FRAXA RESEARCH FOUNDATION UPDATE

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A PUBLICATION OF FRAXA RESEARCH FOUNDATION

Working toward a cure for Fragile X

PHOTO: CONNIE BRUKIN, COLD SPRING HARBOR LABORATORY

> "NEVER doubt that a small group of thoughtful, committed citizens can change the world. *Indeed, it's the only thing that ever has.*"
>
> — Margaret Mead

10th annual Fragile X Banbury Meeting

SCIENTISTS FROM AROUND THE WORLD GATHER TO TACKLE FRAGILE X

SCIENTIFIC MEETINGS ARE ESSENTIAL for quickening the pace of research. Meetings allow for the sharing of new data and preliminary results, avoiding the lengthy publication process. New ideas are exchanged, research plans refined or revised, and collaborations are formed.

In early April, the 10th Fragile X Meeting was held at Cold Spring Harbor's Banbury Center on Long Island, New York. These conferences were initiated in 1999 by FRAXA and have been funded primarily by NIMH ever since. The 3-day meetings are attended by only 36 researchers in an intimate setting which encourages collaboration and discussion.

This year's theme was *New Developments in Fragile X Syndrome from Basic Mechanisms to Therapeutics*. After each scientist presented his/her latest work, energetic discussions followed with critiques, questions and suggestions all offered with one purpose: to further the understanding of Fragile X and to find effective treatments.

The meeting began with photos, videos and stories to show the human side of Fragile X to those who are most familiar with the disorder in flies or mice. With the characteristic magic of Banbury, this led smoothly to presentations of RNA pathways, signaling cascades and synaptic mechanisms.

The next day focused on developmental aspects of Fragile X and therapeutics in animal models, and the meeting concluded with discussions of current and future possibilities for human treatments. The amount of information shared was staggering, so we'll share just a few examples here:

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FRAXA'S SCIENTIFIC ADVISORY BOARD GAINS NEW MEMBERS

Report from Washington | $2 Million in New Research Awards | Clinical Trials | New Faces **SEE PAGE 2**

FRAXA Research Foundation is a nonprofit, tax-exempt charity run by parents of children with Fragile X syndrome. Fragile X syndrome is the most common inherited cause of mental retardation and autism, affecting approximately 1 in 4000 males and 1 in 6000 females. FRAXA's mission is to fund research aimed at finding effective treatments and a cure for all children and adults with Fragile X.

REPORT FROM WASHINGTON

By Mary Beth and David Busby

THE CHILLY WINDS OF INAUGURAL WEEK IN Washington were soon replaced by sunny warmth — reflecting the passage of the American Recovery and Reinvestment Act (ARRA), which includes:

❖ **an extra $10 billion for The National Institutes of Health (NIH)!** This is added to its Fiscal Year (FY) 2009 appropriation of $30 billion.

❖ **an "earmark" of $100 million for "Autism Related Disorders", which we assume includes Fragile X.** (The NIH has announced that it will commit roughly $60 million of its ARRA funds specifically to this, and FRAXA researchers are expected to receive a substantial share.)

What does this mean for Fragile X Research? A lot. It is a signal opportunity to move science forward while keeping scientists, both seasoned and novice, working!

The ARRA funds are required to be spent within 2 years. Because of this, much of the new money will go to enhance and expedite research that is in progress or that has recently gone through the review process. But we are assured that some of the funds will go to new two-year research grants. Luckily, over 100 Fragile X-related research projects are presently "in the mill" at the NIH. In FY2008, the NIH spent about $26 million on Fragile X research projects across 8 of its Institutes and Centers. (See crisp.cit.nih.gov for abstracts of these.) FRAXA researchers are prominent recipients of these project grants. We are confident that their work will be enhanced and expedited by these new funds.

More good news: At the urging of the Fragile X community, the NIH established an "NIH Research Coordinating Group" last year. Its leadership coordinates and stimulates collaboration of Fragile X Research across all of NIH. This seems to be working well and should be particularly effective in this new climate.


DAVID AND MARY BETH BUSBY OUTSIDE THE CAPITOL BUILDING

Please write to Senator Arlen Specter, a long-time champion of Fragile X research to thank him on behalf of your child for hanging tough to get the additional $10 billion in stimulus funds for NIH. His address is: The Honorable Arlen Specter, United States Senate, Washington, DC 20510.

FRAGILE X GAINS RECOGNITION FROM THE AUTISM COMMUNITY


DAVID BUSBY, JR., AND JACK BUSBY, SONS OF MARY BETH AND DAVID, WERE FEATURED ON AUTISM SPEAKS' WEBSITE.

Fragile X discoveries — specifically the mGluR theory and clinical trials of fenobam — and related drugs are among Autism Speaks' Top Ten Research Advances of 2008.

Two key facts make Fragile X research a worthy investment for finding a cure for autism: 1) Fragile X is the most common genetic cause of autism and 2) The cause of Fragile X — a single missing protein — is understood, whereas the roots of autism are still unknown, in most cases.

WANT FASTER UPDATES?

Get realtime updates by joining FRAXA's free email list at fraxa.org

FRAXA'S SCIENTIFIC ADVISORY BOARD GAINS NEW MEMBERS

FRAXA is run by parents, but we do not operate alone. Our Scientific Advisory Board, which includes 3 Nobel laureates, has evolved with our research portfolio and we have been fortunate to gain the expertise of key members of the pharmaceutical and biotechnology industries. **Please join us in welcoming two new advisors:**

Mike Snape, PhD

CHIEF SCIENTIFIC OFFICER

Neuropharm Group, PLC
London, UK

Dr. Snape is a founder of Neuropharm and, with his wife Rose, is a parent of a young person with autism. He has over twenty years of experience in pharmaceutical development and is named as an inventor on five pharmaceutical patents.

Dr. Snape began working with FRAXA in 2006, after discovering FRAXA's studies on the internet and concluding, on the basis of those studies, that developing a Fragile X treatment would fit well into Neuropharm's programs. The result is the recently completed trial of fenobam in adults with Fragile X.

Graeme Bilbe, PhD

GLOBAL HEAD FOR THE NEUROSCIENCE DISEASE AREA

Novartis Institutes for BioMedical Research
Basel, Switzerland.

Dr. Bilbe began his career at Ciba-Geigy in 1989 and now directs research into neurodegenerative and psychiatric diseases at Novartis.

When asked why he chose to work in industry, Dr. Bilbe said, "The idea of converting pure science in a directed way, bringing scientific results to the patients, caught my interest."

After attending FRAXA's 2004 Banbury meeting, Dr. Bilbe launched Novartis' Fragile X research progam – an effort so successful that an investigational new drug (the mGluR5 antagonist AFQ056), is now being tested in Fragile X patients in France, Italy, and Switzerland. Dr. Bilbe was back at Banbury this year.

BELOW: DR. MIKE SNAPE
BOTTOM: DR. GRAEME BILBE

10th annual Fragile X Banbury Meeting

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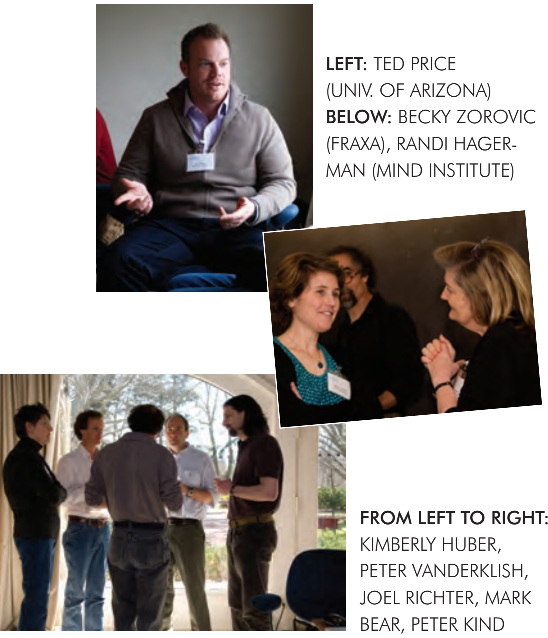


LEFT: TED PRICE (UNIV. OF ARIZONA)
BELOW: BECKY ZOROVIC (FRAXA), RANDI HAGERMAN (MIND INSTITUTE)

FROM LEFT TO RIGHT: KIMBERLY HUBER, PETER VANDERKLISH, JOEL RICHTER, MARK BEAR, PETER KIND

- The signaling pathways through which brain cells communicate are now better understood. Each step in pathways involving FMRP may be a therapeutic target.
- There is a connection between Fragile X and pain pathways. One first-time participant, Dr. Ted Price, gave a talk about peripheral nerves, FMRP, and pain. Dr. Price got his start in Fragile X research several years ago thanks to 86 FRAXA listserv members who responded to a survey about how their children responded to injuries.
- A growing number of basic research studies now support the mGluR theory — that drugs which reduce signaling through the mGluR5 pathway could effectively treat Fragile X. There was a real sense of optimism that drug development is on track. After all, it was a Banbury meeting five years ago that first interested Novartis scientists in Fragile X. Now their lead mGluR5 antagonist (AFQ056) is in clinical trials for Fragile X!

Most gratifying of all were the informal discussions between researchers who were trading advice, brainstorming new ideas, and designing their next experiments. For those of us who are donating or raising money for this research (almost all these projects depend on FRAXA funding), we can take comfort in the fact that some of these discussions may have saved scientists months (or even years) of wasted time using the wrong mouse strain or a sub-optimal technique. Fragile X scientists, while extremely competitive, share information and collaborate with a spirit of common purpose.

FRAXA RESEARCH GRANTS 2009

Working toward a cure

This year, more than 50 university teams have applied to FRAXA seeking a total of $7 million — an impressive measure of the growing level of interest in Fragile X research.

Despite the economic downturn, FRAXA was able to fund a fair number of high-quality projects, thus bringing more outstanding researchers into the field.

We expect to fund nearly $2 million in direct research grants in 2009, and the work being done now is more impressive than ever.


ASHA BHAKAR

Mark Bear, PhD
Asha Bhakar, PhD

MIT — $45,000

Development of a high-content synapse assay to screen therapeutics for the treatment of Fragile X Syndrome

Dr. Asha Bhakar, a postdoctoral fellow in Dr. Mark Bear's MIT lab, will employ a state-of-the-art automated high-throughput screen to test existing drugs. She will use this system to measure changes in dendrites and AMPA receptor expression in cultured Fragile X neurons, before and after treatment with thousands of available compounds.
This could identify unexpected therapeutic compounds that are ready to use right now.

David Nelson, PhD

BAYLOR COLLEGE OF MEDICINE — $60,000

Fragile X Mutant Mouse Facility

New genetic technology has enabled the development of improved hi-tech mouse models of Fragile X. These genetically advanced mice are essential for testing potential treatments. Through funding by FRAXA, a Fragile X Mutant Mouse facility has been established at Baylor College of Medicine. The laboratory of Dr. David Nelson at Baylor College of Medicine is now distributing 14 of the latest models to interested scientists at little or no cost. The 14 mouse strains are described at www.fraxa.org (Research Resources section).

Joshua Corbin, PhD
Molly Huntsman, PhD

GEORGE WASHINGTON AND GEORGETOWN UNIVERSITY — $50,000

Rescue of GABAergic transmission defects in the amygdala in the FMR1-/- mutant mouse model of Fragile X Syndrome

Dr. Joshua Corbin and Dr. Molly Huntsman will study inhibitory circuits in the amygdala (the "emotional center" of the brain) of the Fragile X mouse. Their studies incorporate both genetic and pharmacologic rescue protocols, which, used together, could identify new treatments.

Peng Jin, PhD
Xuekun Li, PhD

EMORY UNIVERSITY — $45,000

Small Molecule Screen using Fragile X Neural Stem Cells

Drs. Peng Jin and Xuekun Li are setting up another kind of high-throughput screen using neural stem cells from knock-out mice to identify small molecules which may be therapeutic in Fragile X. This innovative project uses the proliferation of stem cells as the primary read-out, likely yielding more robust and rapid results than previous approaches.


PENG JIN AND XUEKUN LI


AIDAN SILVERTON AND HIS DAD, KIMBALL

Elizabeth Berry-Kravis, MD, PhD

RUSH UNIVERSITY MEDICAL CENTER — $5,000

Aidan Silverton Student Fellowship

Dr. Elizabeth Berry-Kravis will direct The Aidan Silverton student fellowship at Rush University. This research fund, established by Aidan's uncle, Dr. Craig Silverton, will support an undergraduate or medical student research project on Fragile X each summer for four years. Each project will be directly relevant to development of treatments for individuals with Fragile X. This summer, the goal is to develop biomarkers in blood to measure the mGluR pathway in Fragile X patients.

Laetitia Davidovic, PhD

CNRS, VALBONNE, FRANCE — $30,000

Pharmaco-metabonomic study of FXS treatment efficacy

Dr. Laetitia Davidovic has moved from Quebec to France, where she will study the "metabonomics" of Fragile X, and look for available drugs which can correct the cellular metabolism of Fragile X neurons. This is a novel approach to finding new treatments for Fragile X.

Olivier Manzoni, PhD
Marja Sepers, PhD

INSERM, BORDEAUX, FRANCE — $45,000

Dysruption of endocannabinoid mediated synaptic plasticity in the NAc of FMR1 null mice

Drs. Olivier Manzoni and Marja Sepers at INSERM in Bordeaux, France, are working on an innovative project to examine the endocannabinoid system in Fragile X. They have identified abnormalities in the function of this system, which is so named because cannabinoids (like marijuana or THC) stimulate these pathways. Most importantly, drugs are in development which could ameliorate this dysfunction.

Stephen Warren, PhD
Joshua Suhl, PhD

EMORY UNIVERSITY — $45,000

A new model for epigenetic events in Fragile X Syndrome: induced pluripotent stem cells

The team received outstanding reviews for their plan to develop pluripotent stem cells to test potential treatments for Fragile X. This new technology allows regular live cells from a human donor (for example, skin cells) to be converted into stem cells which can form long-lived cultures. This would allow for testing of potential therapeutic compounds on human Fragile X cells.


JOSHUA SUHL

Efthimios Skoulakis, PhD

INSTITUTE OF MOLECULAR BIOLOGY AND GENETICS, GREECE — $33,750

Efficient screening for pharmaceutical amelioration of Fragile X behavioral deficits in Drosophila

Dr. Efthimios Skoulakis will conduct the first FRAXA research project in Greece, where he has developed novel behavioral assays with Fragile X fruit flies. He will use these techniques to study the major signaling pathways involved in Fragile X and to test a number of pharmacologic rescue strategies.

Miklos Toth, MD, PhD
Ji-eun Oh, PhD

WEILL MEDICAL COLLEGE OF CORNELL UNIVERSITY — $45,000

Genome-wide epigenetic marks in Fragile X: new therapeutic targets and approaches

Based on recent findings that FMRP acts as a transcription factor (controlling transcription from DNA to RNA, rather than translation from RNA to protein), Drs. Miklos Toth and Ji-eun Oh of Cornell University will investigate which other genes' transcription are altered in the absence of FMRP. This has the potential to identify many new treatment targets.

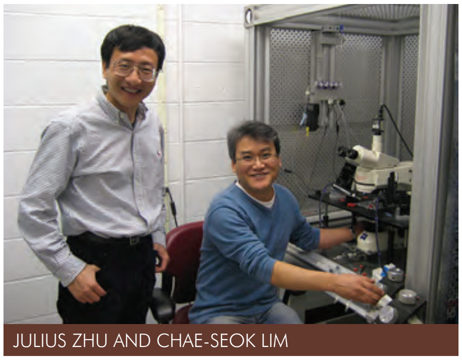

JI-EUN OH

Julius Zhu, PhD
Chae-Seok Lim, PhD

UNIVERSITY OF VA SCHOOL OF MEDICINE — $49,801

Serotonergic rescue of synaptic plasticity in FMR1 knockout mice

Dr. Julius Zhu was a FRAXA Postdoctoral Fellow many years ago at Cold Spring Harbor. Now he is a professor at the University of Virginia and he is still working on Fragile X, with a special interest in the Ras signaling pathway. Dr. Zhu and Dr. Chae-Seok Lim will investigate the potential therapeutic effects in this pathway of a number of drugs which work via serotonin receptors.


JULIUS ZHU AND CHAE-SEOK LIM

FRAXA RESEARCH GRANTS 2009

Working toward a cure

FRAXA funded a large number of projects last year, thanks to the success of the Buffett Challenge, so the bulk of our funding this year is going to pay to renew these projects for a second year. Exciting results are pouring in, and manuscripts for publication are heading out to leading scientific journals around the world.

There are more projects than can be described in this newsletter, so please see www.fraxa.org or contact FRAXA for details on these exciting projects.

TREATMENT TARGET: MGLUR5

Mark Bear, PhD
Dilja Krueger, PhD
MIT — $40,000
Investigating a role for metabotropic glutamate receptors (mGluRs)

UPDATE: Drs. Bear and Krueger are developing new tests of learning in Fragile X mice, something which has proven hard to measure so far. They have come up with some interesting tests and they are now using drugs like MPEP and viral vectors (i.e. gene therapy) to reverse deficits in attention, learning, and other executive functions.

Karen O'Malley, PhD
Vikas Kumar, PhD
WASHINGTON UNIVERSITY, MO — $60,000
Role of cell surface versus intracellular metabotropic glutamate (mGlu5) receptors in opposing FMRP function.

UPDATE: Dr. O'Malley's lab studies the function of mGluR5 inside the cell. We usually talk about these receptors working on the cell surface, but it so happens that they are active inside the cell, too. Just as cell surface mGluR5 function is abnormal in Fragile X, it is likely that intracellular mGluR5 function is abnormal, contributing to Fragile X pathology.

Cara Westmark, PhD
James Malter, MD, PhD
UNIVERSITY OF WISCONSIN — $60,000
Utilization of Fenobam to Reduce APP and Abeta in Fragile X Mice

UPDATE: The team has identified another protein normally regulated by FMRP; like some others, APP is elevated in Fragile X mice and humans. APP, also known as Amyloid Precursor Protein, is thought to have a role in Alzheimer's Disease, and it is known to be elevated in some cases of autism. Thus, APP is a potentially valuable biomarker for autism and Fragile X, and treatments which reduce APP (like mGluR5 antagonists) may be effective in treating many conditions where too much APP is a problem.

Femke deVrij, PhD
Ben Oostra, PhD
ERASMUS UNIVERSITY, ROTTERDAM — $60,000
Understanding the mechanism of mGluR5 directed therapy and the involvement of the miRNA pathway in Fragile X syndrome

UPDATE: The team at Erasmus University have identified several behavioral abnormalities in KO mice, and they are using mGluR5 antagonists to rescue them, while also looking at abnormalities in dendrites and the mechanisms behind them.

MORE TREATMENT PROJECTS

Paul Lombroso, MD
Susan Goebel-Goody, PhD
YALE UNIVERSITY — $85,000
The Role of STEP in Fragile X Syndrome

UPDATE: Dr. Lombroso's lab at Yale has found that a protein called STEP is essential for the internalization of AMPA receptors, and this protein is overexpressed in Fragile X. He's trying to rescue function in KO mice by crossing with STEP knockouts (thus reducing STEP levels) and then he'll try small molecules (i.e. drugs) which inhibit STEP to treat the Fragile X mice. Preliminary results are very promising, and STEP inhibitors are a topic of intense interest to pharmaceutical companies.

Stephen Haggarty, PhD
Surya Reis, PhD
HARVARD/MASSACHUSETTS GENERAL HOSPITAL — $75,000
Characterization of Small Molecule Modulators of Lithium Using a Human Neural Progenitor Cell Model of Fragile X

UPDATE: The group have established human Fragile X neural stem cells in a high-throughput screen, and they are testing thousands of compounds to see which can block the key enzyme GSK3, either alone or in combination with lithium. This work has the potential to identify available drugs which could enhance the therapeutic effect of lithium, which has been demonstrated to be helpful for some people with Fragile X. *(see FRAXA.org, Research Reports section, Elizabeth Berry-Kravis).*

Len Kaczmarek, PhD
Vali Gazula, PhD
YALE UNIVERSITY — $60,000
Regulation of FMRP-Slack potassium channel interactions by mGluRs and protein kinase C

UPDATE: Dr. Len Kaczmarek and his group at Yale have discovered an important new mechanism by which mGluRs regulate potassium channels in neurons, and have found that this system is disturbed in Fragile X. This may explain a number of Fragile X symptoms, and may be another point of therapeutic intervention in Fragile X.

Iryna Ethell, PhD
Douglas Ethell, PhD
UNIVERSITY OF CALIFORNIA AT RIVERSIDE — $80,000
Targeting Matrix Metalloproteinases to Treat Dendritic Spine Malformation and Behavioral Defects in Fragile X Mice

UPDATE: Ethell and colleagues continue their breakthrough research on the role of extracellular enzymes called MMPs, and how they regulate the shape of dendrites. They have already identified minocycline as an off-the-shelf therapeutic, but there are other targets for drug discovery in this pathway.

Thanks to a directed grant of $20,000 from Jerad and Julie Chao, whose 3-year-old son has Fragile X, FRAXA has been able to increase this project budget and Dr. Ethell will add an additional graduate student to the team. This will dramatically speed up their efforts to find additional therapeutic alternatives to minocycline.

Joel Richter, PhD,
Tsuyoshi Udagawa, PhD
UNIVERSITY OF MA — $40,000
Functional Interplay between FMRP and CPEB: CPEB, a Potential Target for Fragile X treatment

UPDATE: Dr. Richter is an expert in the regulation of protein synthesis, and his studies focus on a protein called CPEB. Together with his postdoc, Dr. Udagawa, he is investigating the possibility that reducing CPEB activity could treat Fragile X.

Eric Klann, PhD
Hanoch Kaphzan, MD, PhD
NEW YORK UNIVERSITY — $55,000
Targeting of Translational Control Proteins to Reverse Phenotypes in Fragile X Syndrome Model Mice

UPDATE: The group at NYU are examining the function of the mTOR pathway in Fragile X. This critical signaling cascade is widely involved in cell growth and synaptic plasticity, and is known to be defective in several forms of autism. They will attempt to rescue synaptic plasticity in the KO mouse by genetic reduction of one part of the mTOR pathway, an enzyme called S6K1.

DISEASE MECHANISMS

Gary Bassell, PhD
Viji Nalavadi, PhD
EMORY UNIVERSITY — $40,000
Regulation of dendritic mRNA transport and translation at the synapse by FMRP phosphorylation

UPDATE: Drs. Bassell and Nalavadi are studying the transport role of FMRP and the precise mechanism by which FMRP gets many mRNAs to the right place in the cell, then helps them get translated into protein. This information will lead to other potential points of intervention, and candidate genes for autism.

Kendal Broadie, PhD
Cheryl Gatto, PhD
VANDERBILT UNIVERSITY — $40,000
Spatial and temporal requirements of FMRP function in neurological mechanisms

UPDATE: The Vanderbilt team have made significant progress in understanding the specific times and places in the fruit fly brain which require FMRP for proper development. The simplified system of fruit flies helps us to understand the far more complicated human brain.

Maria Victoria Tejada-Simon, PhD
UNIVERSITY OF HOUSTON — $60,000
Rac-dependent regulation of neuronal morphology in Fragile X Syndrome

Dr. Tejada-Simon is studying alterations in a key regulatory protein called Rac; like some other proteins, its levels are elevated in Fragile X. She will be testing the hypothesis that inhibition of Rac can rescue Fragile X synaptic function.

William Greenough, PhD
UNIVERSITY OF ILLINOIS — $25,000

Dr. William Greenough at the University of Illinois has been distributing Fragile X knockout mice to the research community for a number of years and will continue this activity over the coming year.

CLINICAL TRIALS IN PROGRESS

Trials of new treatments and interventions are currently underway in individuals with Fragile X, at sites across the U.S. and beyond, and many are seeking participants, including these:

ARBACLOFEN — MULTI-CENTER TRIAL
This study aims to evaluate if an investigational medication, Arbaclofen, can manage the irritability associated with Fragile X. Sponsored by Seaside Therapeutics, this trial is being conducted at Rush University Medical Center in Chicago, the MIND Institute in Sacramento, CA, Riley Hospital for Children in Indianapolis, the University of North Carolina, Vanderbilt in Nashville, Seattle Children's Hospital, Children's Hospital Boston, and University of California-Los Angeles.

BRAIN IMAGING STUDY — NIH, BETHESDA, MARYLAND
The National Institutes of Health is seeking men (18-24 years) with fragile X syndrome for a study to determine how well they can accept lying down in a scanner. This study has minimal risk, requires one outpatient visit lasting about 4 hours, and participants will be compensated.

ARIPIPRAZOLE (ABILIFY) — INDIANA UNIVERSITY
This trial is testing aripiprazole (Abilify) in the treatment of Fragile X. The investigators, Dr. Christopher McDougle and Dr. Craig Erickson, believe that aripiprazole will decrease aggression, self-injurious behavior, agitation, and repetitive behavior commonly observed in individuals with Fragile X. Ages 6 to 35 are eligible.

TMS (TRANSCRANIAL MAGNETIC STIMULATION) — BOSTON
With a grant from Harvard, Dr. Jonathan Picker is investigating cortical plasticity in individuals with autism spectrum disorders and Fragile X syndrome using noninvasive transcranial magnetic stimulation (TMS). TMS is an experimental way to transiently activate specific brain areas through the scalp. It has been used for the past 20 years in neurology and psychiatry.

For more information about participating in these and other trials, please visit ***fraxa.org*** *(Get Involved section) or* ***clinicaltrials.gov***

FUNDRAISING

FRAXA's mission is to find effective treatments and ultimately a cure for all children and adults with Fragile X. If you've ever wondered where FRAXA gets the money to support so much research (more than $17 million in total since 1994) you might be surprised to learn that almost every penny has been donated or raised by friends and families — thousand upon thousands of generous people. We receive no government funds. FRAXA is truly a grass roots organization.

These are many — but not all — of the events hosted around the U.S. to support FRAXA in the past few months. Since our overhead expenses are only 5% *(see page 11)*, most of the funds raised have already been put to good use — on research to cure Fragile X.

How can you help most? Please consider an automatic monthly donation online at fraxa.org. It is easy for you, incurs no fees, and can be ended anytime. For FRAXA, knowing that funds will come in every month means we can commit to supporting new research grants, from start to finish (typically 2 years). You can also help by attending an event (see page 10) or hosting your own.

Please donate now at fraxa.org or using the enclosed envelope. Thank you!

Art Show ▲

Marblehead, MA

On Feb. 1, Olga Gernovski held a raffle of her art work at the Marblehead Arts Association to benefit FRAXA. Twelve works of art, including 3 large original paintings, were raffled off, raising over $600. Visit www.olgafinearts.com to learn more about the artist and her art. The room was crowded with friends of Olga and Leo Gernovski, whose son Dima has Fragile X, and Leslie and Trevor Eddy, whose daughter Alison has Fragile X. Laura Tranfaglia (daughter of Katie Clapp and Mike Tranfaglia) sold the raffle tickets.

Fall Party with a Purpose

Edina, MN

The Espinosa, Bjerke and Thompson families held a Fall Party with a Purpose to raise money for TeamFRAXA. Kids enjoyed crafts and games and adults enjoyed a beautiful fall day with live music and great food. They raised over $2000.

Marine Corps Marathon ▶

Washington, DC

TeamFRAXA competed in the October 26th Marine Corps Marathon in Washington, DC, raising over $10,000. Christen Thompson and Kari Espinosa (right) were among the runners on the team in honor of all children affected by Fragile X. Our thanks go to Michael Clift for organizing TeamFRAXA.

Casual for a Cause

Holland, PA

The Casual for a Cause Program at Holland Middle School donates funds collected from the staff to deserving individuals and organizations. This year FRAXA was lucky to be chosen and received $340.

Le Roy Football

Central Illinois

This past fall marked the second annual Abraham Zeleznik Fragile X Walk. The Le Roy High School football team, along with Heart of Illinois Conference football members Fieldcrest High School, Tri-Valley High School, Gibson City Melvin Sibley High School, and Ridgeview High School, walked door-to-door in their communities to raise money for and awareness about Fragile X.

In the two years since the inception of the walk, over $17,000 has been raised by hundreds of people in central Illinois who have selflessly contributed to help fund Fragile X research. Amy and BJ Zeleznik, parents of Abraham (4 years old) and Bohdan (2 years old, non-FX), plan on hosting the walk every year. BJ is head football coach at Le

UPCOMING EVENTS?

Calendar at fraxa.org
— check often!

Willie's Bake Sale

Asheville, NC

"On this holiday of Love, who wouldn't Love to help Willie?" That was the tag line for Willie's Bake Sale on Valentine's Day 2009. $1,725.00 was raised, and that's a lot of cookies!

Kate Gregory writes: "We made 12 batches ourselves, and several friends chipped in a few more at the last minute. It was very pretty, and we had a separate table with FRAXA information, pictures of the kids and FRAXA's movie "Hitting the Mark" playing on YouTube. There were many moist eyes after watching that. We live at a boarding school, and the students were very helpful both with set up and purchasing."

JIM CONNOLLY, PACK LEADER, DR. MICHAEL TRANFAGLIA, AND DICK LANGELL, FLANKED BY MEMBERS OF PACK 50.

◀ Can Drive

Georgetown, MA

Cub Scouts Pack 50 of Georgetown, MA, the hometown of the Langell family, donated $375 in February. They raised the money collecting cans. Mike Tranfaglia was thrilled to accept a giant check on behalf of FRAXA.

Mya Ulmer's 7th Birthday ▶

Fairfield, CT

Mya raised $195 in honor of her cousin, Jimmy Grande, who has Fragile X. Thanks Mya! Can't wait 'til you turn eight!

MYA (2ND FROM LEFT, AND SOME OF HER FRIENDS)

Roy High School. "Since we received Abe's diagnosis three years ago, we have strived to use what resources and connections we had to help the FRAXA cause. The outpouring of support from our family, friends, surrounding communities, and last but not least, our football family, has been amazing!" said Amy Zeleznik.

Eight of the conference's 13 schools have participated in the event and they have considered expanding to include other programs in the Central Illinois area for future walks.

And Many More!

These are but a selection of the events and campaigns mounted for FRAXA research since our last newsletter. We would also like to recognize The Shelly Group, Irvine BMW, who staffed a booth for FRAXA at an October event and raised over $1,000, the Rhode Island FRAXA chapter, especially Tom and Leslie Bobrowski, who organized the Fall 2008 5K run, Laura Moodie for running a half marathon in San Antonio to raise funds for FRAXA, Judith Maloney and Debbie Heiman and their family and friends, who hosted the "Be Big and Give" Ohio fundraiser, and the Ladies Golf Organization at Plandome Country Club in Plandome, NY.

On behalf of all families who live with Fragile X, thank you!

FUNDRAISING

UPCOMING EVENTS

LEFT: LEFT PATRICK'S PALS XII WINNING TEAM

MIDDLE: CASEY BOWLER AT MT. RAINIER'S STRONGEST MAN & WOMAN 3

RIGHT: DORIS BUFFETT

Patrick's Pals Basketball Tournament

Cambridge, MA

Saturday, May 30

On Saturday, May 30, the Buckingham, Brown & Nichols gym will be the scene of Patrick's Pals XIII. Started by 5 loyal childhood friends of James Vershbow, whose son Patrick has Fragile X, the event brings pros and Joes together in a double elimination tournament. Recent Patrick's Pals participants include Bob Lobel, Steve Burton, and Ben Watson. Join us to see who appears this year! Contact James Vershbow at pjversh@comcast.net or 617-599-2641.

Walk for Fragile X

Bernville, PA

Saturday, June 20

Held at the Tulpehocken Jr/Sr High School Track, 428 New Schaefferstown Rd, Bernville, PA. Contact Jennifer Mathias at 610-488-1612, 717-813-1289 or LukeJen97@aol.com.

2nd Motorcycle Run to Cure Fragile X

New Castle, Delaware

Sunday, July 26

A bike run starting at Mike's Harley-Davidson in New Castle, followed by BBQ, live band and silent auction. Activities for kids, childcare, and fun and prizes for grownups too! Live band and silent auction. Organized by Jen Nardo, contact her at jlnardo1@verizon.net.

Mt. Rainier's Strongest Man & Woman 4

Sumner, WA

Saturday, August 1

Laurie Bowler of Rainier Crossfit reports that this year's Mt. Rainier's Strongest Man and Woman 4 will be back at The Old Cannery in Sumner. Last year we had 31 competitors from 4 states and we raised $13,000, bringing our grand total donation to FRAXA to just over $25,000. The contest now has its own website where people can go for information and updates: www.mtrainiersstrongest.com.

2nd Annual Robert Langell Golf Tournament

Turner Hill, Ipswich, MA

Monday, September 28

Golf and dinner at the gorgeous Turner Hill mansion. Contact Didi Langell at langelldidi@hotmail.com.

Boston Gala

Seaport Hotel,

Thursday October 8

Join families, friends, researchers and supporters at Boston's Seaport Hotel as we honor Doris Buffett, whose 2007 challenge grant to FRAXA energized volunteers across the country. Celebrate with Ms. Buffett and other distinguished guests Dr. Mark Bear, authors Mary Higgins Clark and Mary Jane Clark, The Sopranos actor Dan Grimaldi, The Weather Channel storm tracker Jim Cantore, Boston trial attorney Harry Manion, and Boston news reporter Kelley Tuthill on October 8th in Boston. Sponsorships and tables now available. Hosted by Liz and Jason Mazzola, and Leslie and Michael Cheverie. Contact Katie Clapp at kclapp@fraxa.org.

7th Annual Fall X Ball

Poughkeepsie, NY

Friday, October 9

The annual gala will be held at the Dutchess Golf and Country Club. For info, please email Ron and Amy Watkins at rwatkins@fraxa.org or call Ron at 845-797-0846. Last year's gala raised over $70,000.

SUPERMARKET REWARD PROGRAMS

AN EASY WAY TO SUPPORT FRAXA, BECAUSE EVERYONE HAS TO EAT!

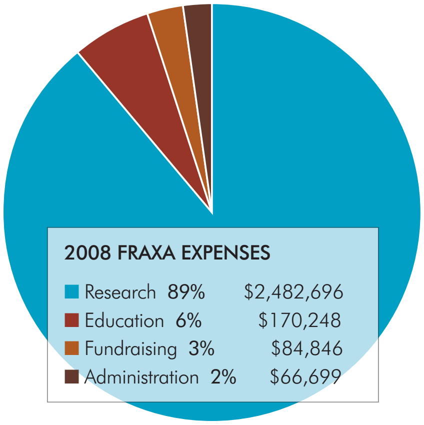
*If you have a **Shaw's** or **Star Market** rewards card, sign up for FRAXA to receive 1% of eligible spending. It's easy, costs you nothing, and could add up to a lot of money for FRAXA. Go to www.shaws.com and go to "Shaw's Cares" and then "community rewards." FRAXA's number is 49001019062.*

If you have any trouble, please contact Becky Zorovic at bzorovic@fraxa.org.

*Do you shop at **Randalls** or **Tom Thumb** supermarkets? If so, please apply for their **Remarkable Card**. The first time you use it, tell the cashier FRAXA's number: 3715. If you present the card each time you shop, 1% of your purchase (excluding pharmacy, alcohol and tobacco) will automatically be donated to FRAXA.*

MESSAGE FROM THE FOUNDERS

Imagine a cure for autism and intellectual disabilities. In 1994, a group of parents of children with Fragile X — the most common inherited cause of intellectual disabilities and autism – dared to dream that big. *This is the mission of FRAXA Research Foundation.*



IN JUST 15 YEARS, FRAXA-FUNDED teams have moved from understanding the cause of Fragile X to reversing signs of Fragile X in animal models. Thanks to magnificent work by 110+ research teams around the world, we are poised to bring newly-discovered drugs into human clinical trials. To help those already afflicted with Fragile X, time is of the essence.

FRAXA leverages every dollar spent in a number of ways. First, we fund research that government agencies might consider too risky, but which often leads to bigger government grants.These grants can be ten times the size of FRAXA grants, and that's a lot of leverage!

Second, FRAXA cannot afford to fund drug development. Developing a single drug costs many millions of dollars. Instead, we fund critical "proof of principle" studies in Fragile X models (like knockout mice and mutant fruit flies.) These studies are powerful inducements to pharmaceutical companies to consider developing their compounds for Fragile X — an indication that they might otherwise consider too rare and risky. FRAXA will continue to seek opportunities to "de-risk" drug development through philanthropic-pharmaceutical partnerships.

Third, when time is critical, what better approach is there than to quickly test thousands of compounds to see if they might reverse signs of Fragile X? FRAXA is now funding several high-throughput drug screens to identify available compounds which demonstrate therapeutic effects in Fragile X model systems. We are leveraging our past research (which enabled development of these systems) against the vast resources of the pharmaceutical industry, which has already developed many thousands of drugs, some still seeking a purpose.

In the current worldwide financial crisis, charities are being hit hard. Fortunately, FRAXA's overhead costs are low, so we are well positioned to weather the storm. We believe that the intelligent allocation of resources will allow us to make uninterrupted progress.

Can we succeed in finding a cure for Fragile X? Absolutely! FRAXA is well known in the rare disease community. Victoria Miller, founder and director of the Trisomy 18 Foundation, recently noted "Whenever I've been in discussions with NIH folks and the topic turns to good examples of effective disease advocacy groups, FRAXA always comes up as the model for how to get things done right on the research front."

FRAXA RESEARCH FOUNDATION UPDATE

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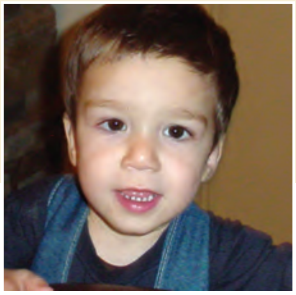

FRAXA is a national 501(c)(3) tax-exempt organization run by parents of children with Fragile X. FRAXA's overhead is 5%, one of the lowest of all charitable organizations. Supporters receive this newsletter and are welcome to participate as active volunteers.

PLEASE HELP...

YES, I WOULD LIKE TO HELP FRAXA:

☐ Member ($25+)
☐ Donor ($50+)
☐ Sponsor ($100+)
☐ Benefactor ($500+)
☐ Research Underwriter ($1000+)
☐ Named Research Fund ($5000+)
☐ Named Research Chair ($25,000+)

Send to: FRAXA
45 Pleasant St., Newburyport, MA 01950

Or donate online at www.FRAXA.org

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