

FRAXA UPDATE

FALL 2003

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FRAXA RESEARCH
FOUNDATION

"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

1994-2004: Ten Years of FRAXA Research

by Michael R. Tranfaglia, MD
FRAXA Medical Director & co-founder

FRAXA Research Foundation will be celebrating its 10th anniversary in January, so it's natural at this time that we look back at how far we've come.

10 years ago, most people in the Fragile X community thought of Fragile X as an irreversible condition, not a treatable disease. Even though the gene that causes Fragile X (FMR1) was discovered in 1991, its function remained mysterious. Now we know much about the normal function of the protein produced by this gene and how its absence causes Fragile X. Indeed, FRAXA researchers have identified a key pathway in the synaptic connections between neurons of the brain that functions excessively in Fragile X. We think this pathway accounts for most of the symptoms of Fragile X. Most importantly, compounds exist which can block this pathway. Some of these are currently being developed as human drugs, so we are testing them in the Fragile X mouse model –

continued on page 3



Andy Tranfaglia with Cookie, pet hamster, and Mike Tranfaglia

Latest Fragile X Research Advances Presented

by Katie Clapp, president and co-founder

This year, at the annual meeting of the Society for Neuroscience in New Orleans, November 8-12, we saw 24 Fragile X studies presented, rather than the dozen or so Fragile X studies of the past few years (and less than five the first year we attended). We are proud to note that 15 of these 24 projects are FRAXA-funded and most of the other teams have also received FRAXA support for related studies. No other source supported nearly as many studies ... not even the U.S. government! This meeting is the

Also in this issue:

- Report from Washington
- Resources for Researchers
- Fragile X Research Day/Fall Fling

premier showcase for neuroscience research, with over 29,000 people in attendance.

Each year, FRAXA hosts a booth at this meeting to recruit new Fragile X researchers and see the work of current FRAXA grantees. This year, Michael Tranfaglia, Katie Clapp, Debbie Stevenson, and Leslie Eddy staffed our booth with help from New Orleans-area parents, Mary Ann Haase and Theresa Wilson. Hundreds of researchers visited us. (See page 4 for descriptions of the most interesting work.) On December 1st, grant proposals will arrive from researchers around the world. After peer review by FRAXA's Scientific Advisory Committee, our Board of Directors will look at FRAXA's available funds and determine which projects can be supported. Donations over the next two months are critical – they will determine how many more scientists can help us solve the mystery of Fragile X!

FRAXA 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 developmental disabilities, affecting approximately 1 in 4000 males and 1 in 8000 females. FRAXA's goal is to accelerate research aimed at the treatment and cure of Fragile X, by direct funding of promising research projects and by raising awareness of this disease.



Report from Washington:

By Mary Beth and David Busby

Fiscal year 2003 is *not* a promising year in Congress for Fragile X research. Each year since 1995, we have asked the Congress and the Congress, in turn, has asked the National Institutes of Health (NIH) and/or the National Centers for Disease Control and Prevention (CDC) to institute or enhance specific Fragile X research projects. In large part as a result of these requests and the letters of our Fragile X Advocates to their Members of Congress, NIH funding for Fragile X research has gone up each year. This year our requests fell on (mostly) deaf ears.

In the Spring we asked the Appropriations Committees of the Senate and House to include in this year's annual Report the following:

1. A state-of-the-science conference on Fragile X research to be sponsored by the NIH.
2. Increased funds for the 3 new Fragile X Research Centers of the National Institute of Child Health and Human Development, NIH.
3. Increased funds for Fragile X research at the National Institute of Diabetes, Digestive and Kidney Diseases (NIDDKD).

4. A study by the National Institute of Mental Health (NIMH) of new Fragile X pharmacological treatments and identification of key molecular targets for drug treatment.
5. Expansion of Fragile X research at the National Institute of Neurological Disorders and Stroke (NINDS), especially to explore the tremor/ataxia syndrome among older male carriers.
6. Expansion of Fragile X – and autism – screening by the CDC's new National Center on Birth Defects and Developmental Disorders (NCBDDD), to maximize prevention potential, minimize impact on families, and promote early intervention.

The Senate Appropriations Committee (but not the House Committee) endorsed our request only to the extent of asking the NIH and the CDC to effectuate our requests #1 and #6.

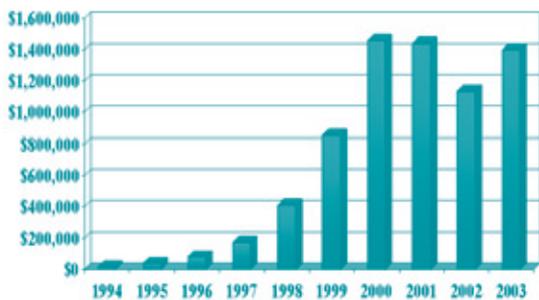
The causes of this lack of responsiveness by the Appropriations Committees are probably:

1. The doubling of the overall NIH budget in 5 years had been accomplished, and the Members of the Committees were not in the mood to push discretionary projects, especially in view of the Iraq war.
2. Failure of your Washington Representatives (us!) to realize the need for special efforts this year. One of our main champions in the House, Congressman Watkins, retired, and several knowledgeable staffers moved.
3. We did not push our FRAGILE X ADVOCATES (you!) to contact their Members as we have in the past.

Lest we become discouraged, let's not forget that since 1995, the Congress has increased NIH spending for Fragile X research from less than \$2 million to \$19.5 million in FY 2003. Also, the CDC's new National Center on Birth Defects and Developmental Disabilities and Disorders is finally getting under way with a very significant budget.

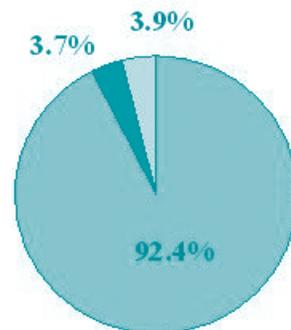
Finally, best of all, FRAXA's own privately-funded research – over \$ 7 million since it was founded in 1994 – is producing the most encouraging and meaningful results of all!

FRAXA Funds Research



FRAXA dollars spent on research grants and fellowships

FRAXA Finances



source: www.CharityNavigator.org

OVERALL RATING: 4 Stars (out of 4)

ORGANIZATIONAL EFFICIENCY

- Fundraising Expenses 3.7%
- Program Expenses 92.4%
- Administration Expenses 3.9%

David's Fragile X Advocates

by Diane Hamsa

As Congress gets to work on appropriations, we will have emails again from Busby.David@dorsey.com. David is our “tour director” on a journey that began in the summer of 1999. We are his advocate journey-men from the north, south, east, and west. Webster’s Dictionary defines journeyman as “any sound, experienced, but not brilliant performer.” We know who the brilliant performer is – our leader, David Busby. His wisdom and expertise have been responsible for the legislative accomplishments aiding Fragile X research. As advocates, our job was to become acquainted with our own representatives in the House and Senate in order to ask their help toward our final destination – effective treatment and a cure. That is where the rubber meets the road.



Robert and Jack Busby

David has been mapping out the best way to go and how we’ll get there. Another adventure with Congress is on its way. We’ll stay the course for increased funding for research and a cure for Fragile X.

Busby.David@dorsey.com, we are with you to help fulfill a dream.

There were a few road blocks, but that didn’t slow us down. The Fragile X Act of 1999 evolved into the Children’s Health Act of 2000. Now, near the end of 2003, we are filled with hope and expectation as research shifts into high gear. Three new research centers are being funded by NICHD. FRAXA does “in house” fundraising with Fall Flings, parties, and the Mary Higgins Clark Galas.

FRAXA: 10 years later continued from page 1

and getting very promising results. *In 10 years we have gone from thinking of Fragile X as untreatable to having a very real, near-term possibility of treatment.*

10 years ago, few scientists were studying Fragile X. A small group of dedicated researchers made significant progress by identifying the FMR1 gene and developing advanced diagnostic tests for Fragile X. However, it was clear from the start that this was a neurological problem and that more neuroscientists would need to be brought into the field. FRAXA has made the recruitment of top neuroscientists its highest priority. We have had great success by reaching outside the small Fragile X research community to bring in new people and new talent. Many leading neuroscientists are currently funded by FRAXA, and most of the major advances in the field have come from their labs. *In just 10 years, Fragile X has gone from an obscure specialty to one of the hottest topics in all of neuroscience!*

10 years ago, government agencies funded relatively little Fragile X research. Total NIH funding of all Fragile X research was just over \$1 million per year, and less than \$40,000 of that could have been considered “treatment-oriented.” In 2004, total NIH funding of Fragile X research will exceed \$20 million, thanks in large part to the lobbying efforts of FRAXA families. In addition, FRAXA has partnered with NIH to co-fund \$1.4 million of treatment-oriented research each year through a special grant program outside the regular funding system. While we think Fragile X research is still extremely under-funded, in the past 10 years we have seen remarkable progress.

10 years ago, FRAXA Research Foundation started by funding a single research grant. We are currently funding more than 30 major projects in labs around the world. Not only has the quantity of the research increased dramatically, but also the quality of the research has increased by leaps and bounds. Ten years ago, Fragile X families were a fragmented group without a common purpose; today, the Internet has brought us together to form an effective advocacy group which lobbies government agencies and raises funds for direct sponsorship of biomedical research.



Andy and Laura Tranfaglia

In the past 10 years, we have seen a remarkable convergence: the scientific community, Fragile X families, and government agencies like NIH have all come to see a cure for Fragile X as not only possible, but just a matter of time. Thanks to your support, we can make this happen as soon as possible. With a lot of help and a little more good luck, we’re sure it won’t take another 10 years.

Research Frontier: New Fragile X Studies Presented at Neuroscience 2003 Meeting

by Katie Clapp

Current neuroscience research on Fragile X spans a great variety of studies. Much of the work focuses on how the Fragile X protein functions and what goes wrong when it is absent. Researchers are now finding that Fragile X mice show a range of problems similar to problems seen in people with Fragile X. The mice show difficulty coping with stress and are slow to learn to distinguish smells (which are central to a mouse's world). They are prone to seizures and there are changes in the fine structure of the neurons in their brains.

Fragile X mice are critical to progress for two main reasons: we can learn more about Fragile X in humans by studying the mice and we can test new treatments on the mice to see how effective they are before considering human testing.

Rather than summarize all 24 studies here, we've included a sampling. For complete abstracts, contact FRAXA or visit www.sfn.org.

Audiogenic Seizures and Effects of mGluR5 Antagonist MPEP in the Fragile X Mouse



QI JIANG YAN,
MICHAEL TRANFAGLIA,
AND ROBERT BAUCHWITZ

Columbia University

Robert Bauchwitz

This study provides the most dramatic evidence to date that mGluR5 antagonists may effectively treat a range of symptoms seen in Fragile X.

Audiogenic seizures can be triggered by very loud sound. The Fragile X knockout mouse is quite susceptible to this kind of seizure. The researchers evaluated an experimental drug, MPEP (a selective mGluR5 receptor antagonist), and found that it was able to abolish these seizures in all strains of Fragile X mice. This indicates that the mGluR5 pathway plays an important role in audiogenic seizures. It also offers a well defined model to investigate the neurobiological and genetic cause of seizures and related deficits in Fragile X Syndrome, as well as potentially serving as a model for testing novel anticonvulsant drugs. This and other studies suggest that mGluR5 antagonists will be useful for treatment of more than just seizures.

Supported by FRAXA

r e s e a r c h

The Fragile X Mouse: Seizure Susceptibility and Electrophysiological Alterations May be Due to GABA System Changes

CARL DOBKIN ET. AL.

Institute for Basic Research, NY

Childhood seizures are common in Fragile X syndrome, and Fragile X mice also show increased seizure susceptibility. This study suggests that seizure susceptibility in Fragile X is increased because absence of FMRP leads to alterations of the GABA system. The team observed electrophysiological changes in the Fragile X mouse consistent with GABAergic system changes. They also found that these changes are reversed in a mouse model, developed by Dr. Robert Bauchwitz, in which a human FMR1 gene has been added into the genome of the knockout mouse. These studies tell us more about how the Fragile X gene works and give some hope that, one day, gene therapy will be a potential treatment for Fragile X.

Supported by FRAXA

A FEW TERMS

FMR1 is the gene that normally produces **FMRP** but is mutated and shut down in people with Fragile X syndrome.

FMR1 Knockout mice have been bred to mimic Fragile X syndrome. They lack the FMR1 gene and therefore also lack the protein, FMRP.

mRNA is code produced by a gene. mRNAs can travel between a cell's nucleus, where all the genes stay, and the cell's dendrites, the extensions which reach out to other cells. Each mRNA contains the code to produce a protein.

synapses are the connections where cells communicate with other cells.

synaptic plasticity refers to changes in shape and structure of dendrites and synapses ... the biological basis for learning and memory.

Olfactory Learning and Memory in a Mouse Model for Fragile X

JOHN LARSON & COLLEAGUES

Univ. of Illinois, Chicago



John Larson

In mice, the sense of smell is critical for navigating their world. The investigators tested Fragile X mice to see if they have defects in distinguishing and remembering smells. They found that Fragile X mice take longer than control mice to learn to distinguish between two smells. This knowledge provides a useful new tool for testing candidate treatments for Fragile X in the mice.

Supported by NIDA (part of NIH), FRAXA Research Foundation, and UIC Campus Research Board

Social Behaviors in the FMR1 Knockout Mouse Model of Fragile X

RICH PAYLOR & COLLEAGUES

Baylor College of Medicine

Behavioral features of Fragile X include cognitive impairment, hyperactivity, attention deficits, social isolation and anxiety, and autistic behaviors such as gaze avoidance. FMR1 knockout mice exhibit several of the physical and behavioral characteristics of the human syndrome.

In this study, Dr. Paylor and colleagues analyzed social behaviors in male Fragile X mice. Although many tests did not reveal differences between Fragile X and control mice, they did see a difference using a tube test of social dominance. In this test, a Fragile X mouse is placed at one end of a tube and a control mouse is placed at the other end. Both mice enter the tube and meet somewhere in the middle; the one who backs out “loses” the match, having ceded territory to the other mouse. Fragile X mice won significantly fewer matches than wildtype littermates, suggesting an impairment in social interaction.

This test offers a simple, easy way to try out potential drug or genetic therapies in mice before considering testing them on people.

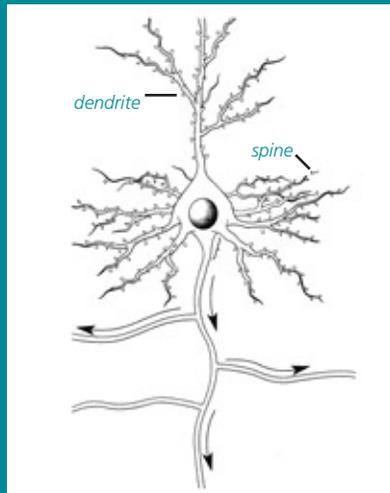
Supported by FRAXA



Rich Paylor

Anatomy of a Neuron

Neurons (brain cells) have branches – dendrites – which have spines where synapses form to make connections with other neurons.



Prolonged Elevation of Serum Glucocorticoid Levels in Fragile X Knockout Mice after Acute Stress

**A.C.BECKEL-MITCHENER,
J.D.CHURCHILL, S.KIM,
C.M.ESTRADA, W.T.GREENOUGH**

Univ. Illinois, Urbana



Andrea Mitchener

This group has examined the mechanism underlying the heightened anxiety that affects most people with Fragile X syndrome. Recent studies have reported that cortisol levels are increased in patients with Fragile X following a stressful event and that this elevated cortisol level fails to return to baseline as quickly as in unaffected individuals.

Dr. Greenough and colleagues have been studying the Fragile X mice and have discovered that, like people with Fragile X, cortisol levels are higher following a stressful event (physical restraint) and take longer to return to baseline. They were looking especially at the hippocampus, an area of the brain that is important in regulating the stress response.

These data suggest that the hypothalamic-pituitary-adrenal (HPA) axis is improperly regulated in Fragile X patients and in the Fragile X knockout mouse. The reason may be that FMRP is required for the proper expression of the glucocorticoid receptor and, perhaps, other proteins involved in the stress response pathway.

Supported by FRAXA Research Foundation and Kiwanis International

Stress-Induced Changes in BDNF and C-FOS Cortical Expression are Altered in Fragile X Mutant Mice

**E.RAMIREZ; G.FOWLER;
C.M.GALL; J.C.LAUTERBORN**

Univ. of Calif., Irvine



Julie Lauterborn

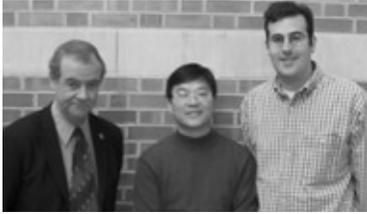
Dr. Julie Lauterborn received a FRAXA grant this year to study the effects of a new Ampakine compound in Fragile X mice. In this presentation, her group demonstrates that Fragile X mice have an exaggerated hormonal response to stress, as do children with Fragile X. They have quantified the stress response difference. This provides more evidence that the HPA hypothalamic-pituitary-adrenal axis is dysregulated in Fragile X syndrome. The HPA axis is an area of intense interest among psychiatrists and endocrinologists, so this may attract new researchers into the Fragile X fold.

Supported by UC Davis MIND Institute

r e s e a r c h

Cerebral Cortical in Vivo Expression of FMRP, but not of FXR1P, is Elevated Following Housing in a Complex Environment

A.W.GROSSMAN, S.H.KIM, K.EDGAR, B.J.DEGRUSH, S.A.IRWIN, I.J.WEILER, W.T.GREENOUGH



Bill Greenough, Im Joo Rhyu, Aaron Grossman

Univ of Illinois, Urbana

Previous studies have suggested that FMRP expression is increased in visual cortex and the motor cortex of rats following experiences that induce structural plasticity (i.e. learning).

Twelve young-adult male rats were housed in a cage of toys whose arrangement became increasingly complex across 20 days of housing. Tissue from these rats was compared with that from littermates housed individually in standard laboratory cages. Rats exposed to the complex environment showed significantly greater FMRP expression in the cortex compared with individually caged rats. Thus FMRP appears to increase its expression in neurons as a result of exploring and learning, tasks which are associated with the development of new synapses. This highlights the key role of the Fragile X protein in the learning process.

Supported by FRAXA Research Foundation, NIMH, NICHD, Kiwanis International

Regulated RNA Binding of the Fragile X Mental Retardation Protein

R.B.DENMAN, N.DOLZHANSKAYA, Y.SUNG

New York State Inst. for Basic Res. Dev Disabilities and Columbia Univ

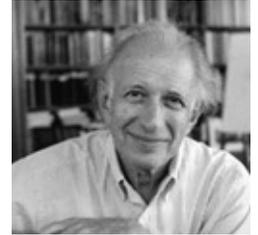
Dr. Robert Denman previously received a grant from FRAXA to study the molecular targets of FMRP. Recently, Dr. Denman has been examining how FMRP's messenger RNA (mRNA) targets are altered in Fragile X syndrome, in turn leading to the clinical and behavioral features of the disorder. In this presentation, the team defines ways in which FMRP is regulated in brain cells. There are several mechanisms by which proteins are turned on and off within cells; these so-called post-translational modifications work in concert with each other to regulate when and how proteins bind to target mRNAs (which contain the codes to produce other proteins). Dr. Denman's team presents a model signaling mechanism by which FMRP normally regulates its interaction with its target mRNAs; this model can explain how some symptoms of Fragile X arise.

Supported By The Research Foundation for Mental Hygiene, NY

Characterization of Fragile X and Other Classes of RNA Binding Proteins in Somata and Neuronal Processes of Aplysia

ERIC KANDEL AND COLLEAGUES

Columbia University



Eric Kandel

Dr. Eric Kandel, who won his Nobel prize just after starting Fragile X research with a FRAXA grant, has been studying proteins that enable learning and memory in the lowly sea slug, aplysia. Dr. Kandel's team has identified dozens of RNA-binding proteins that facilitate synaptic plasticity (the basis for learning and memory) in these slugs. One of these proteins is apFXRP, the slug's equivalent to the human Fragile X protein. The researchers have cloned six alternatively spliced forms of apFXRP, all of which are found in the slug's neurons, and they find that the apFXRP mRNAs can be transported to neurites (developing extensions of neurons which reach out to communicate with neighboring neurons). This is strikingly similar to FMRP in mice, suggesting that further studies will shed light on the function of the Fragile X protein in humans.

Supported by FRAXA, Howard Hughes Medical Institute, NINDS, NIMH, McKnight Foundation

Speaking of mice...

One of the most popular stops at the Neuroscience Annual meeting (aside from FRAXA's booth) was the Neuromice booth because they gave away fuzzy little toy mice. The Neuromice.org folks generously provided us with mice, causing an extraordinary increase in traffic at our booth.

We are currently designing FRAXA Knockout Mice for our booth at next year's meeting, so if you have an idea for a great mouse, let us know!

In Vivo Rates of Cerebral Protein Synthesis are Increased in Fragile X Knockout Mice

M.QIN, J.KANG, C.B.SMITH

Lab. of Cerebral Metabolism, NIMH, Bethesda, MD

Much recent basic research has focused on how the Fragile X protein regulates mRNAs and proteins, because some of these are likely to be involved in related disorders like autism and because some might prove to be useful targets for treatments. An unresolved question is whether FMRP suppresses the translation of other proteins. The aim of this study was to find out whether FMRP suppresses protein translation in the brain in live animals. They measured rates of cerebral protein synthesis in male

u p d a t e .

Fragile X knockout mice and control mice. In all 53 brain regions examined, rates were increased by 5-30% in the Fragile X mice (which lack FMRP). This finding is consistent with the hypothesis that FMRP's role is to suppress of mRNA and protein translation in the brain in live animals.

Funded by NIMH

Ultra High Voltage Electron Tomographic Examination of Selectively Stained Dendrites in Fragile X Mice

J.D. CHURCHILL, I.J. RHYU, M.E. MARTONE, H. MORI, N. YAMADA, M. TERADA, M.H. ELLISMAN, W.T. GREENOUGH

Univ of IL, Urbana, and Osaka Univ, Japan

Human autopsy studies have reported increased density and length of dendritic spines in Fragile X individuals. Recent work has shown similar pathology in Fragile X mice. The present study used ultra high voltage electron microscopy of cortical and hippocampal neurons to confirm and extend previous work. This study confirms that the average length and density of spines are greater in

Fragile X mice than in control mice.

Pruning dendrites is a normal part of human development which occurs throughout life. This and other studies suggest that pruning doesn't happen as efficiently as it should in people with Fragile X. This contrasts with many brain disorders in which cells actually die.

Supported by NIH/AG, NIH/NCRR and FRAXA

STEM CELL TRANSPLANTS GENERATE FMRP IN THE MOUSE MODEL OF FRAGILE X

L.K.K. PACEY, M.M. AXFORD, L.C. DOERING

McMaster Univ., Canada

Neural stem cells have exciting implications for the potential treatment of many nervous system disorders. This team is studying the cellular characteristics and the behavioral effects of FMRP replacement via stem cell transplants in the mouse model of Fragile X Syndrome. Stem cells were isolated from normal mice and cultured to generate large numbers of neurons which produce FMRP. These neurons were then injected into the hippocampus of FMR1 knockout mice. The researchers are currently using a maze to test learning and memory in the mice at various time points after transplantation. These experiments represent the first attempts to replace FMRP by stem cell therapy and test the corresponding functional effects.

Supported by The Fragile X Research Foundation of Canada

RESEARCHERS' CORNER

Last issue, we reported that several antibodies are now available at the University of Iowa Developmental Studies Hybridoma Bank (www.uiowa.edu/~dshbwww/), and that FMR1 knockout mice were being distributed. There has been continued progress:

Mice

Neuromice.org is a consortium of three sites, Jackson Laboratory, Northwestern University, and the Tennessee Mouse Genome Consortium, established by NIH to enhance genomic and genetic tools for neuroscience research by creating new mutant mouse models for neurological/behavioral disorders. The primary goal of

Neuromice.org is to be a research resource center that maintains, characterizes, and, most especially, distributes these mouse lines to interested scientists. Neuromice.org is an initiative funded by six NIH institutes, led by NIMH. FRAXA thanks Dr. Steven Moldin, ... at NIMH, Dr. Joseph S. Takahashi, Director of the Neuromice consortium, and Dr. Martha Hotz Vitaterna at Northwestern University for agreeing to distribute a different strain of FMR1 knockout mouse (C57). These mice should be available to interested scientists within six months.

In addition, Jackson Laboratory will begin distributing the FMR1 knockout mice (on a sighted FVB background) available in the next few months. To check the status of this model, visit <http://jaxmice.jax.org/jaxmice-cgi/jaxmicedb.cgi> and enter Stock #4624.

MPEP for Pre-Clinical Studies

FRAXA has available a supply of the selective mGluR5 antagonist, MPEP, for donation to investigators who wish to test its effects in the FMR1 mouse or other models of Fragile X. The MPEP was synthesized by "Technically, Inc." of Woburn, MA, and has been validated by several labs.

Family Visits

Investigators, fellows, and students researching Fragile X in the lab have gained tremendous insights by meeting children who have the disorder. Descriptions of the fragile X phenotype in the scientific literature can't convey how these children think, behave, and interact. Many FRAXA families across U.S. would enjoy visiting with scientists.

Call Katie Clapp at FRAXA, (978) 462-1866 or kclapp@fraxa.org

FRAXA Fall Fling 2003 Highlights

Raising Awareness and Funds for Research

October 5th, 2003, marked the second annual National Fragile X Research Day, established by FRAXA and endorsed by Congress in 2002. To celebrate, families hosted events around the country and raised a total of more than \$470,000! These funds will enable FRAXA to support more of the new research proposals that will arrive on December 1st.

The key goal of FRAXA Fall Fling is to increase participation: the more events we can hold across the country, in as many states as possible, the better chance we have of getting national media attention for Fragile X.

In addition to the people featured here, we want to thank Cathy Reid and the Piecemakers, who made and auctioned quilts at their Clewiston, Florida church, and Heather and Philip Lopina, whose July barbecue raised both awareness and funds for research.

We are also grateful to Mary B. Porterfield and her family. Mrs. Porterfield passed away this year, and part of her estate was donated to FRAXA in order to support research to help improve the lives of adults affected by Fragile X.

New York: Cocktails in Soho

Elaine Stillerman and Paul Solotaroff hosted a wonderful party and auction at the Soho art gallery loft of their friend, Leor Sabbah, raising over \$12,000. The day after the party, *Men's Journal* published Paul's article about life with his son, Luke, who has Fragile X. Since the story came out, Paul and Elaine have been featured in the media, including MSNBC and the New York Times. The article has been nominated for an award, and Fragile X support groups across the country have been requesting reprints. You can read it at FRAXA's website, www.fraxa.org.

New York: Oldies Dance

Fran Gibb and friends and family recruited a chef from the CIA (that's the Culinary Institute of America) for a dinner and oldies dance in the Bronx. The turnout was terrific, the party raised over \$4,000 and plans are already in the works for next year!

Massachusetts: Evening at the Harvard Club

Boston's Fall Fling was a festive evening hosted by Randy and Chuck Welch. The star of the show was Harvard alum and auctioneer Mo Pratt, whose jokes had everyone in stitches as the bidding prices for basketballs and other sports memorabilia topped \$1000. The evening raised almost \$15,000 and warmed us all up for Boston's upcoming 10th Anniversary FRAXA Gala. In addition, Randy Welch's sister, Jerri Pratt, organized the second annual FRAXA Fun Run at the Bradley-Palmer State Park, raising another \$2800 for research.

Maryland: Fragile X Golf Classic

The Maryland Fragile X Resource Group hosted a September 15th tournament at Bretton Wood golf club in Potomac, Maryland. It included a golf clinic by pro golfer, Fred Funk, a luncheon, the tournament itself, a silent auction, and a dinner and live auction. Thanks to the hard work, careful planning and creativity of chairs Mark and Marla Gruzin and the energetic assistance of Michael and Lisa Kelley, as well as a great crew of volunteers, the event netted \$40,000 for research and an additional \$40,000 for the upcoming International Fragile X Conference in Washington, DC. Many thanks to the Gruzins and the Kelleys and all of the members of the Maryland group who made this event successful and fun.

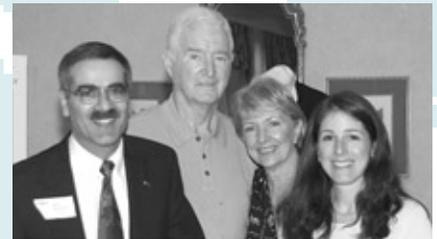
Maine: Barn Sale

FRAXA thanks Julie and Eric Gosselin, Julie Wilson, Tim and Cheryl Peterson, Julie Follett, and their friends for organizing a tremendous barn sale and bake sale which raised \$1000! Maine's Fall Fling was featured in the Portland newspaper as well as local papers, educating thousands about Fragile X.

Ohio: 2nd Annual Irish Night

Judith Maloney and friends raised over \$6,500 at an evening of Irish beer, good food, and dancing ... all of this while Judith was in the midst of moving to a new house!

Ohio – Fragile X Alliance's 7th Annual Golf Benefit



Ara Bagdasarian Herb & Nancy Score, Honorary Chairpersons, Leslie Bagdasarian

On Monday, July 14th, 2003, the Fragile X Alliance of Ohio held their 7th Annual Golf Benefit at Shaker Heights Country Club. It was a landmark day for the Alliance and FRAXA. After a day of golf, dinner guests joined the golfers for cocktails, appetizers and a Silent Auction that was a sports fan's delight. For the dinner program, the "First Down Toward a Cure" video was shown highlighting FRAXA and researchers working on Fragile X. The segment about Jake Porter brought tears to the eyes of everyone in the audience.

The live auction was conducted in humorous broadcast style by special guest, Doug Dieken (former Cleveland Browns player & current radio

Will you host a Fall Fling event in Fall 2004? If we can organize more than 30 events around the US, the collective impact of that many events, small or large, will help us entice the media to feature stories about Fragile X. This year, we did not have enough events to attract their notice.

All events are welcome ... yard sales, bake sales, letter campaigns, runs, walks, bike rides, dinner parties in your home, children's events, pizza parties, bowling tournaments. Need help? We have "To Do" recipes for each type of fundraiser and a list of other parents who have run similar events. We can supply brochures, ideas, and even a FRAXA Files CD with a large collection of resources for volunteers.

Fall Flings

announcer). Returning Honorary Chairpersons Herb & Nancy Score were on hand to meet guests as well.

The highlight of the evening came when Ara Bagdasarian invited the Chairman & CEO of his company, TravelCenters of America (TA), up to the podium. Mr. Ed Kuhn announced that TravelCenters would donate \$25,000 each year for 4 years to FRAXA. It was also announced that the First Data/Western Union Foundation would match TA's contribution, totaling \$200,000 to FRAXA over the 4 years!

In summary, \$100,000 from the 2003 benefit proceeds was donated by the Fragile X Alliance of Ohio to FRAXA and an additional \$50,000 was donated by TravelCenters of America and First Data/Western Union Foundation.



Ed Kuhn, Chairman and CEO of TravelCenters of America announces surprise donation to FRAXA to Ara and Leslie Bagdasarian

The event committee thanks the many Fragile X Alliance of Ohio family members, friends, and the staff at Conferon, Inc. who helped make this event possible and a huge success. If anyone would like a copy of our program or has any questions, please email Leslie Bagdasarian at fraxohio@adelphia.net.

New York: First Annual Fragile X Summer Gala

Ron and Amy Watkins and their family and friends held their first annual dinner gala with silent and live auctions. Best-selling author Mary Jane Clark attended and shared with the guests her experiences as a mother faced with this disorder. Mary Jane's publisher, St. Martin's Press, donated copies of two of her books ("Do You Want To Know A Secret" and "Close To You") for all guests to take home with them. Actor Dan Grimaldi, best known for his role as Patsy Parisi on the HBO series, "The Sopranos" was a rousing speaker, challenging each person to spread awareness to speed the process of finding a cure. The gala was at a country club nestled in the pristine hills of



Niklas Watkins

the Mid-Hudson Valley of New York. At the end of the evening, \$32,000 was raised for FRAXA! For the Watkins, the evening meant much more than the funds. The love and support of their family, friends and other families affected by Fragile X made the evening one of the best of their lives. "For the first time since Niklas' diagnosis, I felt like I was making a difference," said Amy Watkins. "No one could have prepared me for the high I felt that night. Both Ron and I felt we had finally been given the opportunity to share with those around us the importance of finding a cure and how they too could help, just by raising awareness."

Can you imagine playing 136 holes of golf in one day? Now imagine accomplishing this feat on a rain soaked August day. That is exactly what Mike Behan did. Mike is the head golf professional at The Woodstock Golf Club in Woodstock, New York. Behan became aware of Fragile X syndrome when Niklas Watkins was diagnosed nearly four years ago. Niklas is the five year old son of Ron and Amy Watkins.

"Mike called me in the spring to let me know he wanted to play as many holes of golf in one day as he possibly could and attract individuals and businesses to sponsor him on a per hole basis," says Ron. The Watkins never dreamed he could play 136 holes in about eleven hours. When the day concluded, Behan had raised \$5,000. A great deal of awareness was also raised as Behan talked about FRAXA to anyone who would listen.

"Words cannot express how much we value the friendship of Mike and his wife Stacy. This event was their idea and they made it happen," says Ron. The Watkins would also like to thank Elizabeth Spinelli at The Woodstock Golf Club for their donation as well as making the golf course available for the day.

The Watkins have already reserved The Links at Union Vale for the second annual gala on July 31, 2004. They have committed to holding this fundraiser until a cure for Fragile X is found. When *that* happens, they plan to host a party celebrating the hard work and dedication of all families affected by Fragile X.

Philadelphia Reaches for the Stars

On October 8, Cristy Hollin and friends and family held their fourth Philadelphia Fragile X Fundraiser, themed Reach for the Stars. The evening was a huge success, thanks to the tireless efforts of our wonderful Chairs, Robin and Jerry Batoff. Over 250 people turned out to show their support. Upon arrival, each guest was handed a magnetic twinkling star and greeted by two beautiful fairies sprinkling stardust. The song, *When you Wish upon a Star* played over a loud speaker as guests milled about the silent auction, which featured over 270 items.

Guests were treated to a touching video presentation and a live auction. The live auction

included a cruise, trips, visits with Oprah and the Good Morning America Show, a chance to play basketball with Aaron McKie of the 76ers and more! We sold beautiful *Reach for the Stars* jewelry and baseball caps throughout the night, and raffled a trip to Bermuda.

In the end, our hard work paid off and we raised over \$170,000 for Fragile X Research! We gratefully thank Saks Fifth Avenue for sponsoring a pre-event patrons' fashion show and The Children's Boutique of Philadelphia for hosting Fragile X Day, where a portion of the day's proceeds went to Fragile X Research. Finally, we owe our success to our wonderful committee and to all the children who sold raffle tickets at the Gladwyne Super Fresh before the event.



Roger Mudd, Mary Higgins Clark, Michele and Jim Cox

Pittsburgh Gala

This year Pittsburgh was the host city for FRAXA's 6th Annual Mary Higgins Clark Gala. Several hundred old and new FRAXA friends enjoyed an evening of hors'doevres, dinner, dancing and a silent auction at the elegant Omni William Penn ballroom. All were there to support Fragile X research. Honorary chair Mary Higgins Clark added style and grace to the event. We very much appreciate her lending her time to FRAXA. Master of Ceremonies Roger Mudd entertained the audience with his humor and kept the program running quickly and smoothly.



McKayla and Christopher Cox

After dinner, many saw the video, Fragile X, First Down for a Cure for the first time, and there was not a dry eye in the house! We

applaud Debbie Stevenson for producing this incredibly powerful and touching video. Katie Clapp and Dr. Michael Tranfaglia gave exciting updates on the tremendous strides researchers are making towards a potential treatment for Fragile X. Senator Arlen Specter received the Beacon of Light Award for his support of Fragile X Research. We were also

thrilled to give Pittsburgh Steeler Tommy Maddox the first ever Children's Champion Award for his commitment to the advancement of children and his support of FRAXA. Tommy was a true champion, offering insightful comments and staying at the party throughout the night. Pittsburgh's two major newspapers made the gala their cover stories for their society sections, and Pittsburgh's Whirl Magazine also covered the evening. We all felt like celebrities as flash bulbs flickered across the ballroom. Best of all, we could feel the extraordinary warmth and kindness that filled the room. It was one of those rare evenings when everyone seemed to temporarily put aside their personal lives and join together for the good of all affected by Fragile X. It was a night we will always remember, and we would like to thank all who were there in body and spirit.

-Michele and Jim Cox

Nebraska Fall Fling

The community of Scottsbluff gathered together to raise funds for FRAXA at the Scottsbluff Country Club on October 2nd. It was incredible evening. Special guests included Mary Jane Clark, Dr. Mike Tranfaglia, and Dr. Robert Pasternack, Assistant Secretary, Office of Special Education and Rehabilitative Services. Kelley and Ryan

Randels also attended from Omaha, NE. along with their son Cody, who has Fragile X. Kelley is the facilitator of the Omaha Fragile X Support Group. Our two sons, Jack and Jacob were in attendance as well. Excellent coverage was provided from the local newspaper, the Star-Herald. KSTF and KDUH, the two



Jacob and Jack Massey and Mary Jane Clark
photo credit : Roger Holsinger/Scottsbluff Star-Herald

local TV stations, provided television coverage. The evening featured a last-minute silent auction, which was organized after the paper (to our surprise) announced we were having one. What a blessing that was in the end! People who read about it on the front page news came forward and offered items to auction. Sandy Gutwein and her daughter Ashley pulled it all together in less than 48 hours. Items included Denver Bronco tickets, Husker football tickets, Papa Murphy's pizza (one a week for a year), an original painting and a homemade quilt which was donated the day of the event. There were over a dozen items and the auction raised \$2700!

Fifteen event sponsors contributed a large amount of the money raised and more than 150 people attended. The evening can be summed up by an ancient proverb: "A mirror reflects a man's face, but his heart is revealed by the friends he keeps." Our small Western Nebraska community of Scottsbluff demonstrated its love for others by raising \$70,000 for FRAXA Research Foundation. We are humbled and grateful for this overwhelming support and thankful that we live in such a caring community.

- John, Megan, Jack and Jacob Massey

Update from the National Fragile X Foundation

Members of the NFXF will soon be receiving their Fall 2003 Foundation Quarterly newsletter with a special 9th International Fragile X Conference section – including information on our Advocacy Day on Capitol Hill. If, by chance, you're not a subscriber, the conference registration form and related information can be found at www.FragileX.org under the "Conferences & Events" button on our home page. If you didn't heed the call in the last update, please mark your calendars now for June 23-27, 2004 in Washington, DC. We are glad to answer any of your questions about the event, so call us at the number below. The new newsletter also announces our latest project called, "Beyond the I.D.E.A: Adolescents and Adults with Fragile X". Thanks to private seed money, the NFXF will bring together parents, and experts on developmental disabilities and Fragile X who have developed an expertise regarding adolescents and adults and the problems associated with those age groups. One of our objectives is to produce free and user-friendly materials that parents can share with teachers, therapists, employers, group home staff, doctors, etc. These materials will encompass the areas of behavior, communication, medication, counseling, sexuality and other issues that have been identified as problematic for those with Fragile X. We welcome your input.

Robby Miller, Executive Director

1-800-688-8765 or NATLFX@FragileX.org

The National Fragile X Foundation, PO Box 190488, San Francisco, CA 94119

What is it like to Parent a child with Fragile X?

Editor's note: Julie Adams of Wisconsin wrote this note on the FRAXA listserv to help a student who needed information for a school project. You can join the listserv at www.fraxa.org

I applaud the person who came up with the idea of a report on Fragile X Syndrome!!! I'll try to sum up for you, in a few short sentences, what Fragile X Syndrome means to me.

Anything a parent might know about child rearing goes right out the window. Raising a child with FX begins with relearning everything we think we know or did raising our other children. As a parent or sibling of a person with FX, you must work daily on becoming more tolerant, develop the patience of a saint and pretty much become selfless or at least greatly control your own emotions.

You face an entire community of health professionals, educators, neighbors, friends and family,

who do not understand why you do what you do for your child with FX. The general belief is that the child's problems have much to do with your parenting skills, or lack thereof. I have spent 11 years, fighting 3 different school districts to assure my daughters basic safety issues while at school.

My daughter with FX has very limited access or understanding of what life is like compared to her peers. She can't stand loud or unusual noise levels, so she doesn't go to dances, malls, roller rinks, etc., Just being in school is stressful for her. She's not aware of clothing styles, hair/makeup issues. Her best friends are her stuffed animals.

It is very difficult for her to learn. She needs much repetition (months, years) to learn any academics. She will probably never drive a car,

although she thinks she will when she turns 16, she will not go to college or have a career (she wants to be a fire fighter), she will probably not marry or have children (she has a 50% chance of passing on the gene that causes FX, nor could she care for a baby or husband)!

She is the most loving, compassionate person I've ever known. Her sense of humor frequently has me in stitches. While I may feel she is far too sensitive or naive, her desire and will to fit in with the rest of the world, inspires me and gives me meaning and purpose. Parenting a child with Fragile X Syndrome must certainly be one of the hardest tasks on the face of the earth.

Thank you for coming here to get the information you need for this most important topic. Do us all a favor by writing an excellent report!

G R O W I N G T H E T E A M

How you can Help

There are many ways you can help accelerate progress towards effective treatments and a cure for Fragile X. We are now raising money to fund grant applications that will arrive on December 1st. Grant decisions are made in just two months with the help of our scientific advisors, so your money will go to work right away.

Four Stars for FRAXA!

FRAXA has received a 4-star rating from Charity Navigator, the largest independent evaluator of charities in the United States. Receiving four out of a possible four stars indicates that FRAXA excels, as compared to other charities in America, in the area of strong fiscal management. Visit www.CharityNavigator.org on the Web for a nice set of charts rating specific aspects of our organization. Guidestar, www.Guidestar.org, is another site with further details.

Donate a Car



The nonprofit Cars4Charities (www.cars4charities.org or 866-GIVE-4-US (448-3487)) is more efficient than the other groups we have worked with. They will pick up your car, give you a receipt for tax purposes, sell the car, and give over 75% of the sale price to FRAXA.

Combined Federal Campaign

Only 1 in 10 charities qualifies for the Combined Federal Campaign, the nationwide workplace giving campaign for federal employees, and FRAXA is one of them! If you or someone you know works for the government, the post office, or the military, FRAXA's CFC number is 0220.

FRAXA Video

"First Down Towards a Cure"

You can get the new FRAXA movie on video or DVD for \$10. This 11 minute movie features the Bolling family, researchers, Mary Higgins Clark, and Jake Porter, the Ohio high school student with Fragile X whose touchdown inspired stories on TV and in magazines and papers across the country.

FRAXA Gift Memberships

Do you have friends and family members who would like to receive our newsletters? A gift membership to FRAXA is only \$25. Simply call, email or send a note in the mail with the names and addresses of your guest members. The more members we have, the more power we have when we meet with government officials in Washington. Each member is a voice in support of Fragile X research.

FRAXA Holiday Gifts:

Great gifts that promote awareness of Fragile X!



FRAXA T-Shirt

Heavyweight 100% white cotton shirt with the teal

FRAXA logo on left chest. Available in sizes M,L,XL,XX, XXL **\$15**

FRAXA Lapel Pin

Gold-plated "X" **\$10**



FRAXA Umbrella

Pop-up umbrella with white FRAXA logo. Choose from gray, navy blue, or burgundy **\$10**

You can send your order along with a check, or call us at (978) 462-1866 with a credit card number, or order these gifts online at www.fraxa.org

FRAXA RESEARCH GRANTS AND FELLOWSHIPS

Deadlines: May 1 and December 1 each year

FRAXA offers fellowships and grants to encourage research aimed at finding a specific treatment and ultimate cure for Fragile X syndrome:

- Postdoctoral fellowships of up to \$35,000 each per year
- Investigator-initiated grants for innovative pilot studies aimed at developing and characterizing new therapeutic approaches (no funding limit)

FRAXA is particularly interested in preclinical studies of potential pharmacological and genetic treatments for Fragile X and studies aimed at understanding the function of the FMR1 gene. A special RFA has been issued; see www.fraxa.org for details.

FRAXA UPDATE

EDITOR: Katie Clapp, MS

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FRAXA Fall Flingers!

DESIGN: Mary Lou Supple

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FRAXA would like to thank Networx of Newburyport, MA for hosting, at no charge, the FRAXA website and email.

FRAXA 10th Anniversary Spring Galas

**Boston, Thursday, May 20th, The Four Seasons Hotel
with Mary Higgins Clark and Boston Area Celebrities**

Chaired by Harry and Jaime Manion

**Omaha, Thursday, May 6th
Mary Higgins Clark FRAXA Gala**

Special Guests Elieen Naughton and Senator Chuck Hagel

Chaired by Kelly Randels, Diane Hamsa, Carol Parsow, Bob and Sheila Gerhman,
and Cindy McGowan.

Fragile X in the Media

Luke Solotaroff, 6, has Fragile X. Read Luke's story in the November issue of **Men's Journal** ("Me and the X-Man" by his father, Paul Solotaroff). If you missed the magazine issue, you can still read this article online at www.FRAXA.org or call us for a copy.



PLEASE HELP

FRAXA

in supporting research aimed
at treatment for Fragile X

FRAXA is a national 501(c)(3) tax-exempt organization. Every penny you donate goes to research: FRAXA has specific grants to cover all overhead. Supporters receive this newsletter and are welcome to participate as active volunteers.

Yes, I would like to help FRAXA

- o Member (\$25+)
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