



xpressions

Fragile X Research Foundation of Canada Newsletter

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Clinical Trials - Disappointment and Optimism

By Carlo Paribello M.S.M., M.D. President, Medical Director of FXRFC

“...scientists have long understood that even negative results can provide valuable information that points in other possible directions.”

As a physician, clinical researcher and parent of two sons with Fragile X syndrome (FXS), I can certainly understand the frustration experienced by the entire FXS community after two major pharmaceutical companies announced that their experimental drugs had failed to show any benefit to individuals affected with this disorder. In the spring of 2014, Novartis announced that the company had decided to discontinue the development program for its main mGluR5 blocker, mavoglurant (AFQ056), following negative results in large international clinical trials for adults and adolescents with Fragile X syndrome. In September of 2014 Roche made a similar announcement regarding its international, multicentre clinical trial to evaluate the efficacy of its

own mGluR5 blocker (RG7090) in the treatment of Fragile X. They too were unable to demonstrate any significant improvement over placebo in any of the outcome measures used.

However, there could have been a number of reasons for the negative findings and scientists have long understood that even negative results can provide valuable information that points in other possible directions.

As with any medical disorder, scientists compare the normal cellular processes with those that occur in the cells of affected individuals, and then determine where they differ. The parts of the pathway that differ can then be targeted with specific treatments. The mGluR5 antagonists (blockers) that were tested by Novartis and Roche targeted just one of

continued next page,

these potential therapeutic targets, a single receptor that is known to play a key role in synaptic plasticity. In patients with Fragile X syndrome, the absence of a single protein (FMRP) in the brain cells causes excessive production of a number of other proteins that are crucial for maintaining normal structure and function of the synaptic connections between neurons. It was expected that by blocking the mGluR5 receptor, the excessive neuronal production of these other synaptic proteins would reverse the deficit seen in Fragile X. The fact that it did not do so, could mean that only some and not all of the proteins should be suppressed in order to reverse the symptoms of Fragile X. This could also explain why patients seemed to respond better to treatment with minocycline, which inhibits only one protein involved in synaptic plasticity (Matrix Metalloproteinase, or “MMP”). These are just some of the issues that researchers will have to address over the next few years.

The FXRFC and the research community are still optimistic that a targeted molecular treatment for Fragile X can work. Even as this article is being written, there are other potential treatments in various stages of development and testing, that are aimed at other “therapeutic targets”. One such drug is NNZ-2566 (Trofinetide), being developed by Neuren pharmaceuticals. It has an entirely novel mechanism of action compared with other drugs that have been tested for Fragile X syndrome. Neuren Pharmaceuticals has recently completed a phase 2 clinical trial that has successfully established the “proof-of-concept” that will allow them to move forward with developing trofinetide for Fragile X syndrome. In this initial small trial with a relatively short treatment period, Trofinetide was very well tolerated at a high dose of 70 mg/kg twice daily. After only 28 days of treatment, improvements were seen

across the major symptoms of Fragile X syndrome, including higher sensory tolerance, reduced anxiety, better self-regulation and more social engagement. This clinical improvement was observed in both clinician and caregiver assessment, and no serious adverse events were reported. The next step in the clinical development of Trofinetide will likely involve a study in younger children with Fragile X syndrome and may examine a longer treatment duration with higher doses.

Looking at other possible therapeutic targets in Fragile X, recent studies using the *fmrl* knock-out mouse models confirm that there is also a deficit in the production of GABAA receptors in brain cells. The reduced number of GABAA receptors in Fragile X syndrome causes heightened sensitivity to sensory stimuli, anxiety and seizures in up to 30% of patients. Marinus Pharmaceuticals is currently running a Phase 2 “proof-of-concept” study to investigate the use of ganaxolone treatment in children with FXS. Ganaxolone has a high-affinity for the GABAA receptor, and it is anticipated that this drug should increase signaling at existing receptors to normalize GABA-mediated inhibition to reduce anxiety, hyperactivity and learning disabilities associated with this disorder.

These are indeed encouraging results and they really do give meaning to the saying “When one door closes, another one opens”! The FXRFC will maintain its current flexible approach to research funding in order to maximize our ability to identify new “therapeutic targets” that can guide the development of future treatments.

If you would like to explore the entire portfolio of FXRFC funded research, past and present, please visit our website, fragilexcanada.ca and click on “Research Grants”.

Save the date: Sunday June 19th 2016

Please join us for the Annual Fragile X Foundation Family Picnic Day at Variety Village in Scarborough, Ontario on June 19th. This day is also Father’s Day, so what a great way for your family to spend some time together!! Please mark your calendar now. This family filled day is always a fun, safe and easy way for everyone to get to know one another while sharing experiences, stories, and parents can catch up as they laugh together!

Plans are already underway for this year’s picnic and we are looking for high school student volunteers to help the day of. If you know anyone looking for their high school volunteer hours, please have them email Lori at: picnic@fragilex.ca. Duties could include supervising the bouncy castle, helping with the 50/50 draw and setting up sports equipment. They will get a free bbq lunch as well as their volunteer hours.

Please plan to attend with your whole family. More details will follow in our upcoming Spring newsletter and you can check details on our website when we get closer to the date: fragilexcanada.ca

XXX-tra Special People

The FXRFC newsletter often publishes stories about the people that sparked the formation of the Foundation and inspire the ongoing growth and commitment of the FXRFC. If you have a story about anyone with Fragile X syndrome, please send it to us along with a picture. Tell us a funny or heart-warming story, or share a success and allow it to inspire others.

This newsletter's X-tra Special people are Robbie and Adam Laforest. Thank you to their dad Bruce Laforest for sharing their story.

Robbie and Adam Laforest were recent co-recipients of the 2015 Paul Van Steen Achievement Award given annually by the Bridlewood Community Association of Ottawa. This award is given each year to a deserving athlete and community representative of Bridlewood.

Robbie and Adam have not let Fragile X syndrome stand in the way of participating in a wide variety of sporting

activities. They have been involved in Special Olympics for twelve years and currently keep busy year round participating in swimming, soccer, basketball, track and field, golf, and bowling. In previous years they have also participated in cross-country skiing and curling.

Robbie represented the Ottawa region in cross country skiing at the 2010 Special Olympics Provincial Winter Games and won two gold medals.

In addition to sports through Special Olympics, they play hockey for the Capital City Condors. They kayak with the Rideau Canoe Club and have participated in the Canadian Kayak championships on two occasions. They also practice Tae Kwon Do with Adam achieving a third degree black belt and Robbie due to receive his red belt in the near future. In addition to their organized activities, they enjoy biking and downhill skiing.

Adam and Robbie volunteer for many Special Olympic charity events such as the annual Torch Run Police drive, Torch Run Motorcycle Run drive, the Marathon of Sport, and the Staples charity drive. Adam and Robbie also volunteer with the Ottawa Senators Sens Foundation and Adam can be found at many Ottawa Senator games selling 50/50 tickets.



Congratulations Robbie and Adam!

FXRFC Newsletter Designer Volunteer needed!

The FXRFC is seeking a talented graphic designer who could assist with the layout of the newsletter. This could be a shared responsibility and assistance is required to keep producing the newsletter.

If you are interested, please contact Lori at: newsletter@fragilexcanada.ca or call 416-261-2666 for more details.

We also want to give a shout out to some great helpers who assist us with the newsletter. A very dedicated group at Variety Village, made up of adults with various intellectual disabilities, help out with folding the donation forms and the newsletters, and inserting them into the mailing envelopes. We really appreciate their help, and we are told the group really enjoys working on it! Thank you very much!



Report on the 2015 Fragile X Running Teams !

Vancouver:

Team FX Vancouver made up of about 30 runners/walkers joined together on June 28, 2015 to participate in the Scotiabank Vancouver Half Marathon & 5k Charity Challenge. Temperatures were unseasonably warm which made it a bit more challenging for the runners, but everyone came together in good spirits and for a great cause.

Kirsten Madsen led the team in fundraising allowing them to reach close to \$18,000 fundraised. Included in there, the team won an additional \$1,500 for FXRFC for having the third largest average dollars raised per fundraising runner! The team is looking forward to doing it again on June 26, 2016!

Toronto:

October 18th, 2015 was our 5th STWM Charity Challenge in Toronto and was the first time we had snow at the start line! It warmed up little and stayed dry, which was really nice. 42 FX Team T.O. runners helped raise \$38,603!! Very special thanks to all the outstanding 2015 runners.

- Special note, Donna Reid set a personal best (PB) with a half marathon (21.1km) of 1:48.19! Fantastic time, Donna!
- Marcus Covino ran in his first 5km event in 25.08 in honour of his older brother Sebastian. Congratulations, Marcus! What a run!

- All the way from Thunder Bay, Jennifer Kreczmer, Rick & Tammy Galati ran in honour of Jennifer's son Ryan. Thank you for being awesome FX Team T.O. members!
- Shawn Gillespie pushed his son Ty in a stroller and completed the 5k in an impressive 26 min.!

If you would like to participate in a world class event and help raise money for the FXRFC, please email fundraising@fragilexcanada.ca to join one of the Fragile X Teams. You don't need to be an athlete; you just have to want to make a difference for Fragile X research.

Photos on these two pages are from the Vancouver and Toronto Runs in 2015 - Thanks to all participants!



2016 Scotiabank Vancouver 1/2 Marathon & 5k Run Join Fragile X Team Vancouver - Sunday June 26th!

On Sunday, June 26nd Fragile X Team Vancouver will run/walk for Fragile X for the 6th year in a row. Since 2010 the Vancouver run has raised well over \$150,000! The Scotiabank Vancouver 1/2 Marathon & 5k is one of the most scenic runs in the country. There is a friendly atmosphere and is mostly downhill!

There is a discount on the entry fee. The entry fee will depend on which event you choose to participate in and how early you sign up. The sooner you sign up the more you save!

Visit: www.canadarunningseries.com/svhm for all event info. and to join Fragile X Team Vancouver.

Remember, you don't have to be a runner! The 5km run is great for the whole family. Start your training early and contact Team Captain Carrie Lakatos at: carriework@shaw.ca for more information and any questions and join Fragile X Team Vancouver in 2016!

2016 Scotiabank Toronto Waterfront 1/2 & Full Marathon (42.2km & 21.1km) & 5 km Run Join Fragile X Team Toronto! Sunday, October 16th

On Sunday, October 16th Fragile X Team Toronto will lace up our shoes again and run for Fragile X. Last year we had a fantastic group run or walk the 5km and half marathon. No marathoners though.

The Scotiabank Toronto Waterfront Marathon is a world class event and Fragile X Team Toronto has established itself as one of the best STWM Charity Challenge teams. Fragile X Team Toronto has risen well over \$250,000 in five years! So many great memories have been made over the years and we are looking to make more in 2016. Hopefully you'll join us and help make a difference for Fragile X research! Come join in the fun - be a part of our FX Team T.O.!

Please stay tuned for more information coming in the summer issue of the FXRFC newsletter and on our website as the event gets closer.

Not a distance runner? The 5km run/walk is family friendly and many people walk it. The half and full Marathon are challenging, but very rewarding. The entry fee will depend on which event you choose to participate in and how early you sign up. The sooner you sign up the more you save and we can offer a Team FX discount as well! Start your training early and contact Team Captains Jennifer Williams or Ian Shearer at fundraising@fragilexcanada.ca or call 416-419-7108 for more information and any questions - and join Fragile X Team Toronto!

Visit www.torontowaterfrontmarathon.com for all the event info.



The FX Tool Box

The Tool Box is filled with suggestions, helpful hints and coping strategies – tools to make living with Fragile X syndrome easier. We invite you to send in your favourite tools to: toolbox@fragilexcanada.ca for printing in future newsletters. On the FXRFC website, in **Coping with Fragile X**, you'll find a **Helpful Hints** page, where the Tool Box also appears. If you have “tools” you use, let us know!

Here are some great tips for learning with technology, and ways to enhancing learning with family and community activities. Use the strategies below to turn almost any activity into a fun learning opportunity. Please adjust these suggestions to suit your child and family as required.

Technology is constantly around us in smart phones, tablets, gaming devices, and computers. Children are given more information and in a variety of ways, but how can you make the most of technology?

Choose the Right Mode: Children often are very motivated by the sights and sounds of technology devices. There is an abundance of technology and something for every age and ability. Some children have the skills and attention to find icons on smartphones while other children need larger interfaces. Some children will instantly catch on to more complex forms of technology while other children need additional tools and instruction. Some schools have iPads and use them on a regular basis. Some classrooms have adaptive computer equipment such as a screen overlay, a switch, or a modified mouse (e.g. large rollerballs). If these aren't available or haven't been tried, ask someone to lend you equipment to try.

Ask therapists, or members of local organizations for resources. This is a way to try technology and make sure it is a fit before purchasing it. Some children will need instruction and practice with new equipment so be sure to give them time before excluding an item.

Find Learning Opportunities: Handing a child an iPhone, iPad or letting them play on the computer will entertain them, but working with them is an opportunity for learning. Technology frequently is used purely for entertainment when it actually holds many possibilities for learning. Language, social, and academic skills all can be taught through fun videos or games. Children can have fun while working on a variety of skills.

Language Skills: When playing games on technology, ask children questions about what they see or hear or what happened first, then next. Use this as an opportunity to work on answering questions or to expand language.

Academic Skills: Develop learning by teaching colors, numbers, and letters. Choose videos or games that incorporate new concepts. These are just a few examples of the many topics that can be found in videos and games. Expose children to new topics through technology to engage and motivate them to learn.

Social skills: When playing video games, interact with children. Take turns and talk about what is happening in the game. This is a great opportunity for interacting, not just entertaining.

Family and community activities often are viewed as breaks from learning, but they are great opportunities for practicing existing, emerging, and new skills. Try these:

Make Opportunities: Think about opportunities for adding skills throughout the day. For example, if a child is working on initiating interactions, play games like 'Duck Duck Goose' where they have to select a peer to play the game. Then assign a task that involves interacting with peers, like recording the daily snacks brought in by classmates. If children are working on self care skills, involve them in feeding pets, preparing food, or using art materials to provide hand washing opportunities.

Use Materials that Encourage Learning: Many children with social anxiety select independent rather than group activities. Although everyone needs time to themselves, plan activities where children want and have to interact, such as group games rather than video games.

Let Children Be the Experts: Prevent skill regression by letting children be the experts and use skills they already have throughout the day. Plan events where they are in charge of the activity or are paired with a peer to be the group expert. These opportunities allow children to practice and demonstrate their skills to family and friends.

Evaluate Progress: Data collection is an important way to understand current functioning, improvements, and regression. Have materials in easy to access places to track progress. Children can help document progress if the system is created with them in mind. Have a low chart the child can add a sticker or line to when they complete a skill such as putting on their coat or following directions during an activity. This is a positive way for children to participate in monitoring their progress.

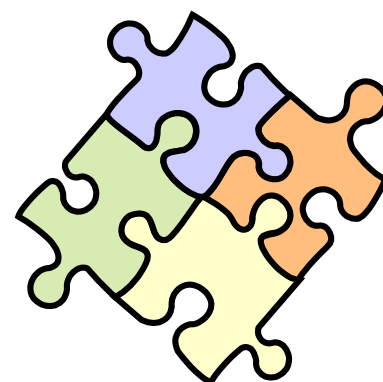
Elaborate on Skills: If a child shows an interest in an activity, be sure to encourage their curiosity. Build on language during the activity by asking questions. If a child is struggling with a skill such as spreading peanut butter, give them a little help, but allow them to complete the task to their best ability. When children show an interest in something new, bring the interest or skill into other environments. For example, if a child is intrigued by a trains going by, look at trains online and create a train picture or collage, make a title, to integrate art, scissor use, and literacy into the learning opportunity.

Bloorview Research Institute

Autism Research Centre

Conducting innovative research programs aimed at improving outcomes and quality of life for children with autism spectrum disorders

Is your child, 21 years or younger, and has a **Neurodevelopmental disorder** (e.g. ASD, Intellectual Disability, Fragile X, Down Syndrome, or an Anxiety Disorder)?



Or is your child **typically developing** and between the ages of 3 - 21 years?

We are currently conducting new research studies across Ontario to understand how genes and biology affect the brain and behaviour in Autism and other Neurodevelopmental Disorders.

We need your help!

POND–Network: Province of Ontario Neurodevelopmental Disorders–Network



Participation may include:

- Activities, Interviews, & Questionnaires
- A blood sample for genetics analysis
- A brain scan (you can get pictures of your brain!)
- A medication trial to find new ways to help children who have ASD



POND NETWORK
Province of Ontario Neurodevelopmental Disorders

To learn more about the POND–Network research project, please contact:
Holland Bloorview

Leanne Ristic 416 425 6220 x 6321 or Susan Day Fragiadakis 416 425 6220 x 6518
Email: lristic@hollandbloorview.ca or sfragiadakis@hollandbloorview.ca

Important Tax Info. - What is a RDSP?

People with Fragile X syndrome have a normal life expectancy, so parents and families have to make long-term plans to provide for their needs. You can contact your local support agencies, like your provincial **Community Living** website or financial institution for guidance in this area. There are workshops and seminars held to guide and advise in the area of financial planning. You may also want to look at a Personal Planning Guide. Contact your Provincial Ministry of Community and Social Services for a copy.

In Canada, the Registered Disability Savings Plan (RDSP) helps parents and other family members save for the long-term financial security of a person with a severe disability. In general, any person under the age of 60 who is eligible for the Disability Tax Credit (Disability Amount) and resident in Canada can establish an RDSP. If the person is a minor, their parent or legal representative may establish the RDSP for their benefit.

Please check out the details like lifetime contribution limits in your province, since they differ from place to place. Anyone can contribute to the RDSP with the written permission of the plan holder. An important point to note is that contributions to an RDSP, unlike RRSP contributions, are not tax-deductible and are not included in income when paid out of an RDSP. Investment income earned in the plan accumulates tax-free. However, grants, bonds and investment income earned in the plan are included in the beneficiary's income for tax purposes when paid out of the RDSP. This is a truly amazing program that can benefit your loved one in the future.

For more information on RDSPs, visit the Canada Revenue Agency Web site at or call 1-800-959-8281 (TTY users call 1-800-665-0354).

Get your donation Tax Receipt and FXRFC Newsletter via e-Mail!

It costs the FXRFC to mail out both our newsletters and income tax receipts.

There are two ways you can help:

By going to our website when you want to make a donation: fragilexcanada.ca Just click on our Donate Now button, and you are linked to Canada Helps where you are able to make a safe and secure donation on-line. You can even designate who your donation is in honour or memory of. You will receive a speedy electronic tax E-receipt and this will keep associated

administrative costs to a minimum, allowing more funds to be directed to the scientific research we fund.

You can also sign up to receive this Newsletter via your email in-box. We encourage you to share an email address with us to receive a colour newsletter in an easy print-at-home pdf format!

Just email info@fragilexcanada.ca and request an electronic version rather than print. Be patient, as it might take us an issue for the switch to occur. Thank you!

This newsletter is published quarterly by Fragile X Research Foundation of Canada and mailed to all our supporters. You can view/download a PDF of the newsletter on our website at www.Fragilexcanada.ca by clicking on Resources. If you do not receive our newsletter regularly or would like us to mail a copy to someone you know, send an email with a complete mailing address to newsletter@fragilexcanada.ca

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Important Information

Did you know FXRFC is on Facebook?

The Canadian Fragile X Research Foundation is on Facebook! Our page is a great forum for our Fragile X families. What a good way to connect with each other, share ideas and info. Feeling isolated? Maybe there is another Fragile X family near by... Check out the FB page & get in touch!

Mark your calendar

Please keep checking the FXRFC website for upcoming events. If you have an event planned in your area, let us know and we'll include it on the site and in our next **xpressions** newsletter issue.

April - May - June, 2016

The Canadian FXRFC Fundraising Parties

Time: you choose! It's not too early to be thinking about holding a Spring Fundraising Party! More details to come on the FXRFC website in the spring.

June 19, 2016

Fragile X Family Fun Day

Time: 11:00 am - 2:00 pm
Location: Variety Village, Scarborough ON.
More details will follow in the next issue. Plan to attend & save the date now!

June 26, 2016

Vancouver 2016 Scotiabank Run

Join Team Vancouver for the half marathon or 5km run. Look for info. on pg. 4 of this newsletter to join the team.

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