



MoGeNews

Issue 4 - March 2015

Editor's Message

We open this latest issue of MoGeNews with an invitation to the entire Molecular Genetics community to participate in an important upcoming event. We are launching our first ever **Career Development Alumni Symposium**, which is focused on building an innovative forum to foster alumni engagement and community building, and to enhance the student and trainee experience. The event will be held in Toronto on **June 4th, 2015** from 1 - 7 pm at The Bram & Bluma Appel Salon at the Toronto Reference Library. It will provide an opportunity for interactive exploration of diverse career trajectories relevant to our students and trainees, networking possibilities to enable advancement in areas of interest, and opportunities to reconnect with former colleagues, mentors, trainees, and friends. There will be a roundtable career discussion and networking session, as well as a career development panel and a wine & cheese reception. We send out a special request to our alumni to participate in this event to serve as career mentors for the roundtable career discussion and networking session. Please join us, and click [here](#) to complete the free online event registration.

It has been an exciting few months for the Molecular Genetics community as we thaw from the deep winter freeze. We hope that you enjoy the latest issue of MoGeNews, which features highlights of many community events, alumni trajectories, research highlights, and coverage of faculty and student achievements.

Sincerely,

Leah Cowen

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Community Events



Photo by Yi Zeng

Toronto hosted the 5th Joint Symposium for researchers from the Shanghai Institute of Biochemistry and Cell Biology and the University of Toronto Faculty of Medicine. The Hospital for Sick Children hosted the event at the Peter Gilgan Centre for Research and Learning on November 11-12, 2014. Scientists presented their latest findings to hundreds of faculty members, staff and students,

and talked about ways to work together. U of T's Department of Molecular Genetics, Donnelly Centre for Cellular and Biomolecular Research and SickKids Research Institute have worked with the Shanghai Institute since 2007. Photograph features left to right: Jian Zhao (SIBCB), Weiguo Zou (SIBCB), C.C. Hui (U of T), Naihe Jing (SIBCB), Howard Lipshitz (U of T), Jinsong Li (SIBCB). Click [here](#) for additional details.



Our MoGen 2014 Holiday Party was held at the University of Toronto Faculty Club on Friday December 12th. The event was well attended by faculty, staff, and students. The party began with a wonderful performance by a jazz trio, as the guests mingled over food and drinks. This was followed by a fun evening of dancing and socializing. Photograph features some of the Cowen Lab members. As always, a great time was had by all and we look forward to the next social event!

Alumni Spotlights



Dr. Gillian Wu, former Dean of Pure and Applied Science at York University, discusses her career trajectory from being the first female graduate student in the Department of Medical Biophysics to her doctoral work with Dr. Helios Murialdo in Molecular Genetics to retirement in January 2015. Gillian provides pearls of wisdom pertaining to genetics of the immune system, women in science, choosing a mentor, and strategies for

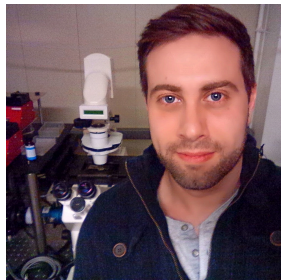
success. Click [here](#) to read more.



Dr. Tomas Babak, Assistant Professor, Department of Biology at Queen's University, discusses his career trajectory from his PhD with Drs. Tim Hughes and Ben Blencowe in the Department of Molecular Genetics to his industrial postdoc at Rosetta Inpharmatics to his senior scientist position at Merck, prior to returning to academia.

Tomas provides insight on strategies to succeed in industry and keep doors open for academia, and his fascination with developing new technologies to address biological questions including ways in

which to exploit high-throughput data sets to understand complex disorders, like schizophrenia and cancer. Click [here](#) to read more.



Dr. Anthony Vecchiarelli, postdoctoral researcher at the NIH, shares his scientific journey from completing his doctoral work with Dr. Barbara Funnell in the Department of Molecular Genetics to winning the Vivash Award to developing a cell-free system to study spatial organization systems at the NIH. Anthony highlights his favourite memories from MoGen, and his passion for science that would

prevail even if he won the lottery. Click [here](#) to read more.



Dr. Andrew Keeping, Supervisor, Development Analytics at ATCO Power Canada Ltd, reflects on his career pathway from completing his PhD with Dr. Rick Collins in Molecular Genetics to joining Boston Consulting Group to leading a business development group. Andrew shares strategies for leveraging skills from graduate school in the private sector, breaking stereotypes, and memories of 2D gels that look like the night sky in

Algonquin Park. Click [here](#) to read more.

Spotlight on MoGen Research Field: Cellular and Molecular Structure and Function

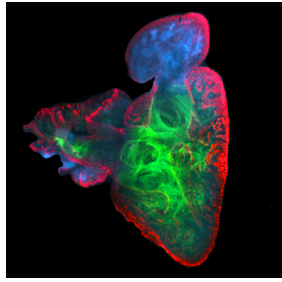


Image from I. Scott. "Getting to the heart of the matter." Adult zebrafish heart stained with Rhodamine-Phalloidin (Red) and showing areas of Bmp activity with a GFP transgenic sensor (Green). Nuclei are stained in blue. The adult zebrafish heart is being used to study pathways that regulate heart regeneration and repair.

Our research interests in the area of *Cellular and Molecular Structure and Function* range from computational protein folding to stem cell biology. Despite the breadth, there are a number of themes that can be identified, all of which are centred on understanding fundamental mechanisms. Several labs are focussed on neuronal development and neuronal tissue function, for example, work that includes the study of neuronal stem cell generation, axon guidance mechanisms and the molecular basis for neural network formation. Central to these efforts is the study of stem cells and the use of a number of different animal models. Cutting-edge techniques involving laser optics and optogenetics are leveraged to study higher-order functions such as learning, memory and locomotion. Stem cells and animal models, including the zebra fish, are also being used to study development and disease in other systems and tissues including the heart and kidney. Collectively, the advances emerging from these efforts are expected to contribute to novel approaches to treating neural and heart tissue

damage, brain cancers in children and Alzheimer's disease in the elderly to name just a few.

Genome stability through successive cell divisions is central to the maintenance of normal cellular function. Not surprisingly, DNA damage and the gain or loss of chromosomes or portions of them are hallmarks of cancer. Several MoGen labs are working to understand DNA repair mechanisms and the processes that ensure proper chromosome replication and segregation. In one collaborative effort, functional genomics, microscopy and mass-spectrometry are being used to study centrosome biogenesis, an important component in the regulation of cell division. In another collaboration, cell-based approaches and x-ray crystallography are utilized to determine how DNA repair enzymes are recruited to double-strand breaks.

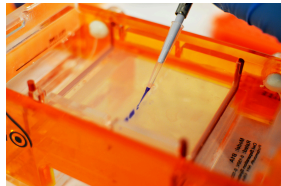
Regulation of gene expression is critical at all stages in the life-cycle of a living organism, and control at both transcriptional and translational levels is the focus of many members of our Department. Core to the effort is the identification and characterization of the DNA- and RNA-binding proteins involved in controlling these processes. Over the past few decades, we have begun to appreciate the important roles played by small RNAs in gene regulation, and a new paradigm for small RNA-mediated gene regulation is beginning to emerge from recent work by MoGen labs. Splicing of pre-mRNA enables both gene regulation and the generation of varied protein isoforms, with exciting new work in this area from MoGen members shedding light on how microexon splicing is controlled in neural development and how the process is misregulated in autism.

The study of protein structure and protein interactions represents another theme among members of the group. Collectively, a wide range of biophysical techniques including NMR and x-ray crystallography, as well as computational approaches, are being used in this research. We study protein folding and quality control, protein-protein interactions, macromolecular assemblies, G

protein-coupled receptors, ion transporters, virus-receptor interactions and protein kinases among others. Intrinsically disordered proteins are now known to mediate cross-talk between signalling pathways, and structural insights into how they perform this role represent one example of cutting-edge research that has recently emerged from our group. MoGen labs are also focussed on the development of novel protein and small-molecule human therapeutics, and notable among these efforts are the use of protein engineering to develop novel antibody therapeutics, the use of bacteriophage as antibiotics and the identification of new drug targets using the membrane yeast two-hybrid assay. Novel functional proteomic approaches are also being used to discover and characterize protein-drug and protein-ligand interactions, which promises to uncover new uses for already approved small-molecule therapeutics.

For a more detailed look at the work ongoing in the *Cellular and Molecular Structure and Function* research field please read the full [Field Spotlight](#).

Research Highlights



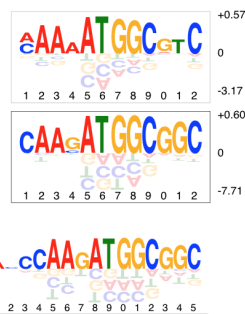
Discovery of tiny gene fragments linked to brain development and autism. (*Cell* 2014 159:1511-23). MoGen team led by Dr. Benjamin Blencowe found that very small segments of genes called “microexons” influence how proteins interact with each other in the nervous system. They

identified a new landscape of splicing regulation that is highly specific to the nervous system. Many of the microexons that they detected are misregulated in people with autism. This article was highlighted in *Cell*, *EMBO Journal*, the *London Free Press*, and the *Toronto Star*. Click [here](#) to read more.



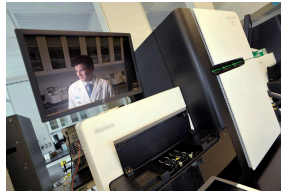
Writing the genetic instruction manual to decode the human genome. (*Cell* 2014 159:1212-26). An international consortium co-led by MoGen professor Dr. Fritz Roth has systematically mapped how 13,000 proteins in the human proteome interact with one another. They found

that proteins involved in cancer are more likely to interact with each other than with other types of proteins. An appreciation of protein interactions is key to deciphering the human genome, just as fixing a car requires more than a list of parts.



Discovery that C2H2 zinc finger proteins greatly expand the human regulatory lexicon. (*Nature Biotechnology* 2015 doi: 10.1038/nbt.3128). MoGen team led by Dr. Tim Hughes performed the first systematic study of the largest group of human transcription factors. They found that the C2H2 ZF transcription factors recognize more motifs than all other human transcription factors combined, and that they broadly bind to regulatory regions. These

transcription factors may have evolved to defend our ancestral genome from damage caused by parasitic DNA. For more details, click [here](#).



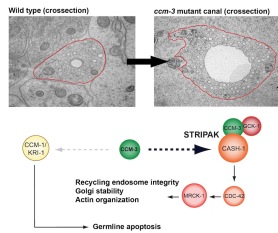
Uncovering distinct genetic causes for sibling's autism. (*Nature Medicine* 2015 21:185-91). Study led by MoGen professor Dr. Stephen Scherer provides the largest whole genome sequencing analysis of families with autism. They discovered that siblings with autism spectrum

disorder often carry different genetic mutations, and that those with distinct mutations showed more clinical variability than those with a shared mutation. For additional details, click [here](#).



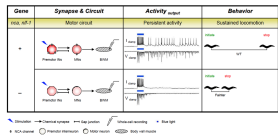
Finding needles in haystacks of genomic data. (*Nature Methods* 2015 12:154-9). An international team led by MoGen professor Fritz Roth develops a powerful computational method to identify disease-associated genes from genome-wide association studies (GWAS). This approach leverages a "guilt-by-association" technique, and

outperformed existing algorithms in an analysis of 100 genome-wide association studies focused on 10 cancer types. Click here to [read](#) more.



Discovery of a molecular basis for disease severity in patients with Cerebral Cavernous Malformation (CCM). (*Nature Communications* 2015 6:6449). MoGen team led by Dr. Brent Derry and Dr. Anne-Claude Gingras uncovers novel

mechanisms underpinning CCM, which is caused by the progressive development of large lesions in blood capillaries, afflicting ~1 in 500 individuals. They identify novel *in vivo* roles of CCM3-STRIPAK in regulating biological tube development and membrane integrity. Click [here](#) to read more.



Discovery of a mechanism by which animals generate rhythmic motor activity that outlasts sensory stimuli. (*Nature Communications* 2015 6:6323). By combining

genetics, optogenetics and electrophysiology, Dr. Mei Zhen's team found that a small groups of premotor interneurons are required for sustained activation of motor output, and that this requires a new class of channel that mediates leak of sodium.



Research establishes that drug combinations could be a powerful approach for fungal infections. (*Cell Reports* 2015 10:809-19). Dr.

Leah Cowen's team discovered that antifungal drug combinations can minimize the evolution of drug resistance, and that pathogens that ultimately evolve multi-drug resistance often suffer trade-offs such that they are vulnerable to killing by immune cells. Click [here](#) to read more.



Dr. Gary Bader's team develops the first app for the MinION - a handheld and inexpensive device that can sequence DNA. ([F1000 Research 2015 4:17](#)). This technology will facilitate the emerging field of personalized medicine. To read more, click [here](#) and [here](#).

Faculty Highlights and Awards

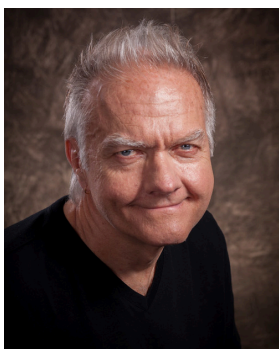


Dr. Julie Lefebvre is awarded a 2015 Sloan Research Fellowship. This early-career award recognizes the most promising scientific researchers working today. Their achievements and potential place them among the next generation of scientific leaders in the U.S. and Canada. Lefebvre's research focuses on how developing neurons precisely organize into neural circuits. For additional details, click [here](#).



Dr. Sachdev Sidhu has won the Protein Society's 2015 Christian B. Anfinsen Award. This award recognizes his contributions to advancing protein engineering, developing cutting-edge basic research reagents and discovering new avenues for disease treatment. Sidhu's research also provides the foundation from which Northern Biologics has sprung. Northern Biologics is a new biotech company backed by the San Francisco-based venture capital firm Versant Ventures. Dr. Jason Moffat and Dr. Sachdev Sidhu of Molecular Genetics

are among the co-founders. The goal: to develop antibody-based drugs to treat cancer and fibrosis. Launched with a \$10 million investment from Versant, Northern Biologics is a joint creation of U of T, the University Health Network's Princess Margaret Cancer Centre and Versant's biotech incubator, Blueline Bioscience.



Dr. Derek van der Kooy, has won the 2015 Canadian College of Neuropsychopharmacology Heinz Lehmann Award. The award recognizes outstanding contributions to neuropsychopharmacology in Canada. Van der Kooy's research focuses on interest and memory, developmental and stem cell biology and the neurobiology of motivation.



Dr. Leah Cowen wins a 2015 NSERC E.W.R. Steacie Memorial Fellowship. These fellowships are awarded to enhance the career development of outstanding and highly promising university faculty who are earning a strong international reputation for original research. Cowen's research focuses on functional genomic analysis of fungal pathogenesis and developing new therapeutic strategies to combat drug resistant fungal pathogens. For additional details, click [here](#).



Dr. Adam Rosebrock receives the 2015 Excellence in Undergraduate Laboratory Teaching in Life Sciences Award. This recognizes sustained excellence in teaching, coordination and/or development of laboratory based instruction in formal Arts and Science life sciences laboratory courses. He is a key innovator of the new course MGY360H1 - Whole-Genome Sequencing and Analysis Laboratory, and is described as an educator who has the ability to build rapport with students and encourage cutting-edge

techniques in research.



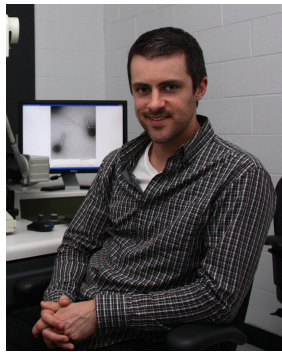
Dr. Janet Rossant is a lead investigator for the Canadian Rare Diseases Models and Mechanisms (RDMM) Network — a first of its kind collaboration. The network was awarded \$2.3 million from the Canadian Institutes of Health Research (CIHR), in partnership with Genome Canada, to advance rare disease research using model organisms. MoGen faculty members serve on the Network's advisory committees: Scientific Advisory Committee (Lipshitz, Rossant) and Clinical Advisory Committee (Cohn).

Graduate Student and Postdoc Highlights and Awards



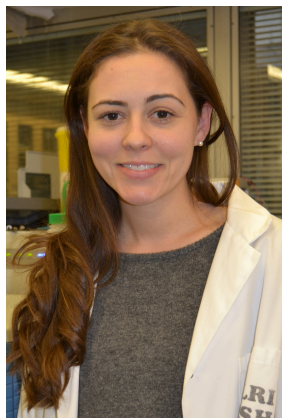
Ken Grisé has been elected as MoGen GSA president. Ken is a doctoral student in the van der Kooy lab. As GSA president his role is to advocate the interests of the graduate student body to the MoGen faculty, other Faculty of Medicine departments and the university at large, and conversely, to keep MoGen grad students apprised of initiatives and issues arising from these different levels of the university. Ken also works with all of the other positions on the GSA to keep the team coordinated and ensure that grad life in the MoGen department is an engaging experience.

Ken says: "I'm aiming to have a very inclusive and open GSA this year. I think open communication between the student body, the GSA, and the faculty will enable us to align our goals and collaborate effectively on our initiatives to generate positive outcomes for the department on all levels. Here's to a great year!"



Dr. Joseph Bondy-Denomy receives a Sandler Fellow position at the University of California, San Francisco. The fellowship is one of the most sought-after postdoctoral positions in the world. Recipients get five years of funding to set up their own labs and research programs. They can hire lab members and apply for external funding — essentially, they become principal investigators. Bondy-Denomy completed his PhD with Dr. Alan Davidson where his studies focused on a bacterial immune system called CRISPR-Cas. For more

details click [here](#).



Dr. Amber Couzens is the recipient of the Canadian Institutes of Health Research-Institute of Genetics (CIHR-IG) Lap-Chee Tsui Publication Award (2014). Dr. Couzens award winning paper published in *Science Signaling* was from her postdoctoral work with Dr. Anne-Claude Gingras and focused on the protein interaction network of the mammalian Hippo pathway to identify mechanisms of kinase-phosphate interactions (*Science Signaling*, 6(302): rs15). Mohamed Solimen, a MoGen student who trained with Dr. Anthony Pawson and Dr. James

Dennis, was a finalist for his *Science Signaling* paper on the adaptor protein p66Shc inhibiting mTOR-dependent anabolic metabolism (*Science Signaling*, 7(313): ra17).



Monika Schmidt is inducted into the American Society of Human Genetics Training and Development Committee (ASHG-TDC). Schmidt is currently pursuing her graduate studies in Dr. Christopher Pearson's laboratory, and will be one of only eight members, including graduate students, post-docs, and early career/industry scientists on the committee. The ASHG, founded in 1948, is the primary professional membership organization for human genetics experts worldwide. The Society's nearly 8,000 members include researchers, academicians, clinicians, laboratory practice professionals, genetic counselors, nurses and others who have a special interest in the field of human genetics.



Molecular Genetics Career Development Workshop Series. After a successful start, the Molecular Genetics Career Development Workshop Series has continued with full force on the last Wednesday of each month under the leadership of Samantha Yammine and Amanda Veri. Our November workshop was entitled, “Where can your

MoGen degree take you?!” and highlighted the success and diversification of our alumni’s careers post-graduation. We were pleased to have the Toronto Sales Rep for Life Technologies, a Toronto-based intellectual property lawyer, and recent graduate working as a scientific advisor at a start-up share their stories to our undergraduate and graduate student audience. We were also excited to share some novel statistics on the department’s alumni.

We focused our January workshop on personal health and wellness, as these are major contributors to academic and personal success. U of T health and wellness expert Cheryl Champagne gave an introduction to mindfulness practice with a mindful eating activity and guided meditation. We had a yoga instructor teach some tension-relieving stretches (do you remember the cramp that only a long day of pipetting can give?!). We sampled and shared some healthy and easy-to-make recipes while going through some of the free resources on campus, and everyone left the event with a full stomach and slightly less stress.

Our upcoming workshops will feature panels of professionals from a variety of different fields, to continue to inspire students and give insights to career opportunities they may not have considered yet. If you have any advice you wish someone had given you when you were a grad student, or if you’d like to be a speaker at any of our workshops, please contact us!



Eric Chapman, Eesha Sharma, and Amanda Veri have been appointed as Graduate Student Ambassadors.

Graduate and Life

Sciences Education (GLSE) Ambassadors are current students who have generously volunteered their time to help students in making their MSc and PhD decision. They are also there to help current students transition into graduate school. Our student ambassadors can answer your questions via e-mail or skype. Contact us to arrange to speak to an ambassador.



Graduate Student Association (GSA) Bake Sale and Food Drive. Every December, the GSA collects non-perishable food donations to donate to local food banks for the holiday season. To help support the food banks even more this year, the GSA

also held a fundraiser where donations were collected in exchange for hot chocolate and baked goods donated by staff and students. The event was a huge success and over \$240 was raised for the Daily Bread Food Bank. Daily Bread Food Bank is a registered charity that supports almost 200 food programs across Toronto, helping to provide food to the thousands of people across Toronto that rely on food banks.

Undergraduate Student Highlights



First Interactive Graduate Student Fair. Dr. Peter Roy of Molecular Genetics spoke in the Graduate and Life Sciences Education interactive webinar for undergraduate students who are considering graduate studies.



Molecular Genetics & Microbiology Student Union (MGYSU) Research Seminar on the Why's and How's of Undergraduate Research. Dr. Leah Cowen spoke to engage students with undergraduate research opportunities.



Innovative Online MoGen Course. We launched our first entirely online course in January - "An Introduction to Medical Microbiology". This course, led by Professor William Navarre, is pioneering in several respects. It is not only the first online course developed by our Department, it is

also the first course at the University of Toronto to be simultaneously available to students inside the school and through the School of Continuing Studies for students outside of the university who wish to learn more about microbiology. This course also pioneers a collaborative approach that is unusual among typical offerings. Many units have been designed in collaboration with scientists and clinicians at Public Health Ontario and St. Michael's Hospital. This foundational online course introduces students to the fundamental principles of medical microbiology as they relate to health and disease. The partnership with hospitals and public health agencies provides a unique opportunity for students to learn directly from professional medical microbiologists.

The design of the course has centred on meeting the needs of students interested in a health related profession. Modules focus on practical topics in infectious disease including diagnosis, antibiotics and antibiotic resistance, infection control, as well as current knowledge about the molecules and genes involved in microbial pathogenesis. Events like the Ebola outbreak happening right now in Africa are used to highlight the most important fundamental concepts in disease transmission, prevention, and treatments. The Ebola outbreak has also been used as a vehicle to discuss health-inequities between wealthy and developing parts of the world.

The course moves beyond the traditional lecture based teaching model. It is not simply a series of one-hour lectures but instead is a mix of multimedia including video vignettes, readings on websites, and assignments that have the students use online databases and tools in infectious disease. The units include interviews with infection control experts, a video tour of a high security "level 4" laboratory, and constantly updated statistics on the Ebola and measles outbreaks. The course also expanded its content in the wake of the measles outbreak to discuss the false rumour that the MMR vaccine causes autism.

The course was incredibly popular from the outset. More than 400 students are currently taking the course, which makes it the largest course taught by our Department. Student feedback has been overwhelmingly positive and the Department is exploring ways of expanding upon the success of this model for future courses.

Closing Thoughts on Funding in Canada



Funding Changes Put Emphasis on Applied Research. Molecular Genetics faculty comment on how changes in government funding are threatening Canada's international standing in biomedical research. Click [here](#) for more details.

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