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MoGeNews

Issue 11 - May 2018

Editor's message

Welcome to our next issue of MoGeNews!

In this issue, we highlight our upcoming **4th Annual Career Development Symposium**, which will be held on **June 4, 2018** at the Chestnut Conference Centre (details below). The event is held to promote interactions between trainees and our many extraordinary alumni from the Department of Molecular Genetics.

Please register!

Graduate students! If any of you would like some experience with scientific writing and would like to contribute to this newsletter, please contact me. For this issue, I specifically would like to thank Jonathan Palozzi, Jon Roth, Ellen Langille and

Amanda Charlesworth for contributions to community events and the alumni spotlight.

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



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4th Career Development Alumni Symposium

Monday, June 4, 2018, 1 pm - 7 pm

Registration is now open! Please join us for an afternoon of discussion with and presentations by distinguished MoGen alumni. The Symposium will be held at the **Chestnut Residence and Conference Centre** in downtown Toronto (89 Chestnut St., Toronto,

ON M5G 1R1).

The afternoon includes round-table discussions (where mentors from various backgrounds meet with ~ 8 trainees), a panel presentation by several featured alumni, and networking sessions to allow trainees, mentors and colleagues to interact one-on-one. The event also provides lots of opportunity for all to connect with friends and colleagues from MoGen.



MoGen alumni, faculty and trainees (MoGen graduate students, postdocs, and MGY undergraduates) are invited. We extend a special invitation to MoGen alumni to sign up as mentors for the round-table discussions. Mentors and panelists will also be invited to an exclusive appreciation lunch before the symposium. Please come and share your career trajectories and experiences with our current trainees!

The 2018 panelists are:

Dr. Michael Brooks, VP of Corporate Development and Strategy, Edesa Biotech

Dr. Masha Cemma, Policy Advisor, Office of the Chief Science Advisor of Canada

Mr. Douglas Hamilton, President and CEO, MetaStat Inc.

Dr. Pamela Kanellis, Senior Director, Canadian Institute for Advanced Research

Dr. Elizabeth Patton, MRC Programme Leader Scientist, University of Edinburgh

Dr. Anthony Vecchiarelli, Assistant Professor, University of Michigan

Registration deadline is May 15. Click [here](#) to sign up and join us!



CAREER DEVELOPMENT SYMPOSIUM

Monday, June 4, 2018 1 pm - 7 pm

With special thanks to our Platinum and Gold Sponsors:





Community Events



Summer Intramural Sign Up!

The playoff season is in full swing and that means spring is finally here! Why not take a break from watching sports to actually play one? This year Mogen will be offering three summer sports

including Coed Ultimate, Coed Flag Football, and Coed Indoor volleyball. Sign up

information and details are available [here](#).

The deadline to sign up is May 15th with leagues starting early June so please sign up early as teams without the minimum number of players will not be entered. For any questions regarding team sign up please contact the sports rep Jonathan Roth (jon.roth@mail.utoronto.ca).

If playing sports with others doesn't fit your fitness goals and you instead prefer to finally cut after bulking all winter, remember to make use of the SGS summer gym bursary. The summer gym bursary provides funding to registered full-time graduate students to help pay for campus facility memberships over the summer months. Details regarding the application process are available on the [SGS website](#) and will be available starting May 15th until around mid-August.



St. Patrick's Day Pub Night

The annual St. Patrick's Day Pub night was held on March 15th, which was celebrated with the huge variety of beers available at Prenup Pub and delicious food to match. Several platters of food including samosas and pesto-fries were kindly provided by the GSA. Everyone was encouraged to dress in their best green attire, and dawned St. Patrick's day

themed stickers also provided by the GSA. The winner of the “Most Spirited Dresser” was Aleksei Shkurin from Tim Hughes' Lab who got a pitcher of beer for his festive attire.



Recruitment Day

MoGen welcomed a new generation of potential graduate students on March 9th to see what our department has to offer. Over 50 recruits travelled from across Canada, as well as the United States and

overseas. Dr. Leah

Cowen gave opening remarks, followed by talks from Neal Sondheimer, Anne-Claude Gingras, and Aaron Reinke. The graduate coordinators then provided an overview of the department and answered questions from the potential students. The GSA organized a pizza lunch and provided an opportunity for recruits to ask questions to current graduate students. After lunch, the GSA members helped the recruits navigate across different nodes to have individual meetings with PIs whose research interested them. Recruits then had a further opportunity to see the breadth of research in our department over drinks and appetizers through the poster session at PGCRL. Dinner at Scaddabush closely followed the poster session, with many faculty members and current students also attending to converse with the recruits. The day was finished off with a pub night at Prenup Pub that was well-attended by recruits and current students alike. Overall, the day was a huge success and we are looking forward to seeing many of the recruits join us in September.



Earth Day Documentary Film Night

MoGen celebrated its environmental side this year with a screening of a documentary film in the CCBR Black room on April 20, 2018. The film was narrated by Sir David Attenborough and showcased some of the diverse ecosystems and animal life on the planet we call home. Snacks and drinks were provided by the GSA, with popcorn to provide a true movie night experience.



Alumni Spotlight



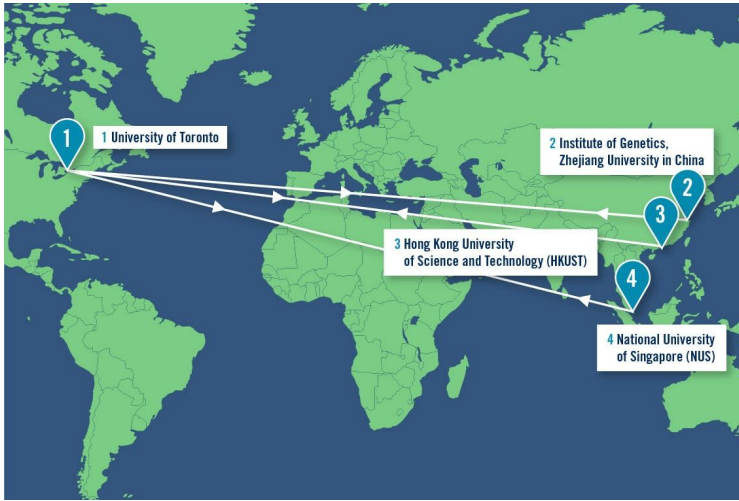
Douglas Hamilton is President and CEO of MetaStat, a personalized medicine company focused on improving survival of patients with aggressive cancer. After graduating with a B.Sc. in Medical Genetics at the University of Toronto, Douglas completed his MBA at the Ivey Business School at Western University and has a successful career working in the US venture capital and biopharmaceutical industries. Mr. Hamilton has held positions of increasing responsibility at Pharmacia Biotechnology, Amgen, and Pfizer, in addition founding PolaRx Biopharmaceuticals and Javelin

Pharmaceuticals. In this spotlight, Douglas recounts his memories from his time at U of T and offers advice on what makes a strong business leader. Click [here](#) for the full spotlight.



International Doctoral Cluster Initiative

The Department of Molecular Genetics has been deeply committed to forging global research alliances with world-class graduate institutions. Our most recent International



Doctoral Cluster (IDC) for the Joint Institute of Genetics and Genome Medicine between the University of Toronto and Zhejiang University in China, now has our first student. **Charmaine Rodrigues will be jointly co-supervised by Dr. C.C. Hui and Dr. Xi Huang in**

MoGen, and Dr. Min-Xin Guan at Zhejiang. Charmaine is studying the role of mitochondria-associated ion channels in medulloblastoma (MB), the most aggressive childhood brain cancer. Read the full spotlight in [U of T News](#).



Research Highlights

High-density proximity mapping reveals the subcellular organization of mRNA-associated granules and bodies. Post-transcriptional regulation of mRNA is a complex process that occurs in distinct compartments within the cell. Cytosolic P-bodies and stress granules, which are respectively associated with mRNA degradation and storage, form by the coalescence of non-translating mRNA and associated proteins. Using

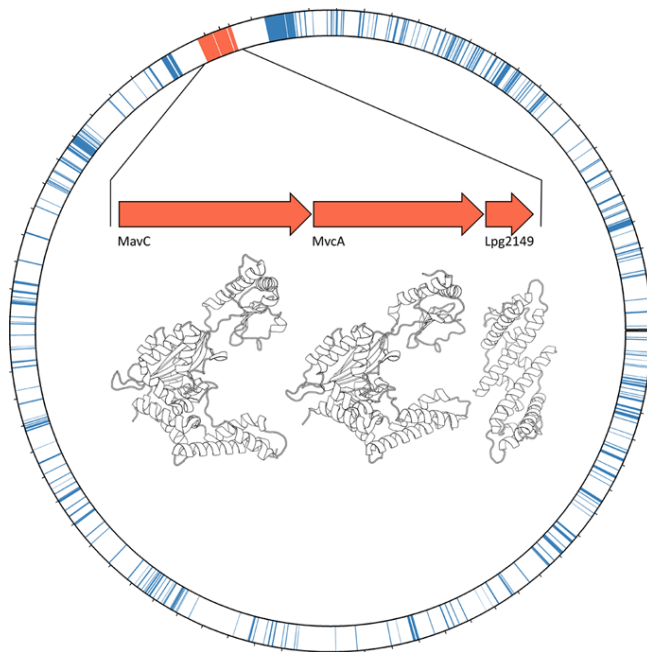


proteomic techniques, a new study led by **Dr. Anne-Claude Gingras**, published in *Molecular Cell*, has discovered new components of stress granules and P-bodies and defined the spatial organization of these structures. Stress granules have been implicated in neurodegenerative diseases such as ALS (amyotrophic lateral sclerosis) and FTD (Frontotemporal Dementia), and the results offer new avenues for identifying the factors that contribute to the development of these granules, as well as provide new opportunities

for exploring the mechanisms that promote ALS/FTD pathologies. Click [here](#) to read more.

(*Molecular Cell* 2018, doi: [10.1016/j.molcel.2017.12.020](https://doi.org/10.1016/j.molcel.2017.12.020))

The first author of the study, Dr. Ji-Young Youn, has been highlighted by *Molecular Cell* in the feature “[Meet the Author](#)”.

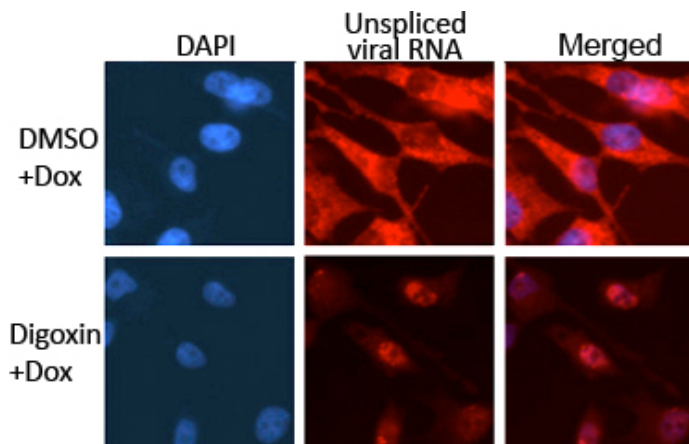


Bacterial pathogens are master manipulators of eukaryotic cell processes.

Legionella pneumophila is particularly adept in this regard, using over 300 translocated “effector” proteins to rewire and replicate inside an evolutionarily diverse range of hosts – from single-celled amoebae to human alveolar macrophages. The specific contribution of the vast majority of these effectors to *Legionella's* pathogenesis remains elusive. A new study led by **Dr. Alex Ensminger and**

Dr. Alexei Savchenko (Univ of Calgary), published in *Cell Reports*, reveals that

two paralogous *Legionella* “effectors”, MavC and MvcA, are injected into the host cytosol in order to deamidate ubiquitin. Through interactions with the E2 protein UBE2N (part of a ubiquitination cascade involved in innate immunity), MavC is able to suppress host NF- κ B signaling in response to a number of cues. Pointing towards the importance of tightly controlling this modulation, MavC and MvcA are directly inhibited by another effector, Lpg2149 - a member of a newly discovered class of regulatory effectors, “metaeffectors,” that target other effectors rather than the host. (*Cell Reports* 2018, doi:10.1016/j.celrep.2018.03.060)



Our ability to fight HIV-1 infection is impeded by the ability of the virus to develop resistance to current drugs.

Research led by **Dr. Alan Cochrane** searches for novel inhibitors of HIV-1 and has identified over 12 cardiotonic steroids (compounds used to treat heart disease) that impede

HIV growth in HIV-infected T cells. A new study, published in *Scientific Reports*, has determined that the signaling pathway used by cardiotonic steroids to alter HIV-1 RNA processing results in a suppression of virus replication. Interestingly, the calcium (Ca²⁺) signaling pathway that confers the effects of these compounds on the heart and is responsible for their toxicity in humans is not required and activation of a separate pathway is needed. Selective activation of the latter pathway can achieve the same inhibition of HIV-1 replication. These findings provide an additional demonstration that manipulation of viral RNA processing can be achieved with small molecules without significant effects on the host cell.

(*Scientific Reports* 2018, doi:10.1038/s41598-018-19298-x)

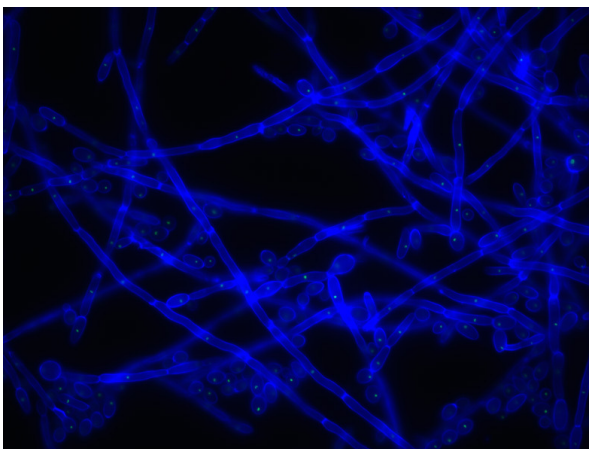
Environmental exposure has a big impact on our health, and determining the interaction between our genomes and the environment is a big challenge for preventive medicine. A new study, led by **Dr. Philip Awadalla**, has found strong evidence that



environmental exposure, including air pollution, has a bigger effect than genetic ancestry on gene expression associated with respiratory disease. The study, published in *Nature Communications*, analyzed the genetic, health and disease data of participants from Montreal, Quebec City and Saguenay (photo), and linked these with environmental

information such as air pollution, walkability and access to food, to see how these factors impact gene expression. The results demonstrate how the local environment directly affects disease risk, and that genetic variation can modulate an individual's response to environmental challenges. Click [here](#) to read more.

(*Nature Communications* 2018, [doi:10.1038/s41467-018-03202-2](https://doi.org/10.1038/s41467-018-03202-2))



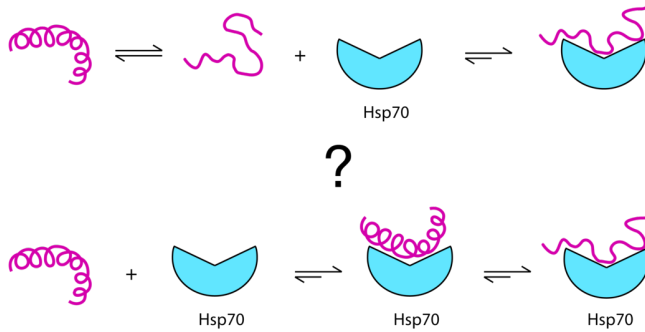
Fungal pathogens such as *Candida albicans* often undergo morphological changes, which allow the fungi to evade the immune system, induce host damage and cause devastating disease. In a recent study published in *PLoS Genetics*, **Dr. Leah Cowen and colleagues** provide new insights into how fungi can sense temperature fluctuations in the host

and respond by inducing its virulence factors. The study uncovers fascinating biology whereby either overexpressing or depleting the levels of a single, environmentally contingent transcription factor, Hsf1, can induce morphogenetic transitions.

Understanding the mechanisms that regulate these morphogenetic switches can lead to the development of novel treatments that disarm the virulence of the pathogen.

(*PLoS Genetics* 2018, [doi:10.1371/journal.pgen.1007270](https://doi.org/10.1371/journal.pgen.1007270))

Molecular recognition forms a central component of biological

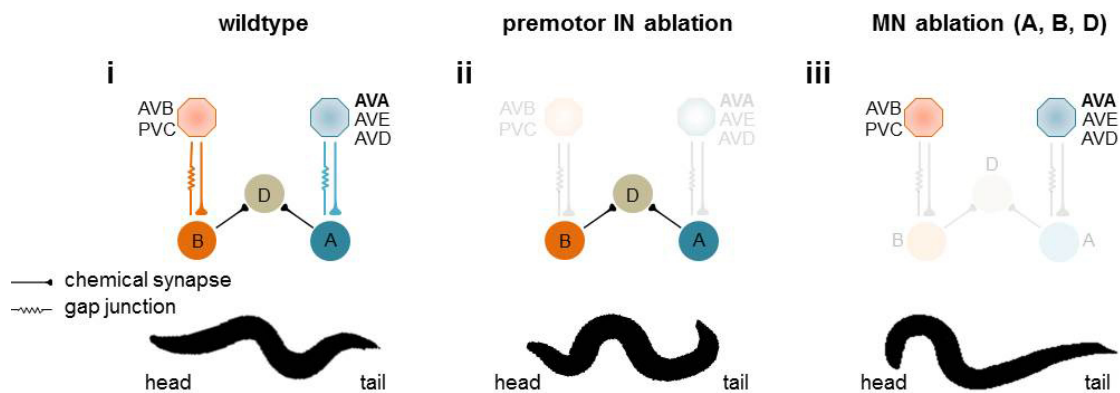


transformations and generally involves conformational changes coupled to a binding event.

Modifications in structure occurring in concert with recognition have typically been understood in terms of two limiting

mechanisms depending on whether the conformational switch occurs prior to (“conformational selection”) or in response to binding (“induced fit”). The relative importance of these limiting mechanisms has been intensely debated because it is difficult to evaluate the molecular flux along the two competing reaction routes. A new study led by **Dr. Lewis Kay**, published in *eLife*, has addressed this debate using the ubiquitous and conserved Hsp70 chaperone, which oversees the integrity of the cellular proteome through its ATP-dependent interaction with client proteins. In order to study the molecular mechanics of this interaction, Dr. Kay and colleagues developed advanced NMR techniques that allowed quantification of the fluxes along the different pathways. The results establish that both bacterial and human Hsp70 chaperones interact with substrates predominantly via conformational selection, that is, they choose conformational states from an ensemble of pre-existing but transient ones. The results point to a conserved mode of client recognition among the Hsp70 family, and highlight the importance of molecular dynamics in this recognition event. (*eLife* 2018, doi: [10.7554/eLife.32764](https://doi.org/10.7554/eLife.32764))

Also, see the [accompanying commentary in eLife](#) by Jiang & Kalodimos.



Proper muscle movement requires the coordinated action of neurons firing rhythmically and at the right time. Central pattern generators (CPGs) are

rhythm-generating neurons and neural circuits with intrinsic oscillatory activities. Across the animal phyla, CPGs are proposed to underlie rhythm of motor behaviors that are either continuous, such as breathing and heartbeat, or episodic, such as chewing and locomotion. The small nematode worm *C. elegans* exhibits rich sensorimotor functions despite a small neuron number; however obtaining a mechanistic understanding on how *C. elegans* motor rhythm is generated has been difficult. A new study led by **Dr. Mei Zhen**, published in *eLife*, shows that multiple oscillators underlie *C. elegans* locomotion. Through cell ablation, electrophysiology, and calcium imaging, they discovered that excitatory motor neurons at the ventral nerve cord themselves function as oscillators. The study illustrates how a numerically simple nervous system can achieve a circuit infrastructure analogous to that of anatomically complex systems, but compressed into fewer layers and cells. (*eLife* 2018; doi: [10.7554/eLife.29915](https://doi.org/10.7554/eLife.29915))



How do genes interact to produce the traits we see as individuals? Research led by **Dr. Charlie Boone, Dr. Brenda Andrews, and Dr. Chad Myers** (Univ of Minnesota) has systematically examined a large network 3-way (trigenic) genetic interactions in the yeast *Saccharomyces cerevisiae*, and compared to an extensive analysis of digenic interactions. Notably, about a third of the trigenic interactions represented novel functional connections that were not observed

in the digenic network, illustrating that higher-order genetic interactions play important roles in phenotypes and modifications to phenotypes in species. The study, published in *Science*, represents the largest of its kind and sheds light on how genes work together to keep cells healthy, paving the way for predicting a person's risk of disease. Click [here](#) to read more.

(*Science* 2018, doi: [10.1126/science.aa01729](https://doi.org/10.1126/science.aa01729))



Faculty Highlights and Awards

Welcome to New Faculty



Dr. Yun Li is a Scientist in the Developmental & Stem Cell Biology program at the Hospital for Sick Children, and has recently joined the Department as an Assistant Professor. She received her PhD at the University of Texas Southwest Medical Center, and her postdoctoral training with Rudolf Jaenisch at the Whitehead Institute at the Massachusetts Institute of Technology. Dr. Li's research aims to understand how the human brain forms, what makes it unique from that of other species, and how disorders like autism impact its development and

function.



Dr. Julien Muffat is a Scientist in the Neurosciences & Mental Health program at the Hospital for Sick Children, and has recently joined the Department as an Assistant Professor. Dr. Muffat received his PhD. from the California Institute of Technology, and completed his post-doctoral training with Rudolf Jaenisch at the Whitehead Institute at the Massachusetts Institute of Technology. His laboratory studies interactions of the nervous and immune systems, with a focus on understanding the role of the resident innate immune cells of the brain, microglia, in neurological and

psychiatric disorders.

Faculty Honours & Awards



Dr. Lewis Kay has been awarded the *2018 Gerhard Herzberg Canada Gold Medal*, Canada's highest honour for science and engineering. The prize, which is accompanied by \$1 million in grant funding, recognizes his role in improving nuclear magnetic resonance (NMR) spectroscopy, technology that elucidates the molecular structure of proteins and other macromolecules within cells.

See the stories in the [Globe & Mail](#) and [UofT News](#).

Canada Research Chairs

Five faculty from Molecular Genetics are Spring 2018 Recipients of Canada Research Chairs (see the story in [U of T News](#)):

Dr. Amy Caudy - *Tier 2 Canada Research Chair in Metabolomics for Functional Enzyme Discovery*. The Caudy lab uses genetic and chemical approaches to study



the metabolome, the chemical intermediates of cellular metabolism; and specifically to characterize the chemical reactions carried out by enzymes of unknown function and place them in context of cellular metabolism and disease.



Dr. Leah Cowen - *Tier 1 Canada Research Chair in Microbial Genomics and Infectious Disease*. Research in the Cowen lab focuses on diverse facets of the biology and evolution of fungal pathogens to understand how microbes exploit the host and cause disease, and to use this knowledge to develop new strategies to thwart drug resistance and treat life-threatening infections.



Dr. Xi Huang - *Tier 2 Canada Research Chair in Cancer Biophysics*. The Huang lab studies the mechanisms by which ion channels regulate brain development and tumorigenesis, and the therapeutic efficacy of ion channel drugs in treating brain tumours.



Dr. Laurence Pelletier - *Tier 1 Canada Research Chair in Centrosome Biogenesis and Function*. The Pelletier lab studies centrosome biogenesis and function, with a particular emphasis on how their perturbation can lead to devastating developmental diseases and cancer.



Dr. Michael Wilson - *Tier 2 Canada Research Chair in Comparative Genomics*. Research in the Wilson lab uses comparative genomic approaches (experimental and computational) to understand disease causing variants in the human genome.



Trainee Highlights and Awards

Dr. Serge Guerousov was awarded the **2017**



Barbara Vivash Award for his PhD thesis, entitled “Functional Consequences of Mammalian-Specific Alternative Splicing Events in RNA Binding Proteins”. Serge’s PhD studies, with Ben Blencowe, examined roles for alternative splicing in the brain. Serge is now a postdoctoral fellow at the Broad Institute of MIT and Harvard.

The Barbara Vivash award is given annually to the graduating student with the best PhD thesis in Molecular Genetics. Click [here](#) to read more.



Brendan Innes (Bader lab) was awarded the **David Stephen Cant Graduate Scholarship in Stem Cell Research**.

The scholarship was endowed by Peter and Sally Cant in memory of their son, David. The award is given annually to a MoGen graduate student who is demonstrating excellence and commitment to the study of stem cell research, and particularly in the areas of neurological disorders, macular degeneration, or stem cell intervention for vision recovery.

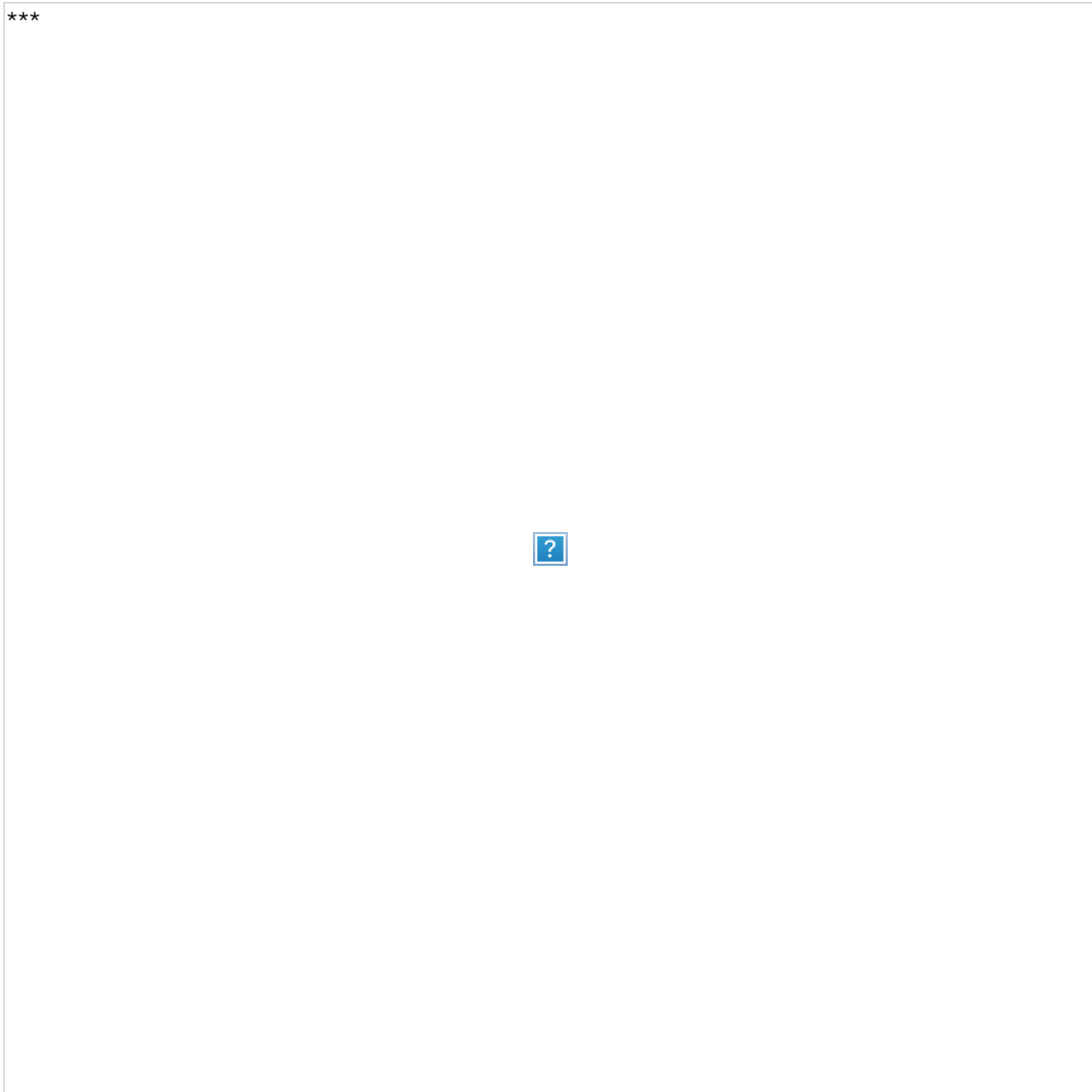


Eesha Sharma (Blencowe lab) has been awarded a **2018 Jennifer Dorrington Award**, for her studies on non-coding RNAs and RNA-RNA interactions at the genomic level. The award was established in 2006 as a tribute to Dr. Jennifer Dorrington, who was a professor in the Banting and Best Department of Medical Research. Click [here](#) to read more.

Samantha Yammine (van der Kooy lab) was



recently featured on [CBC's Cross Country Checkup](#). Samantha is exploiting social media to engage and inform the public about science, scientists and the goals of scientific research. Click [here](#) to read the story in UofT News.



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