

# xpressions

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## FXRFC Awards New Research Grants

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

**Our approach to research funding has always been to maintain a flexible approach in order to maximize our ability to identify new “therapeutic targets” that can guide the development of future treatments.**

The Fragile X Research Foundation of Canada continues its drive to increase the number of scientists working towards finding a treatment for Fragile X. The FXRFC is currently funding six research projects across Canada, and last year it awarded \$112,000 for research aimed at finding a treatment or cure for Fragile X. These projects are currently being conducted at the University of Victoria, the University of Toronto, McGill University and the University of Sherbrooke, and will yield valuable information on the pathology of Fragile X, and should stimulate further research in this area.

Our approach to research funding has always been to maintain a flexible approach in order to maximize our ability to identify new “therapeutic targets” that can guide the development of future treatments. On the following pages of this newsletter are brief descriptions of three projects that the FXRFC started funding in 2014, as presented for you by the researchers. If you would like to explore the entire portfolio of FXRFC funded research, past and present, please visit our website, [www.fragilexcanada.ca](http://www.fragilexcanada.ca) and click on the “Research Grants” link.

These scientists are making significant progress in understanding Fragile X syndrome and it is a direct result of the work funded with your generous donations - please keep them coming!

## Project Title:

### Fragile X gene therapy using Adeno-Associated Viruses

#### *Principal Investigator:*

Dr. David R. Hampson, Ph.D., Professor, Department of Pharmaceutical Sciences, Leslie Dan Faculty of Pharmacy, University of Toronto

Postdoctoral fellow: Jason Arsenault Ph.D.

Fragile X syndrome (FXS) is a genetic disorder that is the most common single leading cause of autism and intellectual disability in males. Caused by a severe down-regulation of the Fragile X mental retardation protein (FMRP), FXS does not have any long term pharmaceutical cures. However, recent advances in gene therapies using Adeno-Associated Viruses (AAV) show promise for future treatments of FXS and a number of other neurogenetic diseases. We thus aim to construct and test a number of biopharmaceuticals that fuse AAV with FMRP so that it can be delivered into the brain cells for the long term amelioration of FXS syndrome. The Fragile X mouse model displays a wide range of

behavioural characteristics (phenotypes) and are excellent models to test this AAV-FMRP strategy. Using molecular biology techniques and protein engineering, we aim to construct a number of AAV-FMRP virus particles, which will be initially tested on stable cell lines and brain cells grown in a test tube. We will look for “selective tropism”, which refers to the virus’ ability to target the right kinds of cells, and then measure FMRP production rates in these cells. We will then identify the most promising selection of AAV-FMRP combinations, and inject them into the brains of Fragile X newborn mice. This will allow us to observe them, to document any “behavioural rescue” during adulthood,

and measure rates of functioning of the newly replaced gene using immunohistochemistry and western immunoblotting imaging techniques. We will then look for correlations between behavioural tests and local neuroanatomical production rates of FMRP in order to gain insight into the precise brain regions and cell types associated with this disorder.

These results will improve our understanding of the neuropathological defects in FXS, and help us devise better gene therapy approaches and approaches that may eventually be used to treat people with FXS.

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## Project Title:

### The rescue of FMRP-related presynaptic long-term potentiation, social interaction, learning and memory deficits in Fmr1 knockout mice

#### *Principal Investigator:*

Dr. Min Zhuo Ph.D., Professor, Department of Physiology, University of Toronto

Postdoctoral Fellow: Kohei Koga Ph.D.

This lab has used a previous FXRFC grant to characterize the phenomenon of long term potentiation (LTP) of synaptic strength, and its correlation with learning and memory function in mice. Dr. Zhuo’s lab reported that the Fragile X mouse model exhibits altered LTP in a part of the brain that is critical for learning and memory, known as the anterior cingulate cortex (ACC). As well, they found that Fragile X mice have a deficit in fear learning behaviour. Although these mechanisms have been studied in the receiving neurons (postsynaptic neurons) of Fragile X mice, the mechanisms of LTP in the sending neurons (presynaptic neurons) is still unclear. To address this gap in knowledge, a new procedure was developed for inducing presynaptic LTP

(pre-LTP) in the ACC, and some molecular mechanisms involved in this process were identified. When pre-LTP stimulation was applied to Fragile X mice, pre-LTP was observed to be defective as well. Preliminary data suggests that after induction of pre-LTP, the distribution of parts of an enzyme known as PKA (Protein Kinase A) in the pre-synapse is abnormal. This can in turn adversely affect neuronal plasticity and communication between neurons.

The FXRFC has renewed this grant so that Dr. Zhuo’s lab can continue to characterize and compare the pre-LTP in normal mice to that of Fragile X mice. They will also study the functional roles of arachadonic acid (ARA) in synaptic plasticity, the molecular mechanisms

involved, and effects on social behaviour in Fragile X mice. The idea for investigating the effects of ARA was prompted by results from a pilot publication reporting that administration of commercially available Aravita (high dose ARA in combination with docosahexaenoic acid (DHA) and a low dose of astaxanthin (an antioxidant) because it showed beneficial effects on social behaviour in people with Autism. ARA, a poly-unsaturated omega-6 fatty acid, is a key pro-inflammatory intermediate. DHA is an omega-3 fatty acid. Both ARA and DHA have been found to be important in neurochemical signal transduction related to brain cell maturation in animals and humans.

## Project Title:

### A definitive method for FMRP Measurement in Fragile X syndrome individuals

#### Principal Investigator:

Dr. Francois Corbin M.D., Ph.D., FRCPC, Biochemistry Department ,  
Faculty of Medicine and Health Sciences , University of Sherbrooke

Master student: Pamela Bouvier

All of the core symptoms of Fragile X syndrome are caused by the absence of FMRP (Fragile X Mental Retardation Protein) in the brain cells of affected individuals. This in turn is a direct result of a mutation in the FMR1 gene that renders it incapable of directing the production of FMRP. Researchers now

know that there is no direct correlation between the size or length of the FMR1 mutation and the severity of symptoms in individuals with Fragile X. However there is a direct correlation between the levels of FMRP in the peripheral blood, and the degree intellectual disability. Therefore, this lab is developing a

simple, accurate technique to measure the FMRP levels in the platelets in the peripheral blood. This will make it easier to diagnose affected individuals, predict cognitive function and may be used as a tool to measure the effectiveness of future treatments.

## Scotiabank Run Update - Join a Fragile X Team!

By Ian Shearer, Fundraising Director, FXRFC

The Charity Challenge Awards for the Scotiabank Toronto Waterfront Marathon was held December 9th, 2014 at Scotia Plaza in Toronto and I'm very pleased to say we won 2nd place in the Overall Fundraising Category. The \$3,000 prize put Fragile X Team Toronto at **\$100,465** for 2014! Our supporters and runners deserve huge congratulations for breaking another FXRFC fundraising record!

It's hard to believe, but in 5 years the Vancouver and Toronto running teams have won **\$16,000** in prize money from Scotiabank and raised almost **\$450,000** for Fragile X research. If we could just get teams in Calgary and Montreal! Anyone who lives in those cities and would like to champion a team, please contact us and we will help & support you!

**Fragile X Team Vancouver** is asking people to join them Sunday, June 28th, 2015. The Scotiabank Vancouver Half Marathon also has a great 5k event. Please contact Team Captain, **Carrie Lakatos** at: [carriework@shaw.ca](mailto:carriework@shaw.ca) for more information.

**Fragile X Team Toronto** will be running again on Sunday, October 18th, 2015.

This event has a 5k, half and full marathon. Team Captains, **Jennifer Williams & Ian Shearer**, pictured here accepting the prize and cheque last December in Toronto, can be reached at: [fundraising@fragilexcanada.ca](mailto:fundraising@fragilexcanada.ca)

For more information and links to both events go to [www.canadarunningseries.com](http://www.canadarunningseries.com)



Come join in the fun - be a part of a FXRFC team!  
Participate and show your support!

# It's the 12th Annual FX Foundation Family Fun Day!!



**Sunday June 21st 2015, 11am-2pm**

Relax and enjoy a wonderful day of fun & fantastic gourmet food (we mean free hotdogs, burgers, veggie burgers & drinks) along with other incredible FX families! Feel free to bring along aunts, uncles, grandparents or whoever supports you & your family. This is your chance to meet other families, and let the kids play at a great facility. There is a fenced-in outdoor green space & patio as well as indoor space in case the weather does not co-operate.

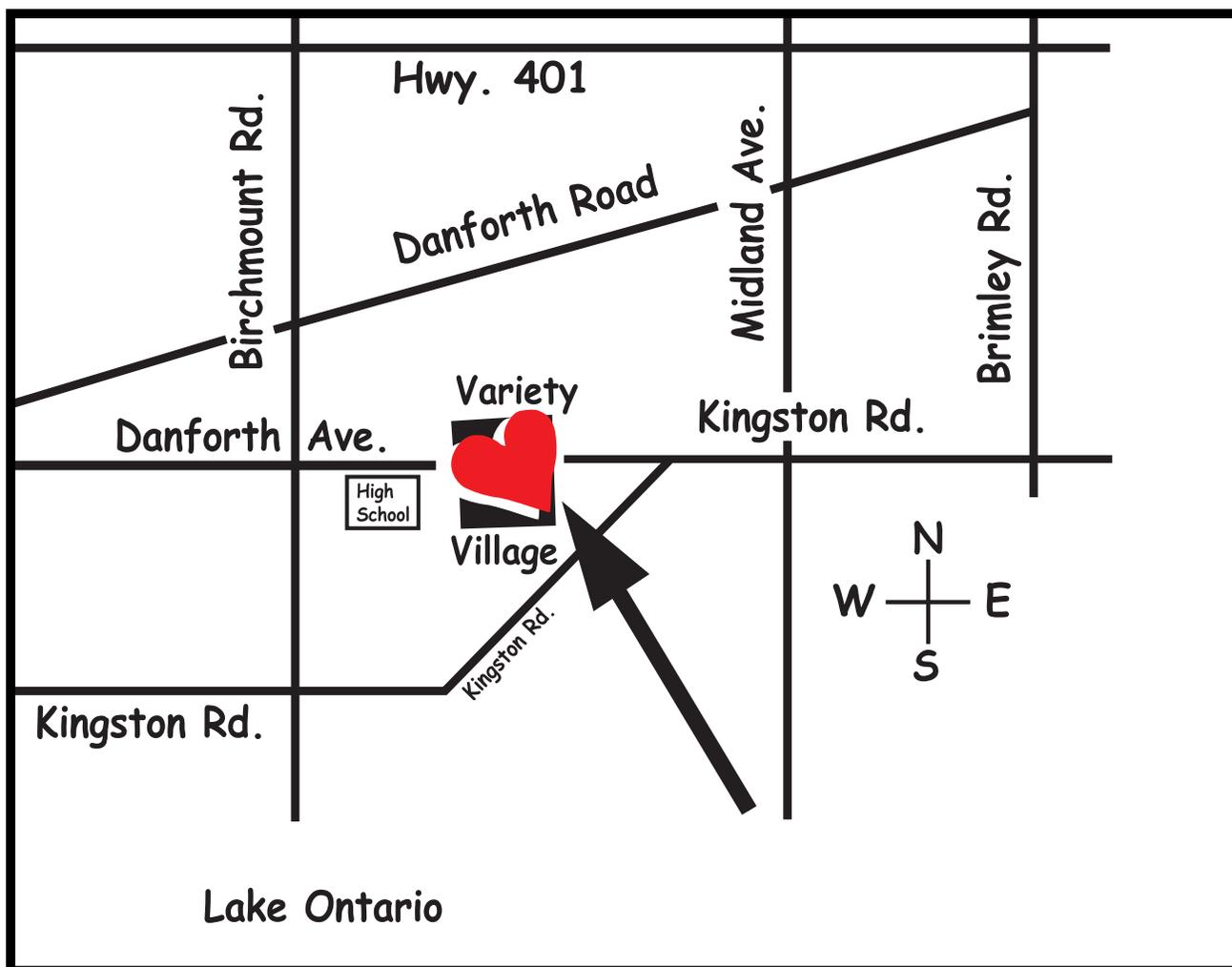
Please RSVP no later than **June 14th**. Contact Jennifer Williams (info. next page) and state how many adults & children are coming in your group.

Bring along your smiles and folding chairs if you have them (but not your pets) and get ready to have a great time, with lots of fun and laughter! There will be lots of play equipment provided, a 50/50 draw, a bubble blowing station & more!

*This year we are again holding a lucky draw fundraiser with great prizes, so bring your wallet! If you have connections & could donate a gift card, tickets to a show or event, or a fabulous prize, please contact Jennifer by May 20th.*

*We are asking each family to contribute one dozen peanut-free treats for the dessert table if you are able - YUM!*





**Variety Village is located at 3701 Danforth Avenue  
Toronto, Ontario M1N 2G2**

for more information on Variety Village, visit <http://www.varietyonario.com/village/>

Please note that you can ONLY exit south off the 401 at Warden Ave. or Brimley Rd.

Also be aware that Danforth Rd. & Danforth Ave. are both in this area.

Variety Village is on Danforth Ave. It's on the south side, and sits next to a high school.

You can park in the school lot if the Village lot is full, then follow the walkway to the Village.

There is a set of traffic lights at Variety Village, so just turn in where you see the sign out front!

**Remember to let Jennifer know by June 14th!**

**Contact Jennifer Williams at 416-724-9052 or email: [fundraising@fragilexcanada.ca](mailto:fundraising@fragilexcanada.ca)**

Please specify how many adults & how many children when you call or email.

Please remember to leave a number where you can be reached, just in case.

Due to limited seating, please bring folding chairs if possible.

**We are also looking for teenagers to volunteer the day of, so please contact Jennifer early if you have a family member that can assist.**

**Thank you and hope to see you on June 21st!**

# Our Athletes Compete in their Provincial Special Olympics & Bring Home Hardware!

## Brothers Do Brampton Proud!

The weekend of January 29, 2015 to February 1, 2015 was a time of great celebration in North Bay, Ontario as Special Olympics Ontario held their Provincial Winter Games. Battling it out in the -30C cold, were **Nicholas** and **Benjamin Paribello**, cross country skiers who compete with the Barrie Striders team in the Central Region. Both young men turned in very fast times, Nicholas in skate skiing and Benjamin in classical skiing. They credit their exceptional fitness to their participation in SOO Bowling and SOO Track and Field in Brampton as well as twice weekly training in Barrie, and personal training with Kerry Dennie's Let's Get Fit in Georgetown. The National Games will be held next February in Corner Brook, Nfld. and with luck, Nicholas with his 4 silver medals and Benjamin with his 2 gold and 2 silver medals will find themselves on The Rock!



*Congratulations to Benjamin (left) and Nicholas (right) on their outstanding achievements in North Bay at the Special Olympics Ontario Winter Games*

## The Québec Special Olympics Provincial Winter Games March 6 to March 8, 2015 in Levis, Quebec

**David Jessome**, shown right, proudly wearing the 3 medals he won in Alpine Skiing – intermediate level at the 2015 Quebec Special Olympics - Provincial Winter Games. Mom, dad, and sister Catherine watched proudly as David skied his way to the podium in the Slalom, Super G and Giant Slalom races.

As mentioned on the Québec Special Olympics website, over the course of three days, more than 350 athletes with an intellectual disability from all over the province competed in the following 7 sports: curling, floor hockey, figure skating, speed skating, snowshoeing, alpine skiing and cross-country skiing. Throughout the Games, the mission staff, as well as several coaches and volunteers were on site to supervise the athletes and to ensure the smooth running of each event.

**Annie Pelletier**, bronze medalist in the Atlanta Olympic games, and the Quebec Special Olympics's honorary patron for the past 18 years, and **Alexandre Bilodeau**, double Olympic champion and Quebec Special Olympics's new ambassador were also there to cheer on and to support the athletes. A wonderful time was had by all. *Congratulations David and continued success!*



# Access 2 Entertainment card – a must!

*This is an opportunity of which everyone should be aware. It is too good to miss!*

By: Myra Sourkes

Launched in early 2005, the Access 2 Entertainment program helps certain businesses provide quality customer service to customers with disabilities. The A2E card is used while attending various entertainment, cultural, recreation or sporting venues not only within your home province but also across Canada.

Through the program, people with disabilities carry a personal A2E card with them and this indicates to the ticket seller that the individual does indeed require the support of an attendant. The card provides free admission or a substantial discount for the support person at the participating venue. The person with the disability pays the regular admission fee.

The Access 2 Entertainment card, administered by Easter Seals Canada, is accepted at most movie theatres across Canada, and many notable

attractions across the country as well, including museums, zoos, recreation centres and special venues like the H.R. MacMillan Space Centre or Vancouver Aquarium in British Columbia, the Museum of Industry in Nova Scotia or the CN Tower in Toronto. The list of participating businesses is expanding all the time, so check the website.

The card is easy to obtain. The person with a disability or their family member submits an application form authorized by a registered health care or disability service provider. The fee is \$20 and the card is valid for 5 years, after which it can be renewed.

Go to [www.access2.ca](http://www.access2.ca) for more information and to obtain an application form.

**DO IT TODAY!!!!!!**

Here is a list of some participating theater chains accepting A2E cards:

- Cineplex Odeon
- Galaxy Cinemas
- SilverCity
- Colossus
- Empire
- Landmark Cinemas
- Rainbow
- Magic Lantern
- AMC
- Capitol

*... and many more attractions!*



## Throw a Spring FXRFC Fundraising Party!

The Canadian Annual Spring Party for Fragile X Research is a unique fundraiser that started in 2009. We asked everyone who received the FXRFC newsletter to participate and the response was wonderful! Various types of parties were held, ranging from a dance in a church basement to a Sunday brunch. Over \$45,000 was raised that year and we'd like to top that amount this year!!

We are asking everyone who has held a party in the past to make it an annual event and anyone who didn't, to pick a date and host an event this year. Here is how it works - instead of collecting pledges, participants host a party to raise money. Your guests are asked to bring a donation to the party. One such party was a fun night at home filled with music, friends and simple food. It was suggested to guests that their donation be about equal to what they'd normally spend on an evening out with friends.

It does not have to be a large or formal affair. In fact, we encourage you to keep it simple, since the idea is to raise funds - not spend your own. You can serve hors d'oeuvres,

wine and cheese or pizza! You could simply organize a board game or movie night and make popcorn! Use your imagination to customize your party and make it your own. What's really important is that we all get together to support research to find the cure for Fragile X.

Join the party today! All proceeds go to fund important Fragile X research projects across Canada. Go to the **What's New** page on [www.fragilexcanada.ca](http://www.fragilexcanada.ca) for more details. You can download everything you need, including both print and email invitations and donation forms. It's that easy! Pick a date that works for you and send out your invitations. Then phone one of your friends' who lives somewhere else in Canada and ask them to commit to holding a party as well. Give them the website information and they'll be all set. It really is easy & fun! Our fundraising team is very excited about the Annual Spring Party and we need you to be as well! Let's make this a Canada wide event!

## Important Information

# Do you know an **XXX**-tra Special Person?

### We are looking for letters, stories, or articles about an extra special person!

The FXRFC newsletter often publishes stories about the people that sparked the formation of the Canadian Fragile X Research Foundation and inspires the ongoing growth and commitment of the FXRFC. If you have a story about a child or adult with Fragile X Syndrome, please send it to us and a picture of the XXX-tra Special Person to share with our readers. Tell us a funny or heart-warming story, or share a success and allow it to inspire others.

If you are planning or have organized a Fragile X fundraising activity or event in your area - big or small - we'd like to hear about it. Anything goes! If you have an announcement or request to make that is related to Fragile X, and would like other families to know about it, please e-mail the Foundation at [info@fragilexcanada.ca](mailto:info@fragilexcanada.ca), or fax the Headquarters at 905-453-0095.

## Get this newsletter by email!

Canada Post increased first-class postage prices significantly in March 2014. This has a financial impact on the FXRFC because it increases our cost to mail out both our newsletters and tax receipts.

You can 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](mailto:info@fragilexcanada.ca) and be patient, it might take us an issue for the switch to occur.



## FRAGILE

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](http://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](mailto:newsletter@fragilexcanada.ca)

The Fragile X Research Foundation of Canada (FXRFC) is a national, nonprofit, tax-exempt charitable organization run by parents of children with Fragile X syndrome and volunteer professionals. Permission is granted to reproduce or distribute this newsletter for non-commercial purposes. We accept donations on-line through our website at [www.fragilexcanada.ca](http://www.fragilexcanada.ca) or by mail or phone at our National Headquarters in Brampton, Ontario.

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### Mark your calendar

#### FXRFC Family Fun Day

**Sunday June 21st in Scarborough, ON**

Join us for this annual event. See pages 4 & 5 of this newsletter for all the details and come have some fun!

#### Scotiabank Runs for FXRFC

**Sunday June 28th in Vancouver, B.C.**

**Sunday October 18th in Toronto, ON**

**Come & participate!**

Fragile X Team needs you! Run or walk! It is a lot of fun for the whole family. If you can't run, join the cheer squad and yell for the team! To join the BC Team contact: Carrie Lakatos at [carriework@shaw.ca](mailto:carriework@shaw.ca) To join the Toronto Team, contact: Ian Shearer or Jennifer Williams at: [fundraising@fragilexcanada.ca](mailto:fundraising@fragilexcanada.ca) We'd really like to get teams in Calgary and Montreal! Anyone who lives in those cities and could lead a team, please contact us and we will help & support you!

If you are not able to join us, please consider helping by sponsoring a FX Team member. Closer to the dates, you can go to the Scotiabank site link & sponsor a FXRFC Team. **More details will follow.**

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