner at Scaddabush with faculty and GSA members could continue to converse with students over some delicious Italian finger foods. The day was finished off with a pub night organized by the GSA at Fran's Upper Deck that was well attended by recruits, current students and faculty alike.

Overall, the day was a success, filled with science, beer, and great conversation. We can't wait to see many of the recruits join us in September!

**All in Green for St. Paddy's Day**
The annual St. Patrick's Day Pub night was held on March 18th at Einstein's pub, which was celebrated with the wide variety of beers available at this well-known U of T watering hole. This year there were many opportunities for students to win free beverages by competing in St. Paddy's day themed trivia, dressing as festively as can be, or by taking a guess at the number of green candies in a jar. There were multiple St. Paddy's day trivia champions that were awarded Einstein's finest brews, giving them all another title to their resume. The most festively dressed winner showed his dedication to the event by wearing his bright green morph suit all night long, making it quite difficult to enjoy his free pitcher. On top of it all, students got to chow down on some classic pub-style appetizers kindly provided by the GSA.

**Bringing Your Childhood Arcade Back to Life**
The MoGen GSA brought us back in time for a night of retro arcade games at Tilt Arcade Bar on April 2nd. Students got to play over 50 vintage arcade and pinball machines for free all night long, along with the opportunity to taste the huge craft beer selection available. The competition was fierce with many students challenging each other in intense car racing games, and others trying to beat top scores in Wack-A-Gator. No matter the game, everyone was able to have a great night of arcade fun reminiscent of younger years to forget about that annoying western blot that just won't cooperate.

**Upcoming GSA Events: Stay Tuned**
The MoGen GSA will be offering a **visit to the Toronto Humane Society on**

**Wednesday, April 24th**. Make sure you don't miss your chance to relax and cuddle up to some adorable furry creatures. In May, our GSA Event Planners, Krista Schleicher and Dustin Ammendolia, keep the good times rolling with a night out to a **Second City Comedy Show on Wednesday, May 29th**. At the end of the month, the GSA will be hosting a celebration filled with wine and cheese for the newly reclassified/qualified PhD students in our department. The GSA's VP Internal Reuben Samson will be making sure all these future PhDs and their colleagues get to enjoy well-deserved night out at the pub night to follow. June events will include a swanky night looking at marine life at the **Ripley's Aquarium Jazz Night (June 14th)** and a **colourful night of fun to celebrate Pride (June 20th)**. In the summer, the GSA already has many events planned to get you out having fun in the sun! This includes a faculty-wide Sports Day, the MoGen BBQ, a beach day, and many more. Stay tuned for details and reminders for all of these events.

\*\*\*

# Research Highlights
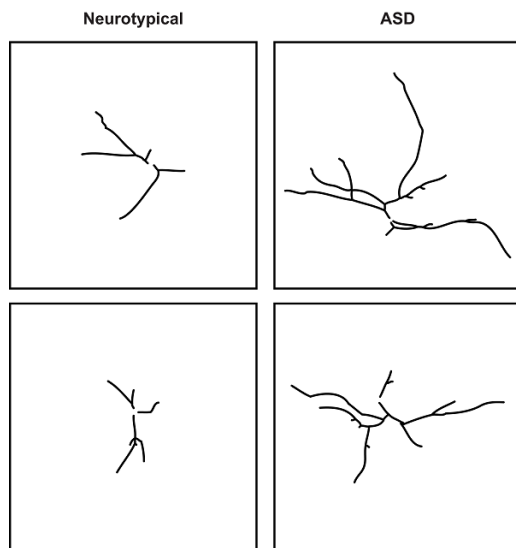


**Mutations associated with autism cause hyperconnectivity of human nerve cells.** Autism Spectrum Disorder (ASD) is associated with different genetic changes, and is thought to be caused by mishaps in brain wiring. A new study led by **Dr. James Ellis, Dr. Stephen Scherer and Dr. Michael Salter** (Dept of Physiology) has found that overactive and overly connected nerve cells result from a mutation found in individuals with autism. The research team focused on mutations in the *SHANK2* gene, and they reprogrammed skin or blood cells to produce stem cells, which were then differentiated to form nerve cells. The team found that nerve cells with *SHANK2* mutations were significantly overconnected compared to controls. They confirmed the result using cells in which *SHANK2* had been knocked out by CRISPR technology, and showed that proper connectivity was restored when *SHANK2* mutations were corrected. The study, published in *Nature Neuroscience*, also illustrates the power of the stem cell approach to produce nerve cells to study their properties and function in the lab, which may also lead to new therapies and drugs to treat neurological disease. Read the full story here.
(*Nature Neuroscience* 2019, doi: 10.1038/s41593-019-0365-8).
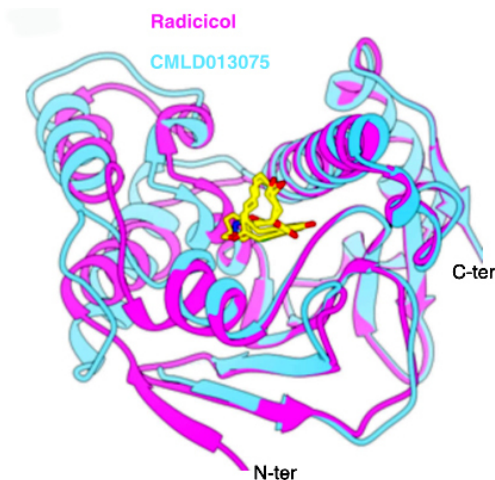


**Targeting the molecular chaperone Hsp90 to combat fungal pathogens.** Fungal pathogens pose a serious threat to public health, especially with the growing population of immunocompromised individuals and the emergence of drug-resistant fungi. Recent studies led by **Dr. Leah Cowen and colleagues** establish that the molecular chaperone Hsp90 provides a promising target for antifungal drug development as it is essential for survival, virulence and drug-resistance of diverse fungal pathogens. Their work, published in *Nature Communications*, reveals the structural basis for species-selective targeting of Hsp90 in a leading fungal

pathogen of humans. Fungal selectivity is crucial to avoid host toxicities associated with inhibition of human Hsp90, as observed with Hsp90 inhibitors under development as anticancer therapeutics. Exploiting enhanced flexibility in fungal Hsp90, the team synthesized a novel Hsp90 inhibitor with >25-fold selectivity for fungal Hsp90 over the human counterpart. In work published in *mBio*, the team demonstrated that Hsp90 regulates cellular responses to antifungal drug-induced stress and controls a transition from yeast to filamentous growth in an emerging multidrug-resistant fungal pathogen, *Candida auris*. This work provides a path towards the development of much needed, resistance evasive antifungal therapeutic strategies.

(*Nature Communications* 2019, doi: 10.1038/s41467-018-08248-w;
*mBio* 2019, doi: 10.1128/mBio.02529-18).
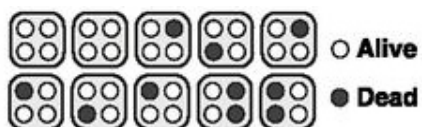


**Why does the same mutation look different in different individuals?** Genetic backgrounds can have a profound effect on the phenotype of mutations, but the molecular mechanisms behind these variations are poorly understood. A new study by **Dr. Charles Boone** and **Dr. Brenda Andrews**, published in *PNAS*, has addressed this question using two strains of the yeast *Saccharomyces cerevisiae* that differ in about 0.2% of their DNA sequence. The research team, in collaboration with Dr. Gerald Fink (Whitehead Institute), examined "conditional essential" genes whose function is necessary in one strain but not the other. The yeast system allowed them to systematically dissect the modifiers involved in background-specific phenotypes. They observed that a complicated set of modifier genes were necessary for this behavior, and that the number and patterns of these modifiers differ depending on the conditional essential gene tested. The ability to predict the impact of modifier genes on mutation is an important goal in genomic medicine, and the results from yeast raise hopes that similar studies will be possible for human cells.
Read the full story here.

(*PNAS* 2019, doi: 10.1073/pnas.1820915116).
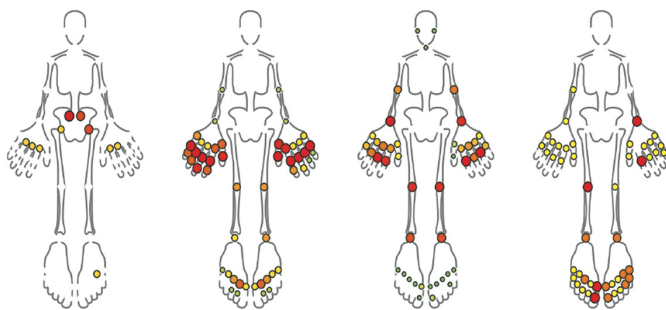


**Using machine learning to predict clinical phenotype and disease trajectories in children with arthritis.** An estimated 24,000 Canadian children suffer from arthritis. There is

no cure and the treatment consists of progressively more aggressive medications. In a recent study reported in *PLoS Medicine*, **Dr. Quaid Morris** and **Dr. Rae Yeung** (Dept of Paediatrics) developed a machine learning tool in which the computer learns to recognize patterns from a sea of data. The research team analysed clinical data from 640 children who had developed arthritis and had not yet been treated with medication. The algorithm was able to classify patients into seven distinct groups according to the patterns of swollen or painful joints in the body. It also accurately predicted which children will go into remission faster and which ones will develop a more severe form of disease. Using these classifications will help decide the appropriate treatments early and prevent unnecessary pain in children affected by arthritis.

Read the full story here.

(*PLoS Medicine* 2019, doi: 10.1371/journal.pmed.1002750).
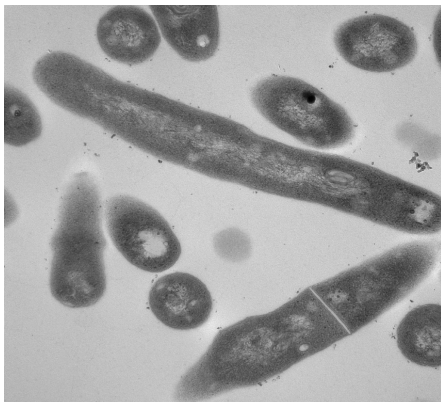


**A recombinant BCG vaccine with enhanced protection against tuberculosis.** Tuberculosis (TB) is the world's deadliest infectious disease, causing 1.6 million deaths and infecting 10 million people in 2017. Bacille Calmette-Guérin, or BCG, is a live attenuated bacterium and the only available vaccine for TB, but has a limited efficacy. BCG vaccine comprises a number of genetically distinct daughter strains that are widely used in the world (over 100 million doses each year). A recent study by **Dr. Jun Liu** and published in *Molecular Therapy* has identified a mutation in a specific BCG daughter strain that reduces its immunogenicity. The mutation is in the *phoP* gene, which encodes a transcription factor that positively regulates over 40 genes in *M.tb*, and is one component of the PhoP-PhoR two-component regulatory system. Based on this finding, Dr. Liu and his research team constructed a recombinant BCG strain that overexpresses the wild-type *phoP-phoR* cassette. In animal models (mice and guinea pigs), the recombinant BCG strain exhibited enhanced immune response and improved protective efficacy against TB. This recombinant BCG is a promising vaccine for future clinical development to replace the current BCG.

Read the story and an interview with Dr. Liu in UofT News.

(*Molecular Therapy* 2018, doi: 10.1016/j.ymthe.2018.08.023).

**An inflammatory response contributes to the development of**
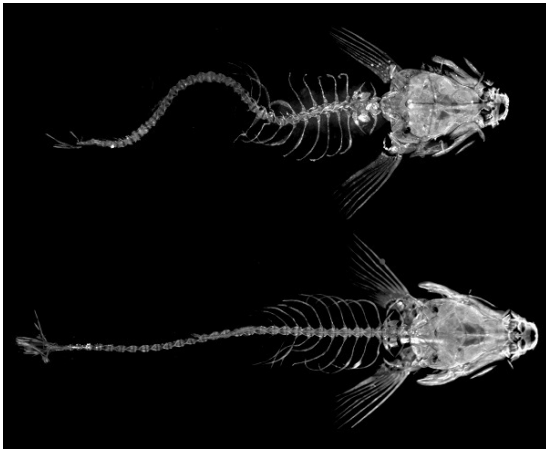
**spinal curvature.** Idiopathic scoliosis (IS) is characterized by three-dimensional curves in the spine that typically arise during adolescence. In addition to affecting humans, IS is also a common deformity found among fish. The zebrafish has emerged as a genetically-tractable model for human scoliosis and other congenital defects. Research led by **Dr. Brian Ciruna** has determined that neuroinflammatory signals, the signals that trigger inflammation in the spinal cord, drive spinal curve formation in zebrafish. A recent study, published in *Science Advances*, examined genes and genetic pathways that were abnormally expressed upon the development of spinal curvature. The lab team found that immune cells associated with inflammation accumulated at the site of spinal curvature, indicating a strong immune response associated with scoliosis. The team also found that suppressing the inflammatory signals with common drugs like N-acetylcysteine (NAC) or aspirin blocked the formation or reduced the severity of spinal curves. The study could have a profound impact on the treatment of idiopathic scoliosis.

Read the full story here.

(*Science Advances* 2018, doi: 10.1126/sciadv.aav1781.)
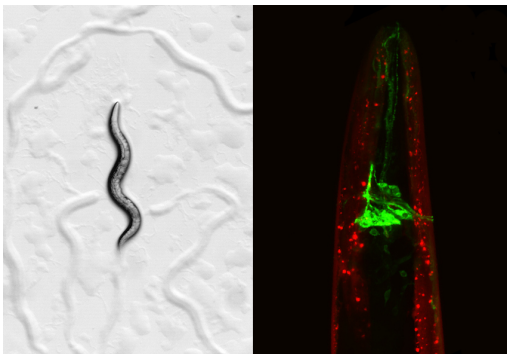


**Why are some memories so difficult to retain?** Memory blocking, also called Kamin blocking, is thought to occur when one "conditioned" memory prevents or blocks a newer one from forming. A new study by **Dr. Derek van der Kooy** and colleagues, published in *Scientific Reports*, has revealed that the problem is one of memory recall rather than establishment. Using the worm *C. elegans* as a simple neurological model, the research team first demonstrated that memory blocking occurs in this organism using olfactory cues, and then examined a protein called EGL-4 (labelled in green) in a single nerve cell in the worm's head, whose movement is required for learning. To their surprise, EGL-4 shifted its position in the cell during blocking the same way it did during normal learning. The results suggest that the memory formed, but could not be retrieved. The study also illustrates that the worm promises to be a powerful system for further

genetic dissection of memory behaviors.

Read the full story here.

(*Scientific Reports* 2019, doi: 10.1038/s41598-019-38939-3).

***



## Faculty Highlights and Awards

**Dr. Stephen Scherer** has been appointed to the rank of University Professor. It is the highest academic rank at the University of Toronto and is usually awarded to no more than two per cent of faculty. Dr. Scherer is internationally recognized for his work studying the structure and function of the human genome. He is the Director of the McLaughlin Centre, and co-founder of the Centre for Applied Genomics at the Hospital for Sick

Children. Read the story in



**Dr. Leah Cowen** has been named co-director of the newly launched CIFAR program on the *Fungal Kingdom: Threats and Opportunities*. The CIFAR team includes diverse experts to understand the unique facets of fungal biology and develop new strategies to mitigate the threats posed by fungi and harness their extraordinary potential. See the story and interview with Dr. Cowen here.



**Dr. Ronald Cohn** has been appointed President and CEO at the Hospital for Sick Children, effective May 1, 2019. He first joined SickKids in 2012 and is a Professor of Paediatrics and Molecular Genetics at the University of Toronto, a renowned clinician in the area of genetic medicine, and Senior Scientist in the Research Institute at SickKids. Read the full announcement here.

\*\*\*

## Trainee Highlights and Awards

**Dr. Monica Wu** has been awarded the **2018 Barbara Vivash Award** for her PhD thesis, entitled "Characterization of two opposing small RNA pathways required for germline homeostasis in *Caenorhabditis elegans*".

Monica's PhD studies, with Julie Claycomb, examined small RNA mediated gene regulatory pathways in the model nematode *C. elegans*.

Monica contributed extensively to numerous projects in the Claycomb lab, including identifying novel gene licensing (instead of silencing) roles for an essential small RNA pathway, exploring the conservation of this licensing small RNA pathway in different nematode species, and defining the roles of a conserved splicing factor in germline small RNA pathways. In her most important and extensive work, Monica characterized a new Argonaute effector (Argonautes are the proteins that interact with small RNAs to elicit gene regulation), which she named VSRA-1 (Versatile Small RNAs Argonaute). In these studies, Monica uncovered novel roles for VSRA-1 in distinct small RNA pathways, including the miRNA and piRNA pathways. This observation redefines our understanding of Argonaute function and points to far more dynamic roles for Argonautes throughout development than previously appreciated.

Monica is now a Research Scientist I at New England Biolabs in Ipswich, MA, where she continues to study RNA biology. At NEB, Monica is developing novel enzymes, reagents and toolkits for rapid large-scale synthesis of homogenous RNA populations to be used in biopharmaceuticals, including RNA-based therapeutics, vaccines and diagnostics.

The Barbara Vivash award is given annually to the graduating student with the best PhD thesis in Molecular Genetics. It includes a significant monetary award, a certificate, and an invitation to present a full Departmental seminar. The date for Monica's seminar will be posted soon on the MoGen website.

**Kaitlin Laverty** (Hughes & Morris labs) has been awarded a **2019 Jennifer Dorrington Award**. Kaitlin's PhD work is aimed at understanding the nature of the specificity of RNA binding proteins (RBP) for their target RNA molecules, using computational biology approaches.

The award was established in 2006 as a tribute to Dr.

Jennifer Dorrington, who was a Professor in the Banting and Best Department of Medical Research. Click here to read more.

***



This newsletter would not be possible without contributions from our community. Thanks to Amanda Veri, Nicole Revie, Erin Styles, David Kim, Jun Liu, and Julie

Claycomb for commentary and photos for this issue.

***



## Links to previous editions of MoGeNews

To access previous issues of MoGeNews, please click on the relevant link:

***

The mogen.news@utoronto.ca address is used to distribute the Molecular Genetics newsletter two to three times a year, plus occasional announcements concerning career symposia and events, to our community. If you no longer wish to receive these emails, you can unsubscribe by clicking the "unsubscribe" button at the bottom of this email. To remove yourself from Faculty of Medicine E-Newsletters, please email address.update@utoronto.ca and include the subject line: Unsubscribe from Faculty of Medicine E-Newsletters.

To update your contact information, click here. Please include your full name and graduation year. If you receive multiple copies of this newsletter, please indicate your

preferred email address.