Barth Syndrome Foundation of Canada

Canadian Newsletter

www.barthsyndrome.ca

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President's Report *by Susan Hone*

Happy Fall everyone!

I am starting off this update with what was the highlight of my summer. After six long years our Global Barth family was able to reconnect at the Biennial International Scientific, Medical & Family Conference in Florida in July! I was so excited to see old friends and was introduced to a number of new families who have joined our group over the past six years.

Canadian Contingent at the 2024 Conference.
Photo submitted by Susan Hone

We had a record number of individuals affected by Barth syndrome attend this year and it is both amazing and sad to see how our group has grown. Canada was well represented at the conference by seven families, researchers, students, and doctors who attended. BSFCa provided financial assistance for five individuals affected by Barth syndrome and one researcher to attend the conference thanks to our generous donors. We also had a dinner one night for the Canadian families at the conference which was funded by an anonymous donor. The dinner was a nice added bonus to the conference, and we would like to express our gratitude to the donor.

One of the highlights for the Canadians was a Researcher from Dr. Robin Duncan's lab at the University of Waterloo, John Zewen Chan, won the prize for the best poster at the poster session. There were 38 posters on display and Mr. Chan's submission on the **Effects of Compound X on Tafazzin-Deficient B-Lymphoblast Growth and Mitochondrial Parameters** was chosen as the winner. Congratulations John!

Conference 2024.
Photo submitted by Susan Hone

At the conference, I attended a meeting with other members of BSFCa along with the leads of the other Barth syndrome affiliates and the Chair and Executive Director of the Barth Syndrome Foundation. We discussed ways in which we could support each other, share ideas, and plan for the future of the organizations.

I am excited to announce the addition of Laurel Pridgen to our Executive Committee. Laurel has two sons affected by Barth syndrome. Welcome aboard Laurel!

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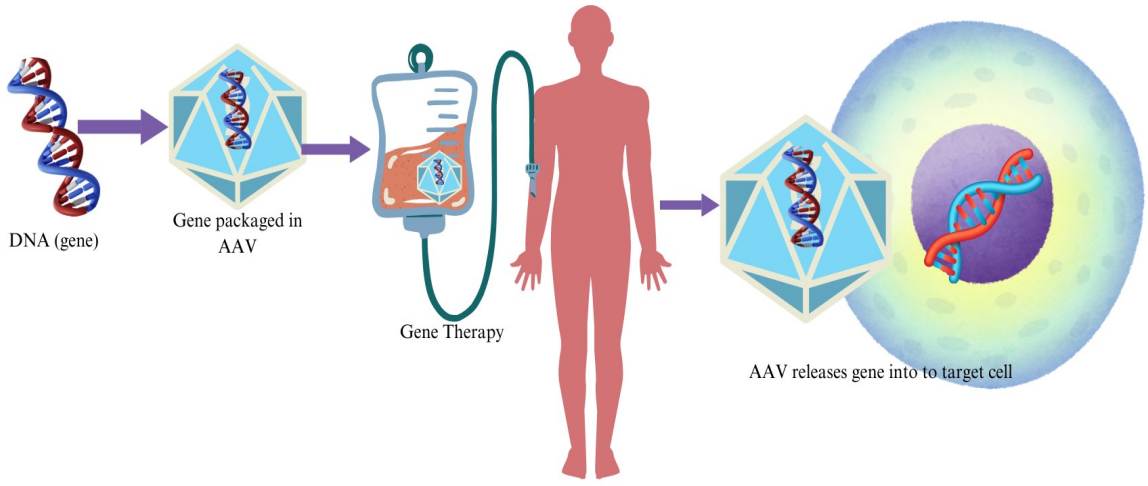
"Enhancing the **lives** and **outcomes** of **Canadian** individuals and families affected by Barth syndrome."

The Road to Gene Therapy *by Christiane Hope*

In recent years, we have heard a lot about gene therapy and Barth syndrome. Although there are multiple approaches to gene therapy, gene addition therapy, in which the non-functional gene is boosted by the addition of a healthy, normal gene, attracts a great amount of interest in our population.

Barth syndrome occurs due to a defect, called a mutation, that occurs in the TAFAZZIN gene. Having a single gene disorder and a relatively small gene, is fortunate as the disease is an ideal candidate for gene therapy. The goal of the therapy is to deliver a full working copy of the gene to reverse the impact of Barth syndrome at its source.

In simple terms, a "package" is created in which a non-defective copy of TAFAZZIN is "wrapped" in a coating called a vector. Currently, adeno-associated viruses (AAVs) are the most popular vectors being used to create the package, as viruses have the unique ability to insert a copy of a gene into DNA. The package along with "promoters" to increase the likelihood that it will be delivered to the heart and skeletal muscles (the target tissues) and NOT to off-target tissues such as the liver is delivered via an infusion into a Barth affected individual. While this sounds simple, there are many curves and hurdles before even a clinical trial is attempted.



The first issue, which scientists are currently working on, is the creation of the package. We need something that when delivered, targets all the organs and tissues that need it, and does not target the organs and tissues that do not. We also need to make sure that the correct amount of package is used—a large enough dose so that it does the job, while at the same time not too much, so there is no adverse reaction to the package. Muscle tissue plus heart represents a large proportion of human tissue, so minimizing overall dose requires a highly targeted package. Immune responses are the principal form of adverse reaction but there can be other toxic effects which must be avoided as well. Before human trials can be authorized, testing is conducted on human (BTHS) cells in a lab as well as animal models including mice and possibly in larger animals.

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Our First Conference Experience *by Laurel Pridgen*

We flew down to Florida this summer with a lot of expectancy, excitement, and hope. The feeling I had when I looked down the conference room hallway and saw the big Barth logo showcased on the display screen was surreal. This conference was planned and organized specifically for my family. Having two boys with a rare condition, it is not often that there is such focused attention on their disease in a way that brings such excitement and hope. As this was our very first time to Florida for the Biennial International Scientific, Medical, and Family Conference, I didn't quite grasp how much attending this conference would mean to me before seeing this logo. We received the Barth diagnosis for our boys, Jonathan (6) and Micah (4) during the Covid pandemic and we began this journey connecting with our Barth community largely online. Also, living in Canada, we are uniquely situated so that the other individuals with Barth who live here are spread out in such a way that meeting in person was not quite an option in the beginning.

We were so fortunate to have a Barth meet-up in Calgary, where we live, a few years ago, which allowed some of our medical team to join in. This meeting in Calgary came at a great time to help us understand the immense value of our Barth community and the need to be connected to build community, relationships, and gain understanding of Barth in each and every season. Coming to Florida this summer was no different. Both my husband and I, less than 24 hours into our stay this summer, both agreed that we couldn't NOT come to each one. Meeting friends who are more like family, who understand more than anyone else what you go through day in and day out, is a special gift and is precious time. Seeing my boys connect with other Barth boys close to their age was not only a cute, but interesting observation. My daughter especially loved Camp Barth and being part of something for her brothers, but in a way that she could enjoy herself and have fun. Hannah told me that "she liked the crafts and making new friends". She was very competitive in the boat race especially and had plans all week as to how her team was going to win.

Team entry in Build-a-Boat Race.
Photo submitted by Laurel Pridgen

Second to the time with other families was the privilege we had to meet medical professionals and researchers who have devoted most, if not all, of their time to working with and for Barth syndrome individuals and families. I will never forget the moment we had with Dr. Taylor, as the boys had their cardiac testing done at the conference and how she was so hands on with them and right there with them at the bedside when imaging was taken. I could see that she

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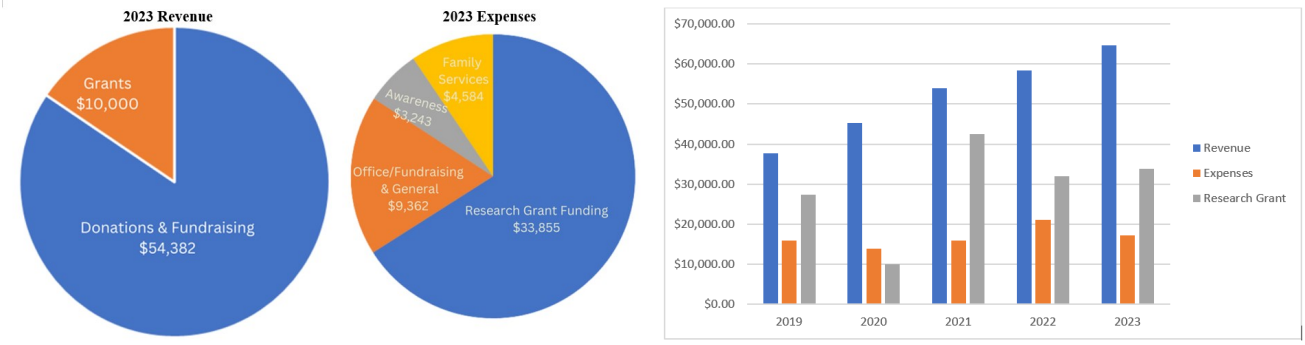
2023 Financial Overview *by Christiane Hope*

The Barth Syndrome Foundation of Canada remains an all-volunteer foundation, and continues to be driven by our unwavering commitment to our mission. We extend our heartfelt gratitude to our donors for supporting our ongoing programs—Family Services, Science & Medicine, and Awareness.

As of December 31, 2023 BSF Canada maintained a healthy financial position.

Five-year trends in Revenues and Expenses



The Road to Gene Therapy continued *by Christiane Hope*

Once those problems are solved, the package needs to be manufactured. Quality control is extremely important so that there are no impurities or empty packages being used, as that would mean a higher dose is needed which leads back to safety issues.

To understand what is needed, how much is needed, and how to produce enough in order to get FDA authorization to start a clinical trial is enormous --$2-5 million US for the GLP pre-clinical work and an additional $10+ million US for a phase 1/2 trial. That is if all the tests are successful, and if there are no hiccups along the way. The Barth Syndrome Foundation is working hard to find partners to help with this endeavour, and whenever we (BSF Canada) are able, we give what we can. It is hoped that we will reach the phase one clinical trial stage within three to five years.

However, while exciting, gene therapy may not be fully curative, and it is possible that it may not work for everyone, as the package includes a virus and individuals who have previously been exposed may have antibodies to it. Additionally, work from other diseases indicates that younger individuals may benefit more than older affected individuals. Despite these hurdles, curves, and mountains to climb, we truly feel that gene therapy is worth pursuing, and we will continue following the road to the end.

Reflections on the NSGC 43rd Annual Conference *by Jessica Wright*

I was recently invited to attend the National Society of Genetic Counselors (NSGC) 43rd Annual Conference in New Orleans by Rebecca McClellan, a genetic counselor who has worked with many Barth syndrome families. It was an experience that was both enlightening and deeply personal. Alongside me was Olivia, a fellow carrier of a genetic condition. Our shared journey provided a unique perspective as we navigated the complexities of our experiences and those of the communities we represent

As we prepared for our session, I felt a mix of excitement and anxiety. Would our story resonate? Would attendees find our experiences compelling? To our surprise, after our presentation, we were met with a flurry of questions, indicating a genuine interest from genetic counsellors eager to understand the perspectives of those directly affected by genetic conditions. Seeing such engagement and curiosity was amazing, and it reinforced the importance of including voices like ours in the conversation.

Throughout our discussions, Olivia and I emphasized the need for genetic counsellors to approach their work with empathy and respect. It's vital to communicate without assumptions, especially regarding women's choices about motherhood. This dialogue highlighted the importance of listening and understanding the individual experiences of carriers, which is crucial for effective counseling.

The emotional weight of our journey was palpable. Both Olivia and I have faced loss, having lost siblings to the very condition we carry. Sharing our stories brought both of us to tears as it was a wave of emotions. I believe that it helped foster a sense of solidarity and understanding within the room. These experiences are not just statistics, but deeply human stories filled with love, loss, and resilience.

After our talk, a group of Canadian genetic counsellors approached us after our session. They expressed a desire for us to speak at their upcoming conference, further amplifying the importance of our narrative. It's a reminder that our experiences can contribute to a broader understanding of genetic conditions and the complexities they entail.

Olivia, Becky, Jessica.
Photo submitted by Jessica Wright

Reflecting on my time in New Orleans, I feel grateful for the connections made and the conversations had. In conclusion, attending the NSGC 43rd Annual Conference was an opportunity to share, and learn, about genetic counseling. As I continue to navigate my journey as a Barth syndrome carrier, I hope to inspire others to engage in these vital conversations, fostering understanding and empathy in the ever-evolving field of genetics.

Panel of NSGC Speakers .*Photo submitted by Jessica Wright*

Pictures of the 2024 Conference

Photos submitted by Susan Hone and Christiane Hope

Our First Conference continued *by Laurel Pridgen*

clearly loves what she does because she cares so much. It meant a lot that she took the time to talk with us and hear a part of her story.

I also was greatly encouraged by the organization and dedication of the BSF staff and team. My biggest take away was that we have the BEST team working to find a way to help save these boys and men. For a rare disease mom, that is honestly such a gift to know that you are in such good hands and that there is passion in the advocacy work that is being done for your children's disease. I greatly appreciate the Barth Syndrome Foundation of Canada for partially sponsoring us for the cost to be able to go and experience this trip. I look forward to next time we get to go to Florida and my hope is more Canadian families can come and join us!

The Pridgen Family. *Photo submitted by Laurel Pridgen*

Congratulations to Adam and Pamela on their wedding this past summer. We wish the happy couple a lifetime of incredible joy, and lasting happiness. May the years ahead be filled with so much love

President's Report continued *by Susan Hone*

In November, the Executive and Board will be having our annual planning meeting to discuss our goals for the next year including possible research funding, an outreach, fundraising efforts, and general organizational requirements.

At last year's meeting, we decided to allocate $15,000 US to assist in funding a grant to David Stokes, PhD, New York University on the **Mechanism of cardiolipin remodeling by TAFAZZIN.**

Strides are being made in the search for a treatment/cure for Barth syndrome. Gene therapy (article included) is one of the avenues being pursued along with the drug elamipretide manufactured by Stealth BioTherapeutics. At a recent Federal Drug Agency Cardiovascular and Renal Drugs Advisory Committee meeting, several families and employees of Barth Syndrome Foundation presented their opinions as to why elamipretide should be approved for use in Barth syndrome. The majority of the committee agreed and the next step in the road to approval will take place in January 2025. Congratulations to all who presented at the meeting and thank you for all your hard work.

Barth Man (Chris Hone) and Emily Milligan, Executive Director of BSF. *Photo submitted by Susan Hone*

As 2024 quickly comes to an end, I wish you all the best and thank you for your continued support.

For donations, please visit

www.barthsyndrome.ca/donate

What is Barth Syndrome?

Barth syndrome is a rare, genetic disorder primarily affecting males around the world. It is caused by a mutation in the *tafazzi*n gene which results in an inborn error of lipid metabolism. This error causes, in various combinations and varying degrees: cardiomyopathy (disease of the heart muscle), neutropenia (an abnormally low count of a type of white blood cell that helps fight off infections), underdeveloped skeletal musculature and muscle weakness, and severe growth delay and exercise intolerance.

While much progress has been made in treating Barth syndrome, unfortunately, it still remains all too often a fatal disorder.

Going Green!

If you have any concerns or are interested in receiving our newsletter via email, please contact us at info@barthsyndrome.ca