



# FXRFC Newsletter

News for Friends of the Fragile X Research Foundation of Canada

Summer 2006 • Volume #10 • Issue #3

## FXRFC and Surrey Place Centre Establish Fragile X Clinic

*Dr. C. Paribello, M.S.M, M.D. President, Medical Director*

We are very pleased to announce that The Fragile X Research Foundation of Canada has established a Fragile X Clinic at Surrey Place Centre in Toronto. Opened in June of 2006, it will serve as a centre to assess and treat patients of all ages who have Fragile X syndrome.

Located in the heart of downtown Toronto, Surrey Place Centre is a community-based organization, providing complex diagnostics, counseling, service coordination, behavioural therapy, and educational programs to people living with a developmental disability and their families. The Centre uses community-based interdisciplinary teams to provide a full range of services and interventions including assessment, counseling, audiology, behaviour therapy, and speech and language therapy. These services are offered free of charge to their clients because Surrey Place Centre receives core funding through the Ministry of Community, Family and Children's Services. The Surrey Place Centre Foundation also raises funds from individuals, corporations, and foundations for additional support. It is affiliated with the University of Toronto, York University, the University of Guelph and many other teaching institutions. It is accredited with the Canadian Council on Health Services Accreditation.

### Why start a Fragile X Clinic?

This will be the first dedicated Fragile X Clinic in Canada and it will serve a dual purpose.

First, it will provide a facility where affected patients and their families can access physicians with the expertise and knowledge to treat this neuropsychiatric disorder. Patients with Fragile X exhibit a unique constellation of problems, and it is important for this medical expertise to exist or else the unique problems of Fragile X patients and their families may go unrecognized and inadequately treated. The clinic can also be used for teaching purposes as it grows.

FXRFC is a nonprofit, tax-exempt charity run by parents and volunteer professionals. Fragile X syndrome is the most common form of inherited mental impairment and developmental disabilities, affecting approximately 1 in 2000 males and 1 in 4000 females. FXRFC's goal is to accelerate research aimed at the treatment of Fragile X, by direct funding of promising research projects and by raising awareness of this disorder.

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Secondly, the newly established Fragile X Clinic at Surrey Place Centre will be in a position to be the first Canadian centre where the research breakthroughs of the last few years will be turned into routine clinical treatments for everyone with Fragile X. For example, recent advances in this field have allowed researchers to identify a key therapeutic target affecting synaptic plasticity in the brain for potential treatment.

Once the Fragile X Clinic is established, it will also conduct clinical trials with new drugs that enhance learning, memory, and cognitive functioning and will therefore put Surrey Place Centre in a position to make a global impact in the field of neuroscience and autism.

## **CLINIC DESCRIPTION**

### **Who will be assessed and treated at the Fragile X Clinic?**

The clinic will assess and treat individuals with a mutation of the FMR1 gene.

### **What is the size of the community that the clinic will serve?**

Currently there are hundreds of known affected families across Canada that are listed in the database of the Fragile X Research Foundation of Canada (FXRFC). However, as a result of improved diagnostic techniques and increased physician awareness, we expect that this number will steadily increase. Patients will be referred to the clinic by the FXRFC. The Fragile X Research Foundation of Canada is a national non-profit organization which is dedicated to funding biomedical research for improved treatment and, ultimately, a cure for Fragile X.

### **When will the clinic be held?**

The clinic will be held every two weeks on Mondays. Each new patient will have a one-hour initial medical assessment. Subsequent case discussions and follow-up appointments will be approximately 30 minutes long.

### **What will the Clinic do?**

Each patient will have a general medical assessment at the clinic with special attention paid to the neglected areas of health in the Fragile X population.



### **Who will assess patients at the clinic?**

All patients will be assessed **Dr. Carlo Paribello M.S.M, M.D.**, (shown here) Family Physician, President, Medical Director, Fragile X Research Foundation of Canada, and **Leeping Tao, RN, MN-ACNP**, Nurse Practitioner, Surrey Place Centre.



## **Referral to Allied Health Professionals**

Following the initial assessment, patients will then be referred to allied health professionals at Surrey Place Centre and Toronto General Hospital as required. Health professionals include a geneticist, an occupational therapist, an audiologist, a speech pathologist, and a psychologist.

The role of each health care professional will be to further assess the condition of the patient and design activities and programs that will enhance their individual strengths and support their weaknesses.

The recommendations that arise from these assessments will then be given to the patient's family members, caregivers, or workers for implementation by their local healthcare providers.

For further information about the clinic and for patient booking, please contact the office of Dr. Carlo Paribello at (905) 453-9366 or e-mail your request to [fxrfc@on.aibn.com](mailto:fxrfc@on.aibn.com).

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## **Fragile X Research - Are we there yet?**

*Dr. C. Paribello, M.S.M, M.D. President, Medical Director*

When we established the Fragile X Research Foundation of Canada in 1997, I predicted that we would have a specific treatment for Fragile X within 10 years. Nine years later, Fragile X researchers believe that they have found a major “therapeutic target” that can be used to specifically treat the core symptoms of Fragile X and possibly autism.

Since the gene was first identified in 1991, researchers have been looking at three main levels in their approach to finding a treatment or cure for Fragile X:

1. Turn on or replace the mutated FMR1 gene.
2. Find ways to replace the FMR Protein in brain cells or
3. Create drugs that compensate for the missing protein. The exciting new development of the “mGluR Theory” of Fragile X falls within the third category.

The absence of the FMR protein in the brain cells of patients with Fragile X cause structural and functional changes at the synapses between neurons. This in turn causes impaired communication between the neurons and interferes with their ability to strengthen connections during the learning process. This process, which has also been referred to as “synaptic plasticity”, is regulated by two delicately balanced pathways known as LTP (long-term potentiation) which strengthens connections, and LTD (long-term depression) which weakens connections.

The problem in Fragile X, appears to be excessive activity of mGluR-LTD and researchers now suspect that this may also be common to many forms of autism spectrum disorders as well. What is particularly exciting about this discovery is that it should be relatively easy to intervene in this hyperactive brain mechanism.

This is why there has been much excitement centered around existing compounds which dampen the mGluR pathway. These compounds are known as “mGluR antagonists” or “mGluR blockers” and some of these drugs are being developed by major pharmaceutical companies for other indications, such as anxiety disorders. This discovery has brought us to the threshold of treatment for Fragile X, and perhaps for autism as well.

The development of the mGluR theory began in **May 1997** when Dr. Greenough at the University of Chicago, reported that FMRP, the fragile X protein, is synthesized in neuronal branches called dendrites, in response to synaptic activity and stimulation of metabotropic glutamate receptors (mGluRs).

In **2002**, an FXRFC funded project in Dr. Peter Carlen’s lab at the Toronto Western Hospital, showed that a major mechanism of communication between neurons is defective in mice which have been bred to model Fragile X. This mechanism, called long-term potentiation (LTP), is one of two main forms of synaptic plasticity, the molecular basis of learning and memory. In the same year in a project started at Brown University, Drs. Mark Bear and Kim Huber made the important discovery that long-term depression (LTD) was also defective in Fragile X mice. This team (funded by FRAXA in the U.S.) found that mGluR-LTD is excessive in the Fragile X knockout mouse.

From these findings emerged the “mGluR Theory” of Fragile X. Researchers proposed that the exaggerated signaling in mGluR pathways is the underlying cause of many cognitive, behavioral, and neurological symptoms of Fragile X and possibly autism.

Subsequent experiments by Dr. Rob Bauchwitz at Columbia University began to test this theory. By treating Fragile X mice with MPEP, a compound which blocks one kind of metabotropic glutamate receptor known as mGluR5, he was able to reverse the hyperactivity and eliminate sound-induced seizures that occurred in these animals.

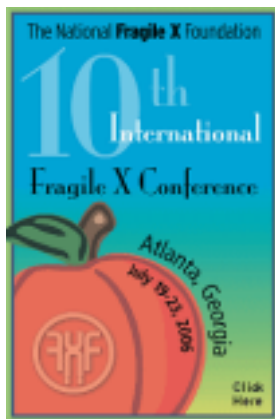
In **2005**, further support for this theory was reported by a team led by Dr. Tom Jongens of the University of Pennsylvania. They demonstrated that fruit flies with a mutated Fragile X gene have learning deficits and corresponding abnormalities in microscopic brain anatomy. Remarkably, when MPEP was fed to these flies, the researchers found that they could reverse, or “rescue” these abnormalities, even when the drug was given to adult flies. Further studies demonstrated that an available drug, lithium, which inhibits mGluR signaling pathways, also rescues Fragile X fly anatomy and cognition.

In **July of 2005** researchers at Hoffman LaRoche reported that Fenobam, a compound used in Phase II/III human trials from 1978-82, is a selective mGluR5 antagonist. In these trials, Fenobam showed that it had some efficacy for treatment of anxiety disorders, but it was never tested in patients with Fragile X. Its patent has expired, so it can now be synthesized and used for experimental basic research.

By **2006** the FXRFC began to actively collaborate with FRAXA and several pharmaceutical companies to bring treatments for Fragile X into clinical trials. The FXRFC will be developing a clinical trial site in Toronto, and will join a consortium of recently established Fragile X clinics across the United States to develop the capacity necessary to advance potential therapies through clinical trials and into routine use.

## Report on the 10th International Fragile X Conference

*Dr. C. Paribello, M.S.M, M.D. President, Medical Director*



In July of this year, I had the honour and pleasure of speaking at the National Fragile X Foundation's 10th International Fragile X Conference in Atlanta Georgia, U.S.A. held from July 19 - 23, 2006.

This conference is highly regarded and is well known for bringing together families, researchers, medical personnel, therapists, and educators in a setting that is specifically designed to optimize interaction among families and professionals. Increased collaboration between researchers, improved treatment skills of professionals, optimized development of individuals affected by Fragile X, and increased understanding of those impacted by the syndrome are the most significant outcomes often cited by previous conference attendees.

The most notable development at this year's meeting was the shift in emphasis from basic molecular studies to potential new medical treatments planned for the next one to two years. Much of the excitement centred around the "mGluR Theory of Fragile X" as the first real breakthrough in the development of a treatment that is specific for the defects seen in Fragile X.

The conference also provided me with an excellent opportunity to meet face to face with families from across Canada. We had known each other through e-mails and phone calls, however the synergy of the group was rejuvenating. It was wonderful to share stories about our children and know that we are all in the same boat.



*The Canadian Contingent*

## TAX TIPS

*By Pam Winthrope, CGA, DFA, Parent, Vancouver, British Columbia*

Did you know that the travel, registration and associated costs of attending the 10th International Fragile X Conference are an allowable deduction on your 2006 tax return?

Do you know that as an individual supporting a disabled person, you have many more allowable expense deductions? The CRA (Canada Revenue Agency) acknowledges the additional financial burden that may be incurred in the support of a disabled person.

The average Canadian taxpayer knows that the CRA allows a non-refundable tax credit for medical expenses such as prescription medication, dental, glasses etc. (The term NON-REFUNDABLE means these credits reduce your federal tax. However, if the total of these credits is more than your federal tax, you will not get a refund for the difference)

Allowable expenses\*\* that the average taxpayer may not be aware of are:

1. Amounts paid for you or a relative to learn to care for a relative who has a mental or physical infirmity. The individual with the infirmity must either live in your household or be dependent on you for support.
2. If medical treatment is not available locally, you may be able to claim the cost of travelling to get the treatment somewhere else.
3. Amounts paid for full or part-time care (including training) in a school, institution, or other establishment that has the equipment, facilities, or personnel needed by people with a certain disability.

You can claim eligible medical expenses paid in any 12-month period ending in 2006 and not claimed in 2005. Generally, you can claim all amounts paid, even if they were not paid in Canada if the dependent is:

- (a) is related to the individual
- (b) has a mental or physical infirmity, and
- (c) is a member of the individual's household or is dependent on the individual for support.

\*\*RC4064(E) Rev. 05 (CRA)

***For further information on this and other disability tax related issues, please email me at [pwinthrope@hotmail.com](mailto:pwinthrope@hotmail.com)***

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## Send in your Articles

The FXRFC Newsletter often publishes stories about the people that have sparked the formation and inspired the growth of the Fragile X Research Foundation of Canada. If you have a story about, and a picture of, a child or adult with Fragile X, please send it to us we will share it in our "X-tra Special Person" feature. Tell us a funny or heart-warming story or share a success.

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! Perhaps it could be a brunch, lunch, or dinner party, a car washing event, football party, bowling, a walk or run, bake sale, cocktail party, a jar for coin collection, garage sale, benefit night at a local fast food restaurant, arranging with local merchants to match any funds raised, etc.

Please e-mail your article for the newsletter to [fxrfc@attglobal.net](mailto:fxrfc@attglobal.net). The deadline for submissions to the next newsletter is October 10, 2006. If you have any questions, please feel free to call us at (905) 453-9366.

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## **October 5th is National Fragile X Research Day in Canada & the U.S.A**

The FXRFC has designated that day as a national fundraising day and would like to use it as both a focal point for raising awareness of Fragile X, and to raise much needed funds for research. Our challenge to you is to think of a Fragile X fundraising activity or event – big or small – to organize in your area on or around National Fragile X Research Day.

Anything goes! Perhaps it could be a brunch, lunch, or dinner party, a car washing event, golf event, football party, bowling, a walk or run, bake sale, cocktail party, collecting a jar of coins, garage sale, benefit night at a local fast food restaurant, arranging with local merchants to match any funds raised – let your imagination soar!

We're hoping to have an event in every province across Canada – and more than one in each province will be even better!! If you're prepared to take up the challenge and organize a fundraiser, we can provide you with brochures and other informational materials. We can also acknowledge and publicize any planned events in the FXRFC newsletter and on our website – just send us an email at: [fxrfc@attglobal.net](mailto:fxrfc@attglobal.net) or phone us at (905) 453-9366. *If everyone pitches in, we WILL find a cure!*

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## **Are You Eating Again!?**

***By Barbara Byers, LL.B., Parent, Vice President FXRFC***

Sometimes I feel like “Our Lady of Perpetual Groceries”. Let me give you a context – I have four sons, aged 7, 11, 12 1/2, and 14 years old. My husband and I are rather modest consumers on the food chain. But our progeny – well look out! They are lean, mean, eating machines. Today, I cooked up two packages of hot dogs. That's 24. My second son ate 10 of them. And he chatted away the whole time, never missing a bite. While son #2 is a “Vast Quantities at a Sitting” eater, my son #1 is a “High Volume Grazer”. Between meals, we will pass in the hall and he will have a mitt full of arrowroots to munch on.

Each Saturday morning, I schlep home the groceries, which always include a “suitable for 15 people” platter of vegetables. I do this to save time. While I cajole people to help me carry in the 25 bags of groceries, they dip and crunch. Within 2 hours, the platter is clean. That gives me just enough time to wash up the sixteen pieces of fruit that will carry them through the afternoon.

Son #3 is now coming into his own. He is a carbohydrate fanatic. His dream meal (and it remains a dream) is a plate full of rice, potato wedges, and plain spaghetti. Within the past three months, he has focussed his snacking on triple decker peanut butter, grape jelly, and honey sandwiches. I figure that the whole wheat bread and peanut butter, along with a glass of milk is a balanced meal... I mean snack.

My fourth son had the potential to be a fussy eater. Luckily his dad is creative and can turn the dinner menu into an imaginary session involving the kid's interest of the month. He loves dinosaurs, so broccoli became a large tree that was eaten by a hungry brachiosaurus. Or the peas were hidden behind a chicken leg, only to be hunted down and devoured by a menacing Bionicle.

As these four handsome boys grow, I am seriously thinking about investing in grocery store stocks. My future is cast. I will be the short lady in the mix, who, after she pairs up the canoe sized Nikes in the front hall, moves into the kitchen, where she'll open a can of apple juice, stick in a straw and hand it to one of the boys to drink with dinner. Bon Appetit!

## **FXRFC Support Groups - We are Growing!**

We are very interested in starting support groups in the other provinces and territories and will provide assistance to anyone able to help out. If you would like to network with other parents of children with Fragile X, or if you would like to volunteer for fundraising events in your area, please contact any of the people below.

### ***National Headquarters***

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Brampton, Ontario, Canada  
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Phone: (905) 453-9366  
E-mail: [fxrfc@attglobal.net](mailto:fxrfc@attglobal.net)

### ***Ontario***

#### **Kitchener-Waterloo Fragile X Support Group**

Teresa Burch, Co-ordinator  
62 Corfield Drive, Kitchener,  
Ontario N2A 3W9  
Phone: (519) 894-3689  
Fax: (519) 894-6333

### ***Quebec Support Group***

Evelyn Lockett  
32 Lakeview  
Baie d'Urfe, Quebec  
H9X 3B1  
Phone: (514) 457-3284  
E-mail:  
[evelyn\\_lockett@hotmail.com](mailto:evelyn_lockett@hotmail.com)

### ***British Columbia Support Group***

Pam Winthrope  
7968-112A Street Delta, BC V4C 4Y6  
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Web: <http://fragilexbc.tripod.com/fragilexbc/>

### ***Alberta***

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*Please become a Friend of The FXRFC in supporting research aimed at treatment for Fragile X. Friends of the FXRFC receive this quarterly newsletter and are welcome to participate as active volunteers.*

## **FXRFC Newsletter**

This newsletter is published regularly and is sent to friends of the Fragile X Research Foundation of Canada (FXRFC). Permission is granted to reproduce and distribute this newsletter for noncommercial purposes.

The Fragile X Research Foundation of Canada (FXRFC) is a national, nonprofit, tax-exempt organization; charitable # 88643 3762 RR0001. You can become a friend of the FXRFC for a tax-deductible donation of \$35 or more per year. The FXRFC is a 100% volunteer organization run by parents and professionals - which means more of your donation goes directly towards research. We now accept VISA and Mastercard payments; simply phone (905) 453-9366 and pass on the details. You may send your cheque or money order to:

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Come visit our site on the web at: <http://www.fragile-x.ca>