

Clinical Trials of Fenobam Have Begun!

FRAXA Research Foundation and Neuropharm, a British specialty pharmaceutical company (www.neuropharm.co.uk), are working together to explore the potential of *fenobam* to treat Fragile X and autism. Fenobam is a compound which reduces mGluR5 activity, which is known to be overactive in Fragile X.

Fenobam was developed in the 1970s for anxiety disorders. It was given to hundreds of people in clinical trials with a good safety record; however, fenobam was never marketed and is now off-patent. No one knew how fenobam worked in the '70s; two decades later, scientists discovered that fenobam blocks mGluR5 – making it of great interest to the Fragile X research community.

Neuropharm secured US Orphan Drug Designation for fenobam in early 2007. In November '07, Neuropharm submitted an Investigational New Drug (IND) application to the FDA to gain permission to conduct human trials in the United States. A month later, the FDA gave Neuropharm the green light to start human trials.

An initial Phase I fenobam trial in healthy volunteers in Nebraska was successfully completed in January.

Fenobam is now being tested in an initial Phase II study in adult males and females with Fragile X. This study is being conducted by Dr. Randi Hagerman at the UC Davis MIND Institute and Dr. Elizabeth Berry-Kravis at Chicago's Rush University. Since mGluR5 antagonists have not been given to people with Fragile X before, this first study uses a single dose of fenobam. The outcomes of this very short-term investigation will determine the feasibility of longer-term studies with fenobam in Fragile X.

Robert Mansfield, Neuropharm's CEO, commented: "We are delighted to announce the commencement of this clinical study in Fragile X Syndrome. The work of FRAXA and researchers such as Dr. Mark Bear has highlighted the potential of mGluR5 receptor antagonists such as fenobam for this patient group. Professors Hagerman and Berry-Kravis are world leading experts in the clinical study of Fragile X and their trial of this targeted treatment is a milestone for those affected by Fragile X Syndrome."

For updates on this program, please sign up for email news at fraxa.org or visit the websites ClinicalTrials.gov or neuropharm.co.uk.

"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



**THANK YOU FOR FRAXA'S
BEST YEAR EVER!**

**EVENTS, PICTURES AND
DETAILS**

See page 8

Dan Grimaldi, of "The Sopranos," and Reiko Aylesworth, of "24", at FRAXA's New York City Gala

Meet FRAXA's
New
Honorary
Board
Members

See page 6

RESEARCH ADVANCES

Correcting Fragile X in Mice

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Scientists have reversed key symptoms of Fragile X in mice by reducing the amount of a single protein in their brains. The protein is mGluR5 – a prime target for developing new drugs to treat Fragile X, and possibly autism, in humans.

MIT researchers led by Dr. Mark Bear, along with Dr. Sumantra Chattarji, of India's National Center for Biological Sciences, published their study, "Correction of Fragile X Syndrome in Mice," in the December 20, 2007 issue of the journal *Neuron*. It was partially funded by FRAXA, which has supported the work of Dr. Bear and colleagues at MIT every year since 2000 and also funds Dr. Chattarji. The study received worldwide media attention because of the possibility that it could help unravel the



mysteries of autism.

The findings support the theory that Fragile X Syndrome stems from too much activation of one of the brain's chief network managers – the metabotropic glutamate receptor mGluR5. People with Fragile X lack a single protein, FMRP. This study found that FMRP and mGluR5 are at opposite ends of a kind of molecular seesaw. They keep each other in check, and without FMRP, mGluR5 signals run rampant.

The scientists were able to correct symptoms of Fragile X in Fragile X knockout mice. These mice lack FMRP and therefore have runaway mGluR5 activity. Using genetic engineering, the researchers created Fragile X mice that also lacked one of the

THE mGluR THEORY OF FRAGILE X

People with Fragile X lack a protein called Fragile X Mental Retardation Protein (FMRP). In the brain, FMRP normally regulates the action of a neural receptor (a kind of protein) called mGluR5. FMRP and mGluR5 keep each other in check, like a molecular seesaw.

Without FMRP, as in Fragile X, the mGluR5 receptor becomes overactive, resulting in an overproduction of various proteins that ultimately disrupt normal brain function and learning. This has become known as the mGluR theory of Fragile X.

two copies of the gene for mGluR5, and therefore had only half the normal amount of mGluR5 expressed in their brains.

"We decided to reduce the mGluR5 levels by 50 percent to reflect what might be a therapeutically relevant condition that would be achievable with carefully titrated drug treatment," said Bear. "Total knockout of mGluR5 has deleterious effects, whereas reducing it by half is innocuous."

Like many humans with Fragile X, mice lacking FMRP have seizures, impaired memory, and accelerated early body growth.

FRAGILE X KNOCKOUT MICE

To create a mouse model for Fragile X Syndrome, researchers have bred a knockout mouse which lacks the gene (FMR1) encoding FMRP. These mice lack FMRP, and they show several characteristics of Fragile X in people: changes in neuron structure, seizures, and learning impairments.

But when mGluR5 was diminished in the Fragile X mice, these problems went away.

Reducing mGluR5 also reversed additional brain abnormalities in mice. The total rate of protein synthesis, normally excessive in the brains of Fragile X knockout mouse, was reduced to normal levels. With less mGluR5, the brain of each mouse no longer formed excessive neuronal connections. The mice did not have the high density of dendritic spines that is characteristic of Fragile X Syndrome.

In this study, researchers used genetic engineering to reduce mGluR5, but the same thing could be accomplished by a drug. Pharmaceutical companies have already developed experimental mGluR5 antagonists, like fenobam, and clinical trials in Fragile X patients are underway (see page 1).

These findings may also lead to further targets for drug discovery, since scientists are now investigating drugs which affect other elements of the brain's mGluR pathway. It should be possible to identify biomarkers – substances which can be measured in the blood – which can identify changes in the function of the mGluR pathway in people with developmental disorders. Biomarkers may enable us to identify people with autism and related disorders who do not have Fragile X, but do have abnormalities in this pathway. It is likely that these individuals would respond to many of the treatments now being developed for Fragile X.

Pictures: Dr. Mark Bear; Dr. Sumantra Chattarji

Where Are We Now?



By Michael Tranfaglia, MD

Basic research funded by FRAXA has greatly enhanced our understanding of Fragile X. The field has now progressed to the point where multiple treatment strategies are being pursued by clinical researchers and pharmaceutical companies around the world. Translational and preclinical research projects funded by FRAXA have demonstrated the efficacy of potential treatments in Fragile X animal models, and human trials are beginning with several of these agents.

A KEY DISCOVERY

The most exciting discovery yet is that excessive mGluR5 signaling is a major cause of Fragile X syndrome. Compounds in development by some pharmaceutical companies can block mGluR5, and these drugs (mGluR5 antagonists) have been shown effective in Fragile X animal models. This has not gone unnoticed by the pharmaceutical industry: several companies have decided to develop mGluR5 antagonists for Fragile X.

TOWARD CLINICAL TRIALS

The first company to announce a drug development program for Fragile X was Seaside Therapeutics (see page 4). Next, Neuropharm, a British company, announced that they would develop fenobam for Fragile X, in collaboration with FRAXA (see page 1). Perhaps most promising of all, two large pharmaceutical companies are currently consulting with FRAXA about possible trials of their advanced mGluR5 antagonists in patients with Fragile X. Stay tuned for further information.

AVAILABLE TREATMENTS

Armed with detailed knowledge of the cellular defects causing Fragile X, researchers have also identified available drugs which can help restore normal function.

Lithium, an available agent widely used in psychiatry, has been shown to reverse many features of Fragile X in fly and mouse models. Clinical trials in children and adolescents with Fragile X were conducted last year by Dr. Elizabeth Berry-Kravis at Rush University in Chicago, funded by FRAXA. Results in this small open trial were promising; a paper detailing the results is expected to be published soon, and larger-scale placebo-controlled trials are being considered.

In addition to lithium, FRAXA-funded investigators have found that the available drugs baclofen, taurine, and minocycline all demonstrate therapeutic efficacy in Fragile X animal models. FRAXA is currently helping to organize clinical trials of all three. These medicines have long histories of safe use in people.

IMPLICATIONS FOR AUTISM

Several drug classes currently under investigation may make a real difference in the lives of children and adults affected by Fragile X. But they may do even more. Since many people with genetically unrelated autism spectrum disorders appear to have defects in the same cellular pathways, many cases of non-Fragile X autism may respond to the same treatments. With continued advances, we believe that the research FRAXA is supporting will ultimately help millions of people around the world.

NEW DRUGS: FROM LAB TO MEDICINE CABINET

The U.S. system of new drug approval is the most rigorous in the world. It takes 12 years on average for an experimental drug to travel from lab to medicine cabinet. 1 in 1000 compounds that enter preclinical testing make it to human testing. Of those, only 1 in 5 make it to the market.

The Food and Drug Administration (FDA) requires three phases of clinical trials before approving a drug:

PHASE I

Involves a small number of healthy volunteers who take the drug to gather information about drug absorption and metabolism, effects on organs and tissues, and side effects at different doses.

PHASE II

The drug is given to a few patients with the specific disease or problem being studied, to learn how effectively the drug can treat disease and to identify short-term side effects.

PHASE III

Involves larger numbers of patients. These studies include treatment and control arms, to seek the benefit/risk relationship of the drug, uncommon and long term side effects, and labeling information.

PHASE IV

Takes place after the drug is approved and on the market; large numbers of patients are followed to ensure the long-term safety and effectiveness of the new drug.

The Orphan Drug Act aims to speed up development of treatments for diseases which affect 200,000 or fewer U.S. residents, like Fragile X. The FDA granted an Orphan Drug Designation to Neuropharm for the use of fenobam to treat Fragile X, so the time required for developing this and other Fragile X treatments could be somewhat shortened.

RESEARCH ADVANCES

WHY FIND MORE TARGETS?

Until a perfect cure for Fragile X is found, effective treatments may consist of drug combinations tailored to individual patients. A drug which works wonders in one child may trigger allergies in another. It will be helpful to have alternative medicines available in cases like this, so FRAXA is pursuing a variety of promising treatment targets as they emerge from basic research projects.

Seaside Awards \$4.5 Million to Vanderbilt University for Targets

Seaside Therapeutics, a biotechnology company based in Cambridge, MA, was founded in 2005 by Dr. Mark Bear, Dr. Randall Carpenter, and others to translate research discoveries into treatments for patients with autism, Fragile X, and other disorders of brain development. FRAXA has been working with Seaside since its inception.

Seaside has licensed a set of mGluR antagonists from Merck, and one of these compounds, STX107, has been shown to reverse Fragile X symptoms in animal models. Seaside is now working to advance STX107 into human trials.

In the meantime, scientists at Vanderbilt University Medical Center, in Nashville, TN, have identified more than 400 other compounds which – like STX107 – inhibit mGluR5. Vanderbilt's high-throughput screening facility can test tens of thousands of small molecules for drug-like activity in a single day.

With the new \$4.5 million award from Seaside, Vanderbilt researchers will use medicinal chemistry, molecular biology, and pharmacology studies to develop compounds that have the properties required for drugs to be used for further study in Fragile X.

"Selectively inhibiting mGluR5 to treat Fragile X is an innovative idea and, with continued success, has the potential to change the way people think about developmental disorders," said Dr. Jeffrey Conn, Director of the Vanderbilt Fragile X project and a member of Seaside's Scientific Advisory Board.

As promising candidate drugs are identified, Seaside Therapeutics will select compounds to carry forward into clinical development for Fragile X. This way, if STX107 does not make it successfully through the drug pipeline (see page 3), alternatives will be ready.

Another Treatment Target: PAK

An international team of researchers, led by Nobel Laureate Dr. Susumu Tonegawa and partly funded by FRAXA, has corrected some symptoms of Fragile X in mice by blocking a normal enzyme called P21-activated kinase, or PAK.

The report appeared in the *Proceedings of the National Academy of Sciences* in July 2007.

Fragile X is caused by lack of a protein, FMRP, which affects dendritic spines – tiny structures on the surface of brain cells (neurons) that enable cell-

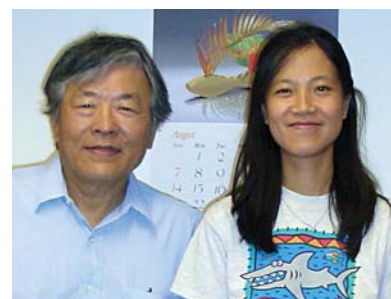
to-cell communication. In Fragile X mice and people, dendritic spines become too long, spindly, and overabundant, which muddies cell-to-cell communication. This has been thought to be the major underlying reason why these patients show behavioral abnormalities," said Dr. Tonegawa.

Like FMRP, the protein PAK also affects the number, size and shape of dendrites – but in the opposite direction. The researchers noticed that when they blocked PAK in the brains of otherwise normal mice, the dendritic spines in these mice became short and thick, and fewer were formed. The mice also had abnormally low levels of electrical signaling.

So the scientists bred mice with both the Fragile X gene mutation and a defective form of PAK with a time-bomb: three weeks after the mice were born, their PAK levels dropped dramatically. A few weeks later, the researchers found that Fragile X symptoms, including excessive movement and difficulty completing memory tasks, were greatly reduced in the mice. When they looked at the mouse brains, the dendritic spines appeared almost normal.

While such genetic manipulation would not be possible in human children, a drug that decreases PAK could potentially treat Fragile X. The fact that the researchers could reverse Fragile X features by reducing PAK well after birth (3-week-old mice are teenagers in human terms) suggests that such a treatment would be helpful even for young adults.

No safe, effective PAK inhibitors are currently available for human use, but several pharmaceutical companies are developing compounds. PAK inhibitors could possibly treat other diseases as well, such as neurofibromatosis (NF) and even arthritis, so FRAXA is actively pursuing these leads.



Pictures (clockwise): Dr. Susumu Tonegawa and FRAXA Postdoctoral Fellow Dr. Mansuo Hayashi; Dr. Kimberly Huber; Dr. Jennifer Ronesi

NEW RESEARCH FUNDED

to be announced in the next newsletter

Report from Washington

Mechanisms Of Fragile X Uncovered

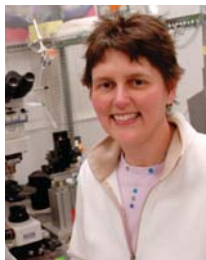
FRAXA-funded researchers at the University of Texas Southwestern Medical Center are uncovering how brain cells are affected in Fragile X.

“I think we’ve discovered a core mechanism underlying Fragile X Syndrome,” said Dr. Kimberly Huber, assistant professor of neuroscience and senior author of a study which appeared in the *Journal of Neuroscience* on January 9th. FRAXA Postdoctoral Fellow Dr. Jennifer Ronesi is the study’s first author.

Dr. Huber’s research with mice focuses on how Fragile X affects communication between cells in the hippocampus, a brain region that is involved in learning and memory. The scientists investigated a protein, called Homer, which serves as a kind of structural support for the glutamate system. Glutamate is the most common neurotransmitter in the brain; brain cells use it to pass signals to neighboring cells.

In Fragile X, the Homer–glutamate support system is abnormally disconnected. Dr. Huber’s group discovered that this results in an inability of brain cells to make new proteins important for learning and memory.

“These results show that Homer plays a vital role making proteins and learning, so it may also indicate where we could target drugs,” Dr. Huber said.



Advocacy Works!

Federal government agencies fund half of all medical research. Thanks to determined and dedicated advocacy by families and friends across the United States, federal funding for Fragile X research has grown from \$1 million to over \$20 million annually in the past decade.

With this increase in spending, and with recent significant advances in understanding Fragile X, comes a growing need to coordinate future funding. More than a dozen government agencies contribute to Fragile X research, and navigating this maze has become difficult for researchers. To address these needs, the Trans NIH Fragile X Research Coordinating Group has been created.

Over the past ten years, the Fragile X community has educated members of Congress about Fragile X. In each of the past three years, Congress has directed NIH to increase and coordinate research efforts related to Fragile X and associated disorders. The 2008 Senate Committee Report on Labor-HHS-Education Appropriations includes this language:

“...urges the NIH, through the NICHD and other participating Institutes, to convene a scientific session in 2008 to develop pathways to new opportunities for collaborative, directed research across Institutes and to produce a blueprint of coordinated research strategies and public-private partnership opportunities for Fragile X.”

The Trans NIH Fragile X Research Coordinating Group has been created in response to this congressional directive. Thanks to the efforts of Dr. Tiina Urv, who is in charge of Fragile X research at NICHD, an impressive eight NIH institutes are participating in the Coordinating Group, along with representatives from other federal agencies, scientists, and advocacy groups. Three working groups; one each for Fragile X Syndrome, FXTAS, and Premature Ovarian Insufficiency, have been formed to identify priority areas of research and obstacles and opportunities. The end result will be a report to Congress which will be available to the public.

We are optimistic that this new initiative will speed future research efforts and foster productive interactions within the NIH and throughout the Fragile X community.

TRANS NIH FRAGILE X RESEARCH COORDINATING GROUP

NIH MEMBERS

NICHD, NIMH, NINDS, NIA, NIDDK, NIGMS, NIDCD, NCI

OTHER FEDERAL AGENCIES

HRSA, CDC, FDA, Department of Education

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FRAXA Welcomes Honorary

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DORIS BUFFETT

Doris Buffett is the founder, funder, and president of the Sunshine Lady Foundation, which has been called “uniquely hands-on, folksy, a person-to-person enterprise – the un-foundation.” Its mission, “to provide opportunities for the advancement of education, well being and new life choices for disadvantaged people,” is rooted in the mid-western values instilled in Doris by her father, Howard Buffett and shared by her brother Warren. In 2007, the Sunshine Lady donated \$500,000 to FRAXA, followed by a \$1.5 million matching grant for a total of \$2 million! “I decided to get involved with FRAXA because I was so inspired by what the parents and relatives were doing. They were thinking outside the box, had unlimited energy, and had the smarts to get things done.” Doris attended high school with Roger Mudd and is a longtime friend of Mary Beth Busby.



JIM CANTORE

If you've watch The Weather Channel during a hurricane, you've seen Storm Tracker Jim Cantore leaning into pounding winds and rain.

Jim's passion for field reporting during extreme weather events is well known. He is known for his ability to "break down" complicated weather events into terms that everyone can understand. Jim is also a parent; his children Christina and Ben are both affected with Fragile X. He is a dedicated and passionate spokesperson for FRAXA; his Public Service Announcement is viewable on YouTube and FRAXA.org and has aired on cable television stations along the east coast.



Board Members

FRAXA has created an Honorary Board to recognize people who show tremendous dedication to FRAXA. These individuals give generously of their time, resources, and efforts to further FRAXA's mission of finding a cure for Fragile X.

MARY HIGGINS CLARK

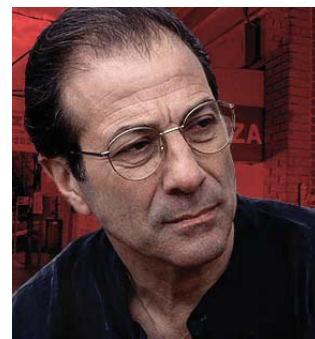
Mary Higgins Clark's fame as a writer was achieved against heavy odds. Born and raised in the Bronx, her father died when she was eleven. Later, left a young widow when her husband had a heart attack, Mary went to work writing radio scripts and decided to try her hand at writing books. Every morning, she got up at 5 AM and wrote until 7 AM, when she had to get her five children ready for school. Now Mary Higgins Clark's suspense novels are world-wide bestsellers.

Mary's involvement with FRAXA began in 1997 when she rocketed the fledgling parent group into a powerhouse for Fragile X research by pledging \$1 million in support over five years. Since then, she has appeared at FRAXA events across the country. Mary's grandson David has Fragile X.



DAN GRIMALDI

Dr. Dan Grimaldi is an actor known for his roles as twins Philly and Patsy Parisi on the HBO TV series, *The Sopranos*. He also played mother-fixated pyromaniac Donald 'Donny' Kohler in the 1980 slasher film *Don't Go in the House*, and has appeared in several episodes on *Law & Order*. He voices 'Frank' for the bestselling computer game *Mafia*. While he is often cast in "tough-guy" roles, in real life Dan holds a Ph.D. and teaches college mathematics and computer science in Brooklyn, New York. Dan became involved with FRAXA many years ago when he attended a gala in New York City; he has been a loyal supporter ever since and always looks forward to appearing at FRAXA fundraisers.



JAMES DENTON

Born in Nashville, Tennessee, James Denton graduated with honors from the University of Tennessee at Knoxville, snagging a degree in advertising as a television/journalism major on the way out the door. Although he spent the next four years selling advertising, Jamie's heart was already in another place, and he headed to Chicago to try his hand at acting full-time. On October 3, 2004, *Desperate Housewives* garnered incredible ratings with its debut episode, with Jamie Denton starring as Mike Delfino, the world's sexiest plumber. Three months later, Jamie was included in *People Magazine's* 2004 Sexiest Men Alive issue. Jamie was the star attraction at FRAXA's recent gala in Atlanta. He was introduced to FRAXA by his childhood friend and FRAXA's newest board member Michael Scott, whose son Morgan has Fragile X.



ROGER MUDD

Roger Mudd has been a newspaper and television reporter for more than 50 years, beginning with *The News Leader* in Richmond, Virginia, CBS News, NBC News, *The MacNeil/Lehrer Newshour* on PBS and finally with *The History Channel*. He is the recipient of five Emmies for his work at CBS, including "The Selling of the Pentagon" in 1972 and "Teddy" in 1979. He has also been a visiting professor at Princeton University and Washington & Lee University. His memoir, *The Place to Be/Washington, CBS and the Glory Days of Television News*, was published this Spring. Roger and his wife E.J. are longtime friends of Mary Beth and David Busby and their sons Jack and Robert, both of whom have Fragile X. Roger has served as Master of Ceremonies at FRAXA galas in many cities, including Boston, Chicago, and Washington, DC.



FRAXA is a grass-roots organization founded in 1994 by parents and still run by parents. FRAXA's mission is to find effective treatments and ultimately a cure for all children and adults with Fragile X.

2007 was FRAXA's best year ever, with over \$5 million raised – more than double any previous year. Doris Buffett, founder of The Sunshine Lady Foundation, challenged FRAXA with a \$500,000 matching grant. Thanks to the outpouring of support from families and friends everywhere, FRAXA far surpassed the challenge. When we raised over \$1.5 million, Ms. Buffett matched every dollar! This means new research, new clinical trials, and new determination to find a cure.

The Sunshine Lady Foundation's Challenge motivated the Fragile X community to dramatically increase fundraising and awareness activities. It has been an exciting time and we are sincerely grateful to Ms. Buffett and to each of you!

The X Ball New York, NY



L to R: Craig Chesley, Debbie Stevenson, David Gregory, Reiko Aylesworth, Eileen Naughton



Katie Clapp, Mary Higgins Clark



Mark Bear, PhD, Jeffrey Stevenson

Debbie and Jeffrey Stevenson, along with Eileen Naughton and Craig Chesley, hosted an extraordinary gala at New York City's Gotham Hall. Special guests included NBC's David Gregory, CNBC's Sue Herera, researcher Dr. Mark Bear, and actors Reiko Aylesworth (from the hit series "24") and Dan Grimaldi (from "The Sopranos"). Over \$800,000 was raised.

4th Annual Walk Canton, IL

More than 315 people raised \$20,000 on April 21st, walking in honor of Parker and Allison Roos, including families from DeKalb, Malta, Washington, Pekin, LeRoy, Plainfield, Cambridge, Bushnell, Peoria, Mackinaw, Lewistown, Farmington, and Canton.

5th Annual Botox Benefit Grand Blanc, MI

Jennifer and Dr. Kimball Silvertan host a benefit each year, and this was the most successful one yet, netting \$8500 for FRAXA.

Golf Tournament London, England

Andrew Neill and friends at the Ealing Golf Club near London raised \$10,000 on May 26th. Andrew and his son Stuart cooked Bar-B-Q all day, feeding all the teams before the rain set in.

Red Tent Reading Group Benefit Miami, FL

Members of Temple Beth Or's Red Tent Reading Group contributed to FRAXA in honor of Marty Gammon's son, Josh.

Pool Party San Diego, CA

Cindy de Gruchy and the Fragile X Center of San Diego hosted a Splash for Cash party in June, raising \$4700 for research.

Picnic South Dartmouth, MA

Thanks to the encouragement of Lisa, Joanne, and Seth Thomas, when Castello Realty hosted their annual picnic to benefit children's causes on July 15th, they selected FRAXA as one of the beneficiaries. Owners Jose and Joe Castello presented a check for \$10,000 to FRAXA.



Buffett Challenge

Charity Poker Tournament

Port Aransas, TX

Across the country on July 15th, CeCe Drake and her four sisters, Shelley, Maren, Katie and Cindy, hosted a poker contest for FRAXA. The Drake sisters have established the organization Fragile X Awareness for Central Texas (FACT, at www.fxsfacts.com).

Fragile X Golf and Dinner

Solon, OH

Ara and Leslie Bagdasarian hosted a golf tournament, dinner, and auction on July 16th. Mary Beth Busby was the featured speaker. This event – the 11th for the Bagdasarians and the Fragile X Alliance of Ohio – raised over \$250,000!

Baseball Game

Montclair, NJ

Three days later, Denise Sabo and her friends and family sold tickets to a New Jersey Jackals game and organized a barbecue for FRAXA.



Standing: Jose S. Castelo, Joe Castelo, Jen King, Alzira Castelo, Lisa Thomas, Tom and Leslie Bowbrowski, Paul Pires. Seated: Maryann Castelo, Sophie and Elijah Bowbrowski, Seth Thomas (with the biggest smile!)

Comedy Shows

Peoria, IL

Comedians Paul and Storm celebrated Fragile X Awareness Day at the Jukebox Comedy Club in a weekend-long FRAXA benefit ending on National Fragile X Awareness Day, July 22nd. Holly Roos organized the event.



←
Jason and
Brandon Welch

Mt. Rainier's Strongest Man

Summer, WA

Hosted by Laurie Bowler of Rainier Crossfit and held at The Old Cannery on July 21st, this contest featured a yoke race, overhead log press, deadlift, bus pull, stone loading, and a farmers walk medley.

Blue Ridge Mountain Ride

Laurel Springs, NC



Mikey Charleton at the Stations Inn Bike Run

Stations Inn ran their annual motorcycle poker run to benefit FRAXA through the Blue Ridge Mountains of North Carolina on July 21st. Riders passed through four states, picking up one card of a poker hand in each stop along the way. They raised over \$6,000.

Bike Run

New Castle, DE

FRAXA's Delaware chapter raised over \$29,000 on National Fragile X Awareness Day, July 22nd, with a motorcycle run. Jen Nardo, Cynthia Worthington, Angela and Matthew Ross, and others hosted a BBQ, live band, silent auction and kids activities.

Pizza Party Fundraiser

Vandalia, MO

The next day, Mike and Carol Schambach hosted their first event ever: a Pizza Hut fundraiser. Carol's family and friends waited tables and local businesses donated door prizes.

Comedy Night

Saugus, MA

Guests enjoyed the antics of four comedians and a special appearance by Mo Pratt at Prince Pizza, on August 2nd. Hosted by Randy and Chuck Welch in honor of their sons, this will be an annual summer event.



FRAXA Office Manager
Melissa Budek and
Alex Doss

Unlimited All-Stars Summer Nationals

Staley, NC

Kart racers from all over the USA met on August 11th in Staley, North Carolina for the Annual Unlimited All-Stars (UAS) Summer Nationals. The races were hosted by the North Carolina Unlimited All-Stars under the direction of Gil Atkinson. Another race to benefit FRAXA is being planned for 2008.



Katie Clapp, the Dog Pound racing club (Hot Dog, Rabid Dog, One-Eyed Dog, Diggity, Dog-daze Dog)

NetWitness Ride for Kids

Chantilly, VA

This motorcycle ride was hosted by the company NetWitness, also on August 11th. Thanks to Jim Charlton and his son, Mikey, Dana Walsh, and the entire organizing team, the ride raised over \$10,000 for FRAXA.

Motorcycle Ride and Auction

New Gloucester, ME

Julie Gosselin and the Maine Fragile X Resource Group organized this ride through the Lakes Region of Maine on August 25th. They raised over \$1500 for FRAXA.

FUNDRAISING

Pole Dancing Contest

Los Angeles, CA



The contestants

Barbara Bott organized this fundraiser at Soul Tree Motion studio on September 2nd. Overheard during the dance: "send your inherent, powerful, female energy to FRAXA!"

Birthday Party

Irvington, NY

Maddy and Wendy Cohen raised \$92 for FRAXA at a 60's-themed party on September 8th at the home of Risa Wells, Israel Perlson and their daughter, Ariana. Maddy & Wendy are the 10-year-old twin cousins of Julian Berg, who has Fragile X, and the daughters of Judy & Alan Cohen. They set up a booth to display FRAXA brochures, magnets, bracelets, and a balloon dog named "Fraxy."

Birthday Party

Montclair, NJ

Shobha Swaminathan threw a birthday party for her son Abhi on September 8th; guests gave donations in lieu of gifts. Later, Shobha also hosted a jewelry party to raise funds.

Golf Tournament

Uxbridge, MA

Gordon Cole and family organized their 2nd annual golf tournament at the Blissful Meadows Golf Club on September 9th, with help from Jack Cashman.

Cash For a Cure Concert

Asheville, NC

Buddy, Carol, Jamie and their Vintage Band performed songs of Johnny Cash, June Carter and the early stars of country. The September 29th concert was hosted by Dr. Kate Gregory.

Buffett Cup Gala

Marblehead, MA

FRAXA raised \$200,000 at the Corinthian Yacht Club on October 4. Honored guests were Doris Buffett, Storm Tracker Jim Cantore, Boston News Reporter Kelly Tuthill, and Roger Mudd. Special thanks go to Mary Lou Supple, Becky and Sasa Zorovic, Leslie and Trevor Eddy, and Liz and Jason Mazzola.

Cocktail Party/Silent Auction

Grandview, OH

Judith Maloney and friends raised over \$20,000 with "The Sun Shines on Fragile X Blues." The band Delta Sheiks performed, and the entire Ohio State University gymnastics team was there as volunteers on October 6.

BarBQ

Omaha, NE

The same day, Sheila Gehrman and the Fragile X Association of Nebraska hosted a western dinner in Omaha – Doris Buffett's home town. The festivities raised over \$20,000.

Atlanta Answers the Buffett Challenge

Atlanta, GA

Elly and Michael Scott hosted An Exceptional Evening Benefiting Fragile X Research at the Sweetwater Brewing Company Headquarters

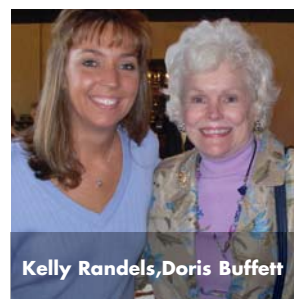


The crowd at An Exceptional Evening in Atlanta; Jamie Denton talking with Teri Hatcher

on October 6th, featuring James Denton who plays Mike Delfino, the world's sexiest plumber, on Desperate Housewives. They raised over \$150,000!

Luncheon

Omaha, NE



Kelly Randels, Doris Buffett

Diane Hamsa hosted an October 7th luncheon featuring Doris Buffett. They raised over \$15,000.

Marathon

Portland, OR

Further west, Nancy Gurman and Lauren Vitalie ran the Portland Marathon, raising funds in honor of Lauren's son Grant and goddaughter Allison Eddy (who is also board member Leslie Eddy's daughter).

Surprise Birthday

Southbury, CT

Jen Weitz threw a surprise birthday party for her husband Jonathan. She asked the guests to make donations to FRAXA in lieu of gifts.

Fragile X Dinners

Yorktown Heights, NY

Nancy Pitcher hosted a dinner and candle light party, and a letter campaign, raising funds in honor of her son Ryan. Nancy's friend Lisa Vanderwerker arranged an evening for Fragile X at a local restaurant; the turnout was so good that the chef called to say he'd never before seen a fundraiser like it!

Coin Toss

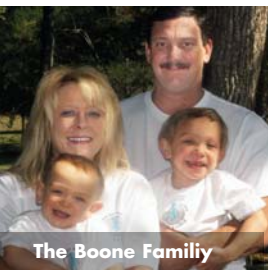
Ypsilanti, MI

In honor of the 43rd birthday of Ted Coutilish – associate vice president of Marketing and Communications at Eastern Michigan University – one of Ted's staff, Meaghan Britton, organized a Coin Toss for Fragile X at Chavez Fountain on October 10 at the Ypsilanti, Michigan campus. Mary Beth Langan and Ted Coutilish's only child, six-year-old Andrew, is affected by Fragile X.

Luncheon and Fashion Show

King of Prussia, PA

Conquer Fragile X Foundation and Cristy Hollin held a show at Neiman Marcus on October 11th, in honor of her son Matthew. They raised over \$67,000 for FRAXA.



The Boone Family

Disc Golf Tournament

Yadkinville, NC

April and Randy Boone hosted this tournament in honor of their son Tyler. They raised over \$6,200.

5K Run/Walk

Cumberland, RI

The October 14th run/walk was hosted by Leslie and Tom Bobrowski and the Rhode Island Family Group; runners included Laura Tranfaglia, Becky Zorovic, and Shorta and Freddy Yuasa.



Joanne & Lisa Thomas, Kerri Hayes, Janice Murphy, Missy Shelley, Leslie Bobrowski

Dream Dinners Fundraiser

San Antonio, TX

The dinner, hosted by Laura Moodie, raised over \$1,500. Also, the 80 teachers at the Bob Beard Elementary School raised \$686 through a Jeans for Genes Day – including Laura.

Jeans to Work Day

Deptford, NJ

Gavin Christopher Gray's mom, Stacy, and colleagues at E. Greenwich Township Schools raised funds by wearing jeans to work.

Bake Sale

Grandview Heights, OH

Maddy Whitley, a student at Grandview Heights High School in Ohio, held a bake sale in honor of Liam and Nolan Maloney.

Gala and Fashion Show

Newport Beach, CA

Andrea Shelly's elegant gala and stunning La Perla fashion raised almost \$250,000.

Fall X Ball

Poughkeepsie, NY

This year, Amy and Ron Watkins raised over \$50,000 at their annual event. In attendance were author Mary Jane Clark, whose son David has Fragile X, and actor Dan Grimaldi.

More Notable Events

Jodi Lancaster held a charity night at Max and Emma's in honor of her children Erin and Alec.

Lisa Haran mailed over 130 letters to friends and family to raise funds.



Laura Tranfaglia

Elissa Boory approached friends and families everywhere, raising over \$62,000.

Kelly Broxterman and her sister sold bracelets in honor of Kelly's daughters Danielle and Amber

and her sister's son Mitchell.

Alan Cohen raised over \$125,000 toward our goal, thanks to his colleagues and friends.

Lois Odom of Venice, FL, raised funds with the help of friends at the Trinity Presbyterian Church of Venice.

The football team at LeRoy High School, along with team members from five other high schools, walked door to door to raise money in honor of Abraham Zeleznik, two-year-old son of Amy and BJ Zeleznik.

Alan Parsow of Omaha passed out envelopes left and right, garnering over \$150,000 of donations to FRAXA.

Dean and Stefanie Clark asked friends for donations in honor of their son Lucas. Tom and Linda Leonard matched every dollar.

Madeline Larsen of Oceanside, NY wrote that as a result of the efforts of four women knitting scarves, they raised \$490 in honor of Ryan Pitcher.

To enter the Tri-County Mall "Magical Evening of Giving" for an after hours shopping gala, shoppers paid Wendy Rollinger of Mason, OH a \$5 donation to FRAXA.

The Virginia Fragile X Resource Group and Michelle Rocker, President, raised dollars and awareness at the "Voices for Fragile X" a capella benefit concert on September 29th.

Lauren Padgett, President of LucasWorks in Magnolia Delaware has pledged to FRAXA 10% of the price of LucasWorks Fragile X Syndrome bracelets sold at her website www.lucasworks.org.

"RAP" of Akron, Ohio, a Single's Discussion Group, held a silent auction on Labor Day. All proceeds were sent to FRAXA by Kristine Atwood.

Dawn Cook, Holly Roos' sister, along with her mom, 2 sisters, and an aunt sold butterbraided frozen pastries and raised over \$1,000 for FRAXA. Dawn writes "how easy it was for the five of us to make a difference."

Thanks to the Buttinger Family, founders and operators of Camp Hillcroft in Billings, NY, the campers voted to support FRAXA and proudly donated some of the proceeds of the Hillcroft's Children's Festival Carnival.

Jack Greenfield celebrated his Bar Mitzvah in August '07; as part of his mitzvah, Jack donated 10% of his gifts to FRAXA.

Melissa and Darren Courtney participated in the Cincinnati Flying Pig Marathon in May '07. Bruce Jackson was their designated runner. Sponsors raised money for FRAXA.

Special Thanks to...

Mary Lou Supple, Richard Colburn, Barry Zamelsky, Barbara Gerber, Carol Burton, Denis and Kira Schmulder, Melissa Morrison, Carrie and Andy Nardelles, Melissa and Robert Shelley, Ethel Rosenblatt, Elaine Stillerman, Deb and Vern Gillan, Cynthia and Brian Casey, the Pessler family, Mary Beth and David Busby, Brian Silver's family and friends, Richard Coe, and Nancy and Jim Hertzog. Thanks also to those who contributed in loving memory of Michael Gerber and John Bodman. Thanks to Patrick Vershbow's Pals, who had planned on 10 annual basketball tournaments but are now planning their 12th! Most of all, sincere thanks and apologies to those we whom we've not mentioned here due to lack of space....

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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 below 7%, one of the lowest of all charitable organizations. Supporters receive our newsletters, email updates, 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+)

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