“Ships on the Horizon” was the motto of this year’s Garrod meeting in Halifax (May 12-14, 2016) which was so excellently organized by Jane Gillis. The agenda was mostly dedicated to treatments and outcomes of inherited metabolic diseases.

CIMDRN presented the first data from our Canadian database on Inherited Metabolic Diseases, and the Canadian Fabry Disease Initiative presented interesting lessons on long term outcomes upon ERT. The schedule contained a well-balanced mix of presentations on evidence and policies in orphan drug development, upcoming innovative therapies, and updates on state of the art treatments for IEM. Mark Tarnopolsky’s presentation on exosome-mediated therapies was a highlight giving hope for patients with mitochondrial diseases. The program was rounded up by a well-attended dietician webinar, a breakfast session driven by patient and parent experiences on rare diseases, and several industry-sponsored symposia. The meeting ended with a session on high throughput technologies for personalized medicine of IEM. The poster session showcased interesting work from students and fellows across the Canadian metabolic centres. Finally, Mark Korson’s presentation on new paradigms for KD in metabolic medicine motivated us as a society to reach out to fellows, residents and students and entice them to become part of our group.

Thank you once more, Jane, all the sponsors, speakers and delegates for making this meeting a true success.

We are all looking forward to next year’s meeting, which will be organized by the Metabolic Teams in Montréal. Please watch out for the final date and program which should be available soon on our website.

Sylvia Stockler, MD, PhD, FRCPC
President of the Garrod Society (2016-2017)
Division of Biochemical Diseases
Department of Pediatrics
University of British Columbia
Editor’s Corner

Dear Friends,

I am very pleased to bring you the latest Garrod newsletter. Our metabolic community is vibrant and is working on many new initiatives and projects. Under the leadership of Dr Sylvia Stockler as our president we have made a number of strides including a very successful Garrod meeting in May 2016. Dr Jane Gillis managed to organize the meeting even when she had moved to Vancouver. It was a very successful meeting in terms of its scientific content as well as the chance to socialize with our friends and colleagues. Please read further about the meeting in the newsletter. Professor Brian Robinson was honored as our pioneer. We learned a lot from him and our other pioneers. Garrod newsletters and the Garrod website serve as a means of communication amongst all of us. I would encourage every one to participate and share their clinical, education and research updates through the Garrod newsletters and the website. I would like to thank Janice Little our research associate who has done a wonderful job with the newsletters and the website.

With best wishes

Chitra Prasad (Editor)

If I may throw out a word of counsel to beginners, it is: Treasure your exceptions! When there are none, the work gets so dull that no one cares to carry it further. Keep them always uncovered and in sight. Exceptions are like the rough brickwork of a growing building which tells that there is more to come and shows where the next construction is to be.

By William Bateson

From the Host of the 2016 Garrod Meeting

From the organizer: I would like to thank all of the speakers, presenters and patients for their truly outstanding presentations, as well as friends of Garrod for making the Halifax Garrod 2016 meeting exceptional.

It was an absolute honour and thrill to showcase my home town of Halifax and reconnect with Maritime colleagues, as well as those from the rest of Canada, The United States, Europe and India! The weather was beautiful and the Marriott Harbour Front provided a cosy and scenic venue for the meeting and brilliant local entertainment. The lobster dinner Gala was a grand celebration and honoured Dr Brain Robinson, this year’s recipient of the Pioneer Award. Dr Andreas Schulze graciously accepted on Dr Robinson’s behalf and shared with us Dr Robinson’s inspirational acceptance message. Drs Annette Feigenbaum and Mark Tarnopolsky shared their experiences and fond memories of Dr Robinson.

I would like to extend a heartfelt thank you to all who traveled to Halifax to attend and participate in, making this year’s Garrod yet another success! I also wish to thank Dr Sylvia Stockler for all of her wisdom, assistance and support in the planning and organizing of this year’s event and the Garrod Executive for their support and guidance and scientific program review.

Thank you for the wonderful opportunity to host such a fabulous and memorable meeting! I look forward to seeing everyone in Montreal for Garrod 2017!

Warmest wishes

Jane
Jane Gillis M.Sc. M.D.
jane_gillis@hotmail.com

Videos can be viewed: http://garrodsymposium.com/garrod2016/videos/

Photos can be viewed: https://flic.kr/s/aHskAerUZx
Upcoming Garrod Meetings
Garrod 2017 - Montréal, QC Tentative dates May 5-7, 2017

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Garrod Website: www.garrod.ca

Please see the Garrod website for further details about the meetings, research grants, abstract submission and travel grants for this year.

Garrod 2018 - Edmonton, AB

Garrod 2019 - Toronto, ON
Our Pioneers

Garrod Pioneer award is bestowed upon an individual who has made a significant and tremendous impact on the clinical & laboratory diagnosis/basic research/management/advocacy of inborn errors of metabolism in Canada. To follow the footsteps of Sir Archibald Garrod a physician scientist, this award gratefully acknowledges a leader who has been an inspiration to his/her peers as well as their students. The decision for the award is made by the Garrod executive and representation from the membership. This award hopes to recognize the pioneer’s contributions and inspire the younger colleagues to strive for the same excellence.

Dear friends and colleagues,

I was born in Derby, in the United Kingdom and I studied at The University of Bristol in England for my Bachelor of Science and for my PhD in Biochemistry. I first came to Canada in 1968 to do a fellowship at the University of Toronto, went back to the UK for three years, then moved to a job at the Hospital for Sick Children in 1973.

The story of how I came to be involved in the Diagnosis of Inborn errors of Metabolism is a complex one but has a couple of points that are worth repeating.

Lesson one: There is a strange history because I was originally hired to investigate the phenomena of neonatal hypoglycemia, in other words babies that have low blood glucose, and this really did not turn out to be a direct problem with energy metabolism. Though we discovered the cause was unrelated, I was made aware that there were patients in the hospital who did have defective mitochondria and abnormal energy metabolism. As a result, I started a collaboration with the metabolic physicians and began to investigate disorders of energy metabolism, particularly those associated with lactic acidemia. This new direction was aided and abetted by Physicians on the staff who took the time to recite case histories to me, and in many cases to meet with the families involved. To this end I owe a lot to Geoff Sherwood, Neville Howard, Joe Clarke, Annette Feigenbaum, Ingrid Tein Andreas Schulze and many others. So lesson one is that basic scientists and physicians are a powerful combination when they work together.

Lesson two also comes from a spirit of collaboration and that is with scientists and laboratory staff. I was not trained in a metabolic disorders lab so I had to develop new testing procedures at the micro level that could be performed on fibroblasts. This involved a lot of tinkering, for which I seem to have an aptitude and a willingness to embrace the new techniques emerging from the world of Molecular Biology. I will never forget the time Fred Sanger gave a lecture at Sick Kids about his new dideoxy sequencing method for DNA. It was so elegant and it convinced me that a new era was in the making. With help from John Callahan and Roy Gravel, I converted half of the lab to Molecular genetics and this was followed by the cDNA cloning of the genes of pyruvate metabolism and other important genes involved in oxidative phosphorylation. With the help of my chief technologist, Nevi Mackay and a succession of talented graduate students and postdoctoral fellows, disease causing mutations were soon defined. In the final years of scientific endeavour, Jessie Cameron joined my laboratory and was responsible for diagnosing the first mitochondrial cases with metabolic defects through exome sequencing. She and Valeriy Levandovsky are carrying on the good work at Sick kids now that I have retired.

Lesson three involves the help I received from the members of the Garrod Society. I owe a debt of thanks to those in Canadian centres who so kindly sent me interesting cases over the years, many of which we solved, though we still have a lot to learn. The spirit of friendly collaboration typified by Grant Mitchell and Mark Tarnopolsky has enabled the progress of scholarship and learning. I could single out a long list of individuals both from here and abroad who have contributed to this communal effort. I thank you all. In accepting this award, I hope that I have convinced you that this “pioneer” had a lot of help and inspiration from many sources and I offer my congratulations and support to “The Garrod Society” for their good works to continue.

Thank you, again for this opportunity to say a few words. I regret that I could not attend in person.

Sincerely,

Brian Robinson.
Canadian Research Initiatives
Please submit your research projects and ideas to be included in this section.

The Canadian Inherited Metabolic Diseases Research Network

As many members of the Garrod Association know, the Canadian Inherited Metabolic Diseases Research Network (CIMDRN) is an inclusive practice-based research network comprised of more than 50 investigators from across Canada and beyond. In support of our research program, which is building evidence to improve care for children who have one of 30 inherited metabolic disorders, CIMDRN is currently recruiting affected children and their families from 13 of 14 participating centres nation-wide. As of July 28, 2016, we have recruited 522 participants.

We are pleased to report that, with recruitment and data collection occurring rapidly at this time, CIMDRN has moved into a new phase of its work. Over the past year, we have begun to focus on the evaluation of data quality and on the analysis of clinical data, including investigation of associations between interventions and outcomes; as well as preparing to implement a survey of participating families to incorporate parent-reported outcomes into our analyses. At the Garrod Symposium in May, 2016, CIMDRN was able to present a comprehensive update on its progress and findings to-date.

As CIMDRN looks toward opportunities beyond its initial funding through a CIHR Emerging Team Grant (2012-2017), we have established a dedicated working group to identify projects and funding opportunities that can build on CIMDRN’s research infrastructure. All CIMDRN members who are interested in these efforts are invited to participate.

And finally, CIMDRN’s collaboration with Mito-Canada has progressed as we prepare to implement a survey of physicians who treat patients with mitochondrial diseases in Canada. The goals of this initiative are two-fold: (1) to better understand care, and variation in care, for mitochondrial diseases in Canada; and (2) to stimulate further high-quality research that will improve health services and outcomes for Canadians living with mitochondrial diseases. We invite any interested members of the Garrod Association to contact our team with questions, etc.

Please contact us if you have any questions or suggestions for CIMDRN at this exciting time!

Beth Potter & Pranesh Chakraborty, on behalf of CIMDRN
bpotter@uottawa.ca
pchakraborty@cheo.on.ca
www.cimdrn.ca

From left:  Laure Tessier, Research Coordinator, Monica Lamoureux, Research Coordinator, Beth Potter, Principal Investigator, Sara Khangura, Research Associate, Kylie Tingley, PhD Student

Pranesh Chakraborty, (Principal Investigator)
Study Recruitment

Looking for participants for a graduate research project being run from the School of Epidemiology, Public Health, and Preventive Medicine at the University of Ottawa. The study is aimed at improving the quality of decision-making regarding the development, use, and reimbursement of treatments for rare diseases. The student is Ms Kylie Tingley, a candidate in the PhD epidemiology program, and Dr Pranesh Chakraborty is a member of her supervisory team, along with Dr Beth Potter, Dr Doug Coyle, Dr Ian Graham, and Dr Kumanan Wilson. As part of her PhD work, Ms Tingley will be consulting with stakeholders to better understand their perspectives on evaluating and synthesizing treatment effectiveness evidence for rare diseases. The results of this study will be used to shape the development of an evidence framework for evaluating evidence for rare diseases.

The study team is seeking individuals with experience in treatment of those diagnosed with an inherited metabolic disease and who may be interested in participating in a 45 to 90 minute focus group about current practices in evaluation and synthesis of treatment effectiveness evidence for rare diseases.

If you are interested in participating, please contact Ms. Tingley at kting022@uottawa.ca. Ms. Tingley will be able to provide full details of the procedures and answer any questions you may have. Participation in this study is voluntary and the protocol has been reviewed and approved by the Ottawa Health Science Network Research Ethics Board and the Children’s Hospital of Eastern Ontario Research Ethics Board.

A review of the genetic variants in Canadian patients with Fabry disease
CFDI (Canadian Fabry Disease Initiative)

The diagnosis of Fabry disease is based on phenotypic, biochemical, genetic and histochemical findings. The correct diagnosis is critical in that it has implications for counseling, insurance and healthcare system costs. There is known genetic heterogeneity in the GLA gene that causes Fabry disease, including variants of unknown significance and benign variants. We reviewed 82 unique variants in the Canadian Fabry Disease Initiative database and determined that there are 61 variants that are pathogenic, 9 that are likely pathogenic, 4 that are benign and 8 that are of unknown significance. We proposed a protocol to try and further categorize the variants of unknown significance as well a strategies for those patients with variants that are benign and likely pathogenic. We highlight importance of ongoing review of genetic variation as well as genetic counseling.

Dayna-Lynn Nevay MSc, CCGC
Genetic Counsellor
Adult Metabolic Clinic

Fabry Research Study
FACTS gene therapy (FAbry disease Clinical research and Therapeutics)

Dr. Jeffrey Medin is pleased to announce that research ethics approval at 3 sites for a phase I clinical trial for gene therapy in patients with Fabry disease. The sites include the QEII Health Sciences Centre in Halifax (Dr. Michael West), the University Health Network in Toronto (Dr. Armand Keating) and the University of Calgary (Dr. Aneal Khan). The trial is entitled Entitled “Autologous Stem Cell Transplantation of Cells Engineered to Express Alpha-Galactosidase A in Patients With Fabry Disease “. Recruitment has been started and as the sites get activated, further information regarding the trial, eligibility, exclusion criteria and contact information is available at clinicaltrials.gov (identifier NCT02800070 ).
Metabolic Education

**Vademecum Metabolicum**

The Garrod Association is one of the proud sponsors of the electronic version of the Vademecum metabolicum with Johannes Zschocke and Georg F. Hoffmann as Editors and Clara van Karnebeek as Editor of the electronic version which is now freely downloadable at [www.vademetab.org](http://www.vademetab.org).


**Metabolic Teaching**

Dr. Mark Korson

The Genetic Metabolic Center for Education (GMCE) shares a common mission with all other stakeholders in the "metabolic disease community" - to raise awareness about these disorders, so that patients are diagnosed in a timely way, and as a result are eligible more quickly for effective and potentially life-saving therapies. As a unique education-focused entity, GMCE believes it will be able to provide unprecedented, ongoing awareness about metabolic disease to important target physician populations, and look to educate both specialists and specialty trainees so they can play more of a role in patient diagnosis and management.

The following integrated resources encompass the capabilities of GMCE:

**Consultation and Clinical Support Service (CCSS)** – A program in which an experienced metabolic physician/dietitian team provides clinical consultative/educational support by HIPAA-secure video-conferencing to providers who need to consider metabolic disease in the differential diagnosis and/or who manage metabolic patients. Includes access to emergency consultation.

**Subspecialty-Specific Conferences** – Live training programs that provide practical approaches to multiple metabolic symptoms within a specific specialty using clinical, interactive, case-based workshops with a focus on metabolic diseases for which treatments currently exist. Our first conference ("Metabolic Approach to Symptoms in the Newborn") occurred last December as a satellite symposium for the annual congress, "Hot Topics in Neonatology". Because of its success, repeat workshops are planned for this annual meeting this coming December and next year as well.

**Interactive Training/Reference Web Site** - A modular learning site for specialists and specialty trainees likely to encounter metabolic patients. The site will host the following:

- **The Lecture Hall** (offering on-line metabolic approaches, grouped together by specialty interest)
- **The Clinic** (recordings of patients/families talking about living with their diseases)
- **The Library** (providing key articles relevant to lectures and patient presentations)
- **Study Hall Forum** (providing educational review and examination preparation)
Patient-As-Teacher Project (the Damian Project) – Live and video streamed opportunities at teaching hospitals and medical schools to learn firsthand from patients/families about living with a metabolic disease. This program already occurs at Tufts and Boston University medical schools each fall and began over 8 years ago. In addition, GMCE is building a library of professionally filmed and edited patient presentations to be used throughout its educational programming, including online electives for specialty trainees. The rationale here is that physicians will be more likely to identify patients with disorders they have seen before.

Industry Training Seminars - An educational outreach to pharmaceutical and other companies that cater to the "metabolic community." This will help upgrade the level of understanding industry employees have about the diseases in which they have an interest so they can interact more knowledgeably with patients and health care professionals.

For more information about GMCE, its mission, or its educational strategy, please visit www.geneticmetabolic.com GMCE also welcomes ideas and collaborations. Let's connect!

New Testing

Newborn Screening

Newborn Screening Ontario (NSO) has started offering diagnostic laboratory services under our new "NSO Diagnostics" division. We are pleased to announce that we are now offering two molecular diagnostic tests using a next-generation sequencing (NGS) approach.

The first is testing for mitochondrial diseases, in collaboration with London Health Sciences Centre and Hamilton Health Sciences Centre (see separate joint announcement in this newsletter).

The second is for diseases targeted by newborn screening in Ontario. This panel currently includes 76 genes associated with the primary and secondary targets of the provincial NBS program. Only the gene(s) related to the suspected disease will be analyzed, and variants in these genes will be reported. This molecular test is not part of the newborn screening process; it is a diagnostic test that can be requested following a screen positive, or if there is clinical suspicion of a disease that is targeted by the Ontario newborn screening panel. For more information, including gene lists and requisitions, please visit https://www.newbornscreening.on.ca/en/diagnostic-testing. Please feel free to contact us by phone or email if you have any additional questions, comments, or suggestions. Specifically, we are planning to update our gene panel shortly and would appreciate any feedback regarding genes you would like to see added – or would suggest we remove.

For general inquiries including pricing, please contact Brigitte Belanger, CCGC at bbelanger@cheo.on.ca or 613-737-7600 x3778. For medical/scientific inquiries, please contact: Dr. Dennis Bulman at dbulman@cheo.on.ca, or Dr. Pranesh Chakraborty at pchakraborty@cheo.on.ca

Mitochondrial Disease molecular diagnostic testing

We are pleased to announce the opening of the “Ontario Mitochondrial Laboratories”, now offering a broad range of molecular testing for mitochondrial diseases. This includes mtDNA sequencing using Next Generation Sequencing (NGS), a variety of nuclear gene NGS panels and sub-panels, mtDNA deletion and depletion testing, targeted mtDNA mutation testing, single gene mutation analysis, and known familial mtDNA or nuclear gene testing.

The Ontario Mitochondrial Laboratories is a collaboration between London Health Sciences Centre, McMaster University Medical Centre, and Newborn Screening Ontario at CHEO (the Children’s Hospital of Eastern Ontario), offering a one-stop shop for mitochondrial disease molecular testing within Canada. The Ontario Ministry of Health and Long Term Care will reimburse the cost of testing for any Ontario patients who meet the test utilization criteria (attached). In order to simplify and streamline the process of ordering mitochondrial disease testing, one web portal (MitoDx.ca) for all three labs will allow healthcare professionals to see what testing is offered, generate a custom requisition, and digitally submit requisitions alerting the lab of an incoming request.
A PDF copy of the requisition (including the Ontario test utilization criteria) is attached to this announcement.

For more information about our services, to access the test ordering system, and to access information about the gene panels provided, please visit MitoDx.ca.

Please feel free to contact us by phone or email if you have any additional questions.

For general inquiries, including pricing, please contact Brigitte Belanger, CCGC at BBelanger@cheo.on.ca or 613-737-7600 x3778.

For medical/scientific inquiries for a specific service laboratory, please contact:

NSO at CHEO: Dr. Dennis Bulman (dbulman@cheo.on.ca), or Dr. Pranesh Chakraborty (pchakraborty@cheo.on.ca)
HHSC: Dr. John Waye (wayne@hhsc.ca)
LHSC: Dr. Tony Rupar (Tony.Rupar@lhsc.on.ca), or Dr. Bekim Sadikovic (Bekim.Sadikovic@lhsc.on.ca)

Support Groups

Camping with CanPKU!

Campfires, cabins and community: Canadian PKU and Allied Disorders welcomes you to our first-ever national camp! What better way to celebrate Canada’s 150th Birthday than by bringing our national PKU community together! Grab your friends and family of all ages - from child to adult, those with PKU and those without - for a weekend full of activities, guest speakers and camp food. Located just outside of Peterborough, Ontario, the camp takes place the weekend of September 22-24, 2017, and registration opens December 1, 2016.

Visit canpku.org/canadian-pku-camp for more details.

If you have any news items, please submit to Janice. Little, Resource Associate, LHSC: janice.little@lhsc.on.ca