

FRAXA UPDATE

SUMMER 2001

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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

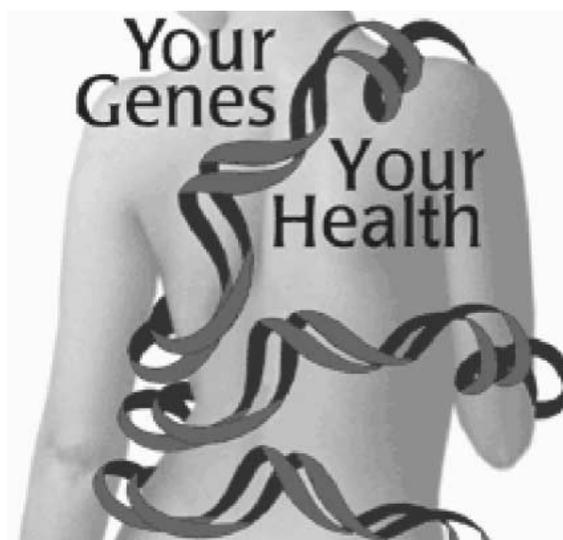
ever has."

— Margaret Mead

NEW RESEARCH FUNDED

In June, FRAXA's Board of Directors voted to award 10 grants and fellowships for cutting edge projects that will bring us closer to finding effective treatments and a cure for fragile X. Much of the research focuses on the fragile X protein, which is lacking in people with fragile X syndrome. Why is this protein so important to learning and memory? Are there ways to compensate for it, or bypass it? These are key questions that investigators are working to answer.

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New Fragile X Website

The DNA Learning Center at Cold Spring Harbor Laboratory has created a new web-based guide to fragile X. Called *Your Genes, Your Health* (vector.cshl.org/ygyh), this interactive site uses a wonderful variety of animations and videos. Cartoons demonstrate how the FRAXA genetic mutation shuts down the fragile X gene so that it cannot produce its normal protein. Dr. W. Ted Brown explains how fragile X is diagnosed and how it can be inherited through

families. Dr. Vicki Sudhalter describes educational strategies and medications that can help reduce anxiety and other common symptoms of fragile X. Dr. Esther Nimchinsky discusses her research aimed at understanding the fragile X protein. FRAXA parents Debbie Stevenson, Mary Lou Supple, Katie Clapp, and Mike Tranfaglia share coping strategies and 9-year-old Laura Tranfaglia talks about what it's like to have a brother with fragile X.

Because this multimedia site requires a fast Internet connection, FRAXA and the DNA Learning Center have also created a CD-ROM version, which is available from FRAXA free upon request with any new donation. (To get the CD, just call or send in a note with your next donation.)

Also in this issue:

- Report from Washington
- Fragile X Awareness Day
- Fundraising Events

The CD-ROM includes the entire DNA Learning Center fragile X site and current FRAXA publications: *Medication Guide for Fragile X*, *Fragile X - A to Z*, *Unlocking Fragile X* video, brochures, and a set of *FRAXA Update* Newsletters. The CD works on PC and Macintosh computers.

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 2000 males and 1 in 4000 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.

FRAGILE X AWARENESS DAY:

Last year, the Senate declared July 22nd to be National Fragile X Awareness Day. This year, we set a goal: to persuade newspapers, radio and TV stations, and municipalities around the world to feature fragile X. Here are a few highlights. If fragile X received publicity in your area, please send it in so we can share the good news in our next newsletter.

... ON VOICE OF AMERICA

On July 23rd, *Voice of America* featured a 1-hour segment on fragile X. Voice of America's daily call-in talk show *Talk to America* is broadcast on radio, TV, and the Internet at www.voa.gov/talk and reaches an international audience of 80 million people! Thanks to Executive Producer Irina Burgener and her husband Robert Burgener for facilitating this broadcast.

... IN CLEARFIELD, UTAH

Martha Mathews writes:

I am thrilled to report that July 3 is Fragile X Day in Clearfield, Utah! A City Councilman asked me why more people were not aware of fragile X. I was asked to give a brief presentation. I presented as much as I could about FRAXA and why its mission is so important to all Americans.

You should receive the original copy of the Proclamation soon. I know that the research will pay off. But the road is a hard one. I am so thankful that many scientists have teamed up with FRAXA. That alone tells the story!

... IN BUFFALO, NEW YORK

Lisa Kowal writes:

I decided that I wanted to try to make a long term difference for my son by raising money for FRAXA. I sent a request to my County office for an "Erie County Fragile X Awareness Day," which was approved! Friday, July 20, 2001 will be the day. I also requested that we be permitted to

hold a fundraiser in the building where I work. It is a large building with thousands of employees and lots of traffic! The Erie County Fragile X Day will give us both the benefit of media coverage and hopefully, an incentive to businesses to participate in a "local" cause.

I then gathered a team of friends together and we mapped out our plan. We will hold raffles at each end of the building, pass out literature on Fragile X and wear FRAXA t-shirts. We have already sent out 80 letters to businesses requesting theme basket donations for our raffle or, if they prefer, a check payable to FRAXA. We will meet our two



Lisa's son Alex Kowal

main goals: awareness and fundraising!

I've decided to establish a FRAXA Chapter here in Western New York. I am grateful for all that the FRAXA team has done to raise funds for Fragile X Research, but think of all that they (we) could raise with each one of us doing a part? Even a small fundraiser when multiplied by many families running one can make a huge difference!

I admit to being a little nervous about this first one since I am new to this, but I am also having a great time doing it. We are already talking about ideas for next year's event!

– Lisa M. Kowal
FRAXA, Western New York Chapter
192 Greenfield Dr., Tonawanda, NY 14150
(716) 694-3030, lisak@buffnet.net

The County of Erie, New York, has issued a proclamation declaring July 20th to be Fragile X Awareness Day. The Erie Proclamation urges "all fellow citizens to support efforts to promote knowledge of the disorder and research projects aimed at treatment. Thank you, Lisa!

Please Consider: Human tissue from people of all ages, donated at the time of surgery or death by people of all ages, or after a miscarriage or pregnancy termination, is a precious resource on which researchers depend. This is not an easy topic to think about, but, for many, there is satisfaction in helping to fight this scourge of our children. You can call Doreen DiMeglio, (800) 847-1539, at the Brain and Tissue Bank for Developmental Disorders in Maryland, or Katie Clapp, (978) 462-1866 at FRAXA to learn more or to register. The MIND Institute in California has a brain bank as well; you can call Dr. Randi Hagerman directly at (916) 734-6348. We will all be working together on this important cause. We would also like to thank Lynne Wolfe for choosing to donate her father's brain to science when, sadly, he died in the spring.

Report from Washington:

by Mary Beth and David Busby

Last year, with your help, the help of other Fragile X advocates, and that of Representatives Delahunt and Watkins, Senators Hagel and Edwards, and other sponsors of the Fragile X Breakthrough Act of 1999, we achieved a landmark victory: passage of the Children's Health Act of 2000.

As you know, among its other provisions, this new law authorized the establishment of at least 3 Fragile X research centers and a loan repayment program to encourage young scientists who conduct pediatric research. The next step is for the Congress to provide funding for these centers and the loan program.

You, your family and friends can help a lot by writing to your Members of Congress (both Senators and your Representative) today asking him or her to support funding for Fragile X research. The sample letter below offers some ideas, but feel free to express your own thoughts.

If you have questions call David Busby at (202 824-8820) or email him at (busby.david@dorseylaw.com).

SAMPLE LETTER:

Date

For Representatives:

The Honorable John Doe
The United States House of Representatives
Washington, D.C. 20515

Dear Honorable John Doe,

For Senators:

The Honorable John Doe
United States Senate
Washington, DC 20510

Dear Senator Doe,

My child (or grandchild, etc.) (name) has Fragile X, the most common cause of inherited mental retardation. Federal financial support for research on Fragile X is authorized in the Children's Health Act of 2000. I am writing now to request your support for an appropriation of at least \$10 million in the fiscal year 2002 Labor - HHS - Education Appropriations Bill.

The Children's Health Act directs the National Institute of Child Health and Human Development to expand, intensify, and coordinate research on Fragile X. It also authorizes the establish-



ment of at least three Fragile X research centers through grants and contracts with public or private nonprofit institutions. To make it possible for health professionals to enter this research field, it authorizes repayment of a portion of their educational loans.

Fragile X is still not well understood, even in the medical profession. Yet it affects one in 2000 boys and one in 4000 girls. One in every 260 women is a carrier. Most children with Fragile X requires a lifetime of special care at a cost of over \$2 million.

Dr. James Watson, Nobel Laureate and discoverer of the DNA Double Helix stated recently: "I became very excited when the fragile X gene was discovered in 1991. It was the first major human triumph of the Human Genome Project. The impact upon affected families rivals that of Down Syndrome. Unlike Down Syndrome, with fragile X there is just one functional protein missing. So we must entice key young scientists now working on nerve cells to focus on fragile X. It has to be a simpler disease to understand and eventually conquer."

Current research efforts hold great promise for the development of safe and effective treatments, but additional support for these efforts is urgently needed. I therefore urge you to do all that you can to provide \$10 million to NICHD for the establishment of Fragile X research centers, and \$2 million to implement the loan repayment program.

I appreciate your attention to this request, and hope I can count on your support.

Sincerely,

Name

Address

THREE NEW FRAXA FELLOWSHIPS AWARDED

Effects of FMRP on Glutamate Receptor Trafficking

ROBERTO MALINOW, PH.D., PRINCIPAL INVESTIGATOR

JULIUS ZHU, PH.D., POSTDOCTORAL FELLOW



Cold Spring Harbor Laboratory; \$35,000

By Julius Zhu and Katie Clapp

When a nerve cell receives a signal from another nerve cell, two things happen:

1. The receiving cell passes the signal on to other cells. The brain is composed of a vast number of cells arranged in a network to receive and process input signals.
2. The receiving cell changes as a result of this experience. In particular, the cell's synapses, where inputs are received, undergo changes. It is now generally believed that the brain learns and remembers things by changing the strength of synapses. People with Fragile X often have difficulty in learning and remembering new knowledge, probably because this mechanism is impaired.

Recent studies suggest that synaptic changes result from the movement in and out of synapses of some proteins known as glutamate receptor proteins. But how is the fragile X protein involved?

Recent research suggests that the Fragile X protein (which is lacking in people who have Fragile X syndrome) regulates the expression of a few important intracellular signaling molecules. Preliminary evidence collected by Dr. Zhu and his colleagues indicates that some of these molecules and their related signaling pathways are involved in controlling glutamate receptor trafficking. Dr. Zhu and his colleagues decided to investigate how these pathways signal the delivery and removal of glutamate receptors in normal mice and then to find out if these signaling pathways are altered in Fragile X knockout mice. (One kind of glutamate receptor is the AMPA receptor, the target of a new class of drugs called AMPAkinases, which are currently being tested in fragile X animals by the Greenough lab, with FRAXA funding.)

Dr. Zhu previously trained in the lab of Nobel prize winner

r e s e a r c h

Dr. Bert Sakmann at the Max Planck Institute in Heidelberg, where the state-of-art multiple whole-cell recording technique was first developed. He is now a postdoctoral fellow in the lab of Dr. Roberto Malinow at Cold Spring Harbor Laboratory. He will combine the multiple whole-cell recording technique with other cutting-edge techniques, including recombinant DNA delivery, and electron and two-photon laser scanning microscopy, to address these questions. The findings of their research may suggest many more molecular targets useful for genetic or pharmacological therapies for fragile X syndrome.

Dr. Zhu's FRAXA fellowship is funded with major support by Tyler Gruzin's friends and family, who believe in his future and are committed to helping find a cure.

Translational Regulation of Fragile X Syndrome Proteins

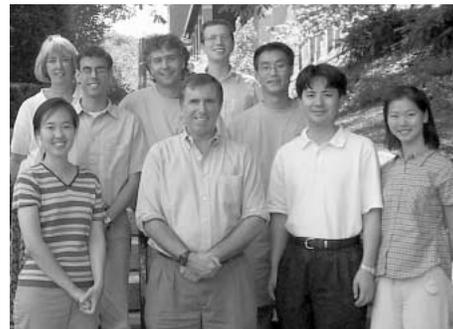
JUSTIN FALLON, PH.D., PRINCIPAL INVESTIGATOR

SANDRA WON, PH.D., POSTDOCTORAL FELLOW

Brown University; \$35,000

By Justin Fallon

Fragile X syndrome is caused by the absence of the FMR1 gene's protein product, FMRP. However, little is known about the normal function and regulation of FMRP or how its loss leads to cognitive impairment. We do know that the translation of RNAs into proteins at synapses (the junctions between nerve cells) is essential for learning and memory. A growing body of evidence suggests a role for FMRP in RNA binding, transport, and/or translation. Intriguingly, FMR1 messenger RNA is present at the synapses and its translation can be stimulated by neurotransmitters. The close relationship between FMRP protein and message and RNA metabolism at synapses provides a pathway to link FMRP function at the molecular level to its role in



update :

GRANTS AND FELLOWSHIPS RENEWED

The following updates were written by Michael Tranfaglia, MD, FRAXA Medical Director

Study of the Synaptic Function of the Fragile X Mental Retardation Protein

CLAUDIA BAGNI, PH.D.

Univ. of Rome; \$28,000; (2000: \$37,000)

Dr. Bagni has developed a promising new method for understanding the translation of the fragile X protein and related proteins in the body and at the synapses of nerve cells. Dr. Bagni is collaborating with several other teams, including Dr. Ben Oostra and Dr.'s Barbara Bardoni and Jean-Louis Mandel, all of whom have received some support from FRAXA.

Restoration of Natural FMR1 Expression in FMR1 Deficient Mice by P1 Artificial Chromosome (PAC) Transgenesis

ROBERT BAUCHWITZ MD, PH.D.

Columbia Univ., \$155,000; (2000: \$90,000); (1999: \$90,000), (1998: \$17,000)

Dr. Bauchwitz's research team is now laying the groundwork for an eventual cure for fragile X by determining exactly which DNA sequences must be present for normal functioning of the fragile X gene FMR1. Most genes (including FMR1) contain far more material than is actually translated into protein, making them very large and hard to work with in their natural state. Dr. Bauchwitz is working to find the minimum functional length of DNA which will replace the defective fragile X gene. This is a first step in developing practical gene therapy for fragile X.

Special thanks to our Research Funding Partner, The Preiser Fund of Long Island, in honor of Jonathan Preiser and in memory of Marilyn Garret. We also gratefully acknowledge Eric Rosen for all he has done working alongside Dr. Bauchwitz. This past year he has been a tremendous help in our quest to reach our goals.

Studies of Synaptic Regulation of Protein Synthesis and Possible Therapeutic Approaches to Fragile X

WILLIAM GREENOUGH, PH.D.

Univ. of Illinois; \$194,000; (2000: \$238,000); (1999: \$136,000); (1998: \$150,000); (1997: \$55,000)

We now know that one of FMR protein's primary functions is to regulate protein synthesis in dendrites (the receiving end of synapses) in response to neural activity; however,

higher functions in the brain. Therefore, an understanding of the translational regulation of FMRP is necessary for understanding the molecular mechanisms leading to Fragile X mental retardation.

We are investigating the molecular mechanisms of activity-induced Fragile X protein synthesis using a combined molecular, cellular and biochemical approach in cultured neurons and in mice. Of special interest is the potential role of a particular process, recently identified in our laboratory, by which synaptic mRNAs are translated into proteins. The mRNAs encoding FMRP and a related protein, FXR2P, contain unique tags indicating that they may be regulated by this process. The overall goal of our studies is to understand the role FMRP plays in translating other proteins and thereby strengthening and/or weakening synapses and, ultimately, enabling learning and memory. Such information could contribute to designing strategies and treatments for overcoming the loss of FMRP in Fragile X syndrome.

Molecular Basis of Fragile X Syndrome

LYNNE REGAN, PH.D., PRINCIPAL INVESTIGATOR

LILI ARAMLI, PH.D., POSTDOCTORAL FELLOW

Yale University; \$35,000

By Katie Clapp

A normal role of the Fragile X Protein, FMRP (which is lacking in fragile X syndrome) is to bind and interact with a number of RNAs (RNAs are direct products of genes) within nerve cells. Presumably these RNAs have important roles, which may be disrupted when FMRP is not present, leading to symptoms of fragile X syndrome. The Regan lab team has been working to identify these RNAs and their functions in the brain. Dr. Aramli will use a combination of approaches to identify the RNA targets of FMRP, to establish their significance in living animals, and to investigate the role of the interaction between FMRP and the RNAs. She will also use a variety of biophysical techniques to understand the mechanisms of these interactions. Understanding these effects may lead to possible therapeutic interventions, even providing information for the design of drugs to rescue some of the normal interactions between FMRP and the RNAs it binds.

this involves many other proteins in a complex biochemical pathway. Some of these other proteins could be valuable “targets” for development of potential therapies involving small molecules (i.e. simple drugs). The Greenough group has been the world leader in precisely delineating this pathway, and their highly productive work continues.

Behavioral Characterization and Therapeutic Interventions in FMR1 Knockout and Transgenic Mice

RICHARD PAYLOR, PH.D.

Baylor College of Medicine; \$110,000; (2000: \$109,000)

Although the fragile X mouse model has been available for several years, it has proven to be surprisingly difficult to pinpoint specific measurable and reproducible cognitive and behavioral differences, compared to normal mice. Dr. Paylor is a leading expert on cognitive and behavioral paradigms in mice, and he has designed an extensive battery of tests to measure the actual differences in fragile X knockout mice.

Unfortunately, the city of Houston, Texas was hit by a terrible flood this spring, and Baylor College of Medicine sustained significant damage to equipment and labs. Dr. Paylor and others at Baylor have done a wonderful job recovering from the storm.

Reactivation of the FMR1 Gene in Fragile X Patients Cells in Culture

GIOVANNI NERI, PH.D.

Catholic Univ., Rome, Italy, \$18,000; (2000: \$32,000); (1999: \$30,000)

Dr. Neri’s group has previously shown that it is theoretically possible to reactivate the FMR1 gene by demethylation and to produce some normal protein, even from fragile X cells with a full mutation. However, the chemical demethylation used for this effect is far too toxic for use in humans, and methylation is a widespread mechanism for regulation of gene expression in all cells, so the potential for harm from non-specific demethylation is too great to allow consideration as a therapeutic option. Dr. Neri and colleagues are continuing their work to identify more specific ways to reactivate the gene, which could be of use in potential therapies.

Transgenic Mouse Model of Fragile X Syndrome: Temporal and Spatial Restriction of FMR1 Expression in Mouse Forebrain

ERIC KANDEL, MD,

Columbia Univ., \$110,000; (2000: \$150,000); (1999: \$150,000)

The fragile X knockout mouse, developed by Dr. Ben Oostra in the Netherlands, has been available for some time; it entirely lacks the fragile X protein throughout its life and displays some symptoms which closely resemble the human fragile X syndrome. While this is a useful model for telling us what the gene does, it cannot tell us some very important things, such as when during development the fragile X gene is used most, or where in the brain it performs any of its several known functions. However, the new technology of conditional knockout mutation allows the gene to be selectively deleted in various brain regions, or turned on and off at will during different stages of development — powerful tools for answering the when and where questions. Nobel Laureate Dr. Eric Kandel is leading this ongoing project; he reports that the conditional knockout mouse has been bred and is now ready for testing.

Transport of the Fragile X Protein and Generation of Monoclonal Antibodies to FMRP, FXR1 and FXR2

ALAN TARTAKOFF, PH.D.,

Case Western Reserve Univ.; \$80,000; (2000: \$93,000); (1999: \$30,000); (1998: \$30,000)

One of the less well-studied functions of the fragile X protein is its role in transporting other proteins and/or mRNAs from the nucleus to the dendrites of nerve cells. Dr. Tartakoff is an expert in studying the nuclear transport mechanisms and is working to define how this process works in the case of fragile X.

Dr. Tartakoff has also received a grant from FRAXA to develop and distribute antibodies to the fragile X protein, FMRP, and related proteins, FXR1p and FXR2p. In the first year of this grant, Dr. Tartakoff has developed three monoclonal antibodies which are now available to other investigators (see article in the **RESEARCHERS’ CORNER**). We are extremely grateful to Dr. Tartakoff for tackling this particular project, because the lack of good, widely-available antibodies has been a bottleneck which has slowed progress in the fragile X field.

Researchers' Corner

This new section of the FRAXA Update is intended especially for researchers. Along with providing direct research grants and fellowships, FRAXA aims to increase the pace of progress by providing opportunities for scientists to interact to benefit from the expertise of others. As Fragile X becomes an ever more highly specialized and complex field, no one person or lab can realistically solve the mystery of fragile X alone. The field will progress ever faster if collaborations flourish and more investigators apply their particular talents and expertise to the challenge. Please email kclapp@fraxa.org to submit an item for the next FRAXA Update.

NEW! Researchers' Fragile X Listserv

Recently, several scientists have suggested that we establish an email exchange for researchers. Accordingly, all investigators, postdocs, and graduate students who are active in fragile X research are cordially invited to join the new FRAX-L listserv, kindly sponsored by Dr. Stuart Brown, Assistant Dean of Students at University of Connecticut, and member of the FRAXA "family."

The goal of the Researchers' listserv is to advance biomedical research by facilitating information exchange, collaborative inquiries, requests for reagents, and so forth. Although fragile X research is a competitive field, recent meetings and many other exchanges have demonstrated that it is also a very collaborative field. We hope that FRAX-L will be a useful tool and that the participants will help to make it successful. All of the families affected by fragile X have so much to gain.

How can this listserv be most useful to the fragile X research community? Discussions might address behavioral/animal models, the roles of FMRP, reagents, protocols, troubleshooting, etc. If it becomes active, it can be divided into topics as time goes on. Whenever possible, we will post announcements of new grants and Requests for Applications that might be of interest.

This Researchers' listserv is a counterpart to the very active general fragile X listserv that FRAXA established in 1995. If there is ever a need for family input or a call for subjects for an experiment, we will be happy to post it to the general listserv, collect responses, and report them back to investigators.

Researchers can join FRAX-L by sending an email to kclapp@fraxa.org Everyone can join the general fragile X listserv at www.fraxa.org/html/listserv.htm

Available: Continuous Performance Task Software

We have designed a computerized Continuous Performance Task (CPT) that I think is quite appropriate for assessing attention and impulsivity in both mental-age-matched typically developing individuals and individuals with fragile X syndrome. I would like to offer it to other researchers who might be interested in measuring such variables. It is based on the classic attention paradigm of two parts: 1) hit the space bar when you see a red square; 2) hit the space bar when you see a red square that follows a blue triangle. The program automatically tallies hits and false alarms and takes about 12 minutes to complete. The use of a D prime statistic will be helpful when covarying out participant's attention on other higher level cognitive tasks. The CPT was written with E-prime software (formerly called MEL), so you may have to buy E-prime.

I want to send this offer out to the community because we spend so much time (and money) designing nifty measures and then a lab in the next town over designs a VERY similar tool, and the next thing you know, we have failure to replicate results. I would love to have more of an exchange of experimenter-designed measures in the community.

Mina C. Johnson-Glenberg, Ph.D.
Waisman Center, 529A
University of Wisconsin - Madison
1500 Highland Avenue
Madison, WI 53705-2280
phone: 608/ 262-6768
fax: 608/ 265-4103
johnsonglen@waisman.wisc.edu

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Researcher's Corner

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Available: Monoclonal Antibodies Which Detect Human FMRP

Last year, FRAXA provided a grant to Dr. Alan Tartakoff at Case Western Reserve University to produce monoclonal antibodies to human FMRP. Over the past several years, it had become clear that one major roadblock in the field has been the relative lack of specific FMRP antibodies. The first antibodies are now available. Dr. Tartakoff reports:

We have used recombinant fragments of human FMRP carrying a (his)6-tag at the N-terminus (RNA, 5, 1248 (1999)) to immunize FMR1 knock-out mice (Jackson Lab). 35 hybridoma supernatants react with distinct recombinant fragments of FMRP (judging from ELISA assays and Western blots) and three detect intact FMRP upon Western blotting of HeLa cell lysates.

These three IgG monoclonal antibodies (7B8, 2F5, 6B5) react with the fragment of FMRP extending from the N-terminus to residue 204, as judged by ELISA and Western blotting. They detect a single protein band in lysates of HeLa cells and normal human fibroblasts and this band is coincident with the signal which is detected by the commercial (Chemicon) antibody number 2160. It is obviously distinct from bands in HeLa extracts which react with polyclonal anti-FXR1 and anti-FXR2 antibodies. This is surprising since the recombinant fragment of FMRP with which this antibody reacts is nearly identical to N-terminal sequences of FXR1 and FXR2. The new antibodies give no specific signal in Western blotting using lysates of fibroblasts from a Fragile X patient.

Small samples of culture supernatants are available and we have recently initiated production of corresponding ascites. Investigators wishing to obtain samples should contact Dr. A. M. Tartakoff, Pathology Institute, Case Western Reserve University School of Medicine, 2085 Adelbert Road, Cleveland, Ohio 44106 (amt10@po.cwru.edu). Since supplies are limited at present, investigators should request samples only if they intend to use them for specific experiments in the near future. Investigators interested in any of the MAb's which do not react with intact FMRP in Western blots should describe the experiments they envisage. Ongoing immunizations have begun with fragments of FMRP, FXR1 and FXR2 which are altogether distinct.

Neuroscience Faculty Search

In September 2000, the Eunice Kennedy Shriver Center for Mental Retardation, Inc. merged operations with the University of Massachusetts Medical School. In partnership with the Medical School, the Shriver Center announces a major effort to expand its programs in translational and basic neuroscience. The Center's mission is to understand neurological and behavioral development, with special emphasis on mental retardation and developmental disabilities, and there is a particular interest in conducting research on fragile X.

Positions open include Associate Director of Research, Translational Neuroscience and several Neuroscience Faculty positions at the rank of Assistant or Associate Professor within the Neurobiology of Developmental Disorders Division (formerly Biomedical Sciences). For more information, consult the website: www.shriver.org. Potential applicants may contact: William J. McIlvane, Ph.D., Chairman, Faculty Search Committee, E. K Shriver Center, 200 Trapelo Road, Waltham, MA 02452, phone 781-642-0153
William.McIlvane@umassmed.edu.

Update from the National Fragile X Foundation

We hear you! The results of our extensive Fragile X Needs Assessment can be found in the Summer 2001 issue of the Foundation Quarterly. Based on the 463 surveys returned, we have begun work on a series of specialized pamphlets that will address the topics you told us were important.

Many of you have already begun to contact the NFXF in regards to the 8th International Fragile X Conference to be held in Chicago, July 17-21, 2002. Let me reassure you that we are already hard at work preparing for that important event. We hope you are planning on attending! The registration form will be available on October 1, 2001. Look for it in our Fall 2001 Foundation Quarterly,

or online at FragileX.org. Of course, we're always happy to mail or fax you a copy.

The NFXF now has its entire, 200 + page website on CD. To purchase the FragileX.org Website CD — a low-cost alternative to going online — be sure to contact us at 1-800-688-8765.

I hope you were able to spend National Fragile X Awareness Day in a way that was meaningful to you and your family.

Robby Miller, Executive Director
PO Box 190488 / San Francisco, CA 94119
NATLFX@sprintmail.com

Fragile X Research Meeting Held at Banbury



Paul and Randi Hagerman, Sally Till, Steven Warren and Ted Brown

clear that a growing number of scientists are becoming interested in fragile X, and that progress is accelerating, especially the area of identifying proteins and RNAs which work with the fragile X protein in the brain. Planning is under way for next year's meeting, which will focus on proteins and RNAs.

The second annual Fragile X Banbury meeting was held at Cold Spring Harbor, New York, in March. Funded by the National Institute of Mental Health (NIMH), with additional support from the National Institute of Child Health and Human Development (NICHD) and FRAXA, these small, intense meetings enable scientists to present and discuss new findings. This year's meeting made it



Jennifer Darnell and Robert Bauchwitz

Advocating for Research

FRAXA members have been involved in many events aimed at shining the spotlight on fragile X research. Here are a few examples.

Working with the National Institutes of Health (NIH)

FRAXA Medical Director Mike Tranfaglia, Vice President Mary Beth Busby and President Katie Clapp have all helped to evaluate research funded by the National Institute of Child Health and Human Development (NICHD) and the National Institute of Mental Health (NIMH). Katie served on an advisory group which recommended guidelines for the NICHD's priorities over the next 5 years. She has served on NIMH study sections to evaluate research proposals. Mike Tranfaglia and Mary Beth Busby have both served on teams evaluating NICHD-funded Mental Retardation Research Centers. FRAXA members are also working with NICHD on their new fragile X brochure.

A Congressional Luncheon FRAXA and two dozen advocacy organizations, including the National Fragile X Foundation and Conquer Fragile X Foundation, have formed the Coalition for Children's Health to advocate full funding for the Children's Health Act. In June, the Coalition sponsored a Congressional luncheon, entitled **Expanding Federal Research Efforts at NIH for Childhood Diseases and Disorders**. Mary Beth Busby, FRAXA Vice President and mother of Robert and Jack, who both have fragile X, addressed more than 50 key congressional staffers, on behalf of the all of the groups.



"Brain Breakthroughs" with Mohammed Ali

In June, the Society for Neuroscience held a luncheon on Capitol Hill called **Brain Breakthroughs: Delivering Results**. The Society brought together NIH leaders, neuroscience researchers, and a few representatives of advocacy organizations, including FRAXA's Katie Clapp. The goal: to educate Members of Congress who sit on health-related committees and other key players about neuroscience and the real impact research has on the lives of their constituents. The stars of the luncheon were Mohammed Ali, who has Parkinson's disease, and his wife Lonnie, who spoke eloquently about what neuroscience research could mean for her family.

FRAXA Booth at Society for Neuroscience Annual Meeting

The Society for Neuroscience is a professional society of researchers who study brain disorders. Every year, FRAXA staffs a booth at the Annual Meeting, where over 20,000 neuroscientists gather, including most of the researchers FRAXA currently supports. We see presentations of current research, talk with "our" researchers, and recruit new investigators to the fragile X field. This year's meeting is November 10-15 in San Diego.

FRAXA EVENTS

Help FRAXA Accelerate Research

FRAXA has been fortunate to have grown exponentially, from a simple idea in 1994 to a million+ dollar research foundation today, thanks to many generous supporters who are committed to improving the lives of everyone with fragile X. This year, the economy has slowed, and this has hurt FRAXA's fundraising. At the same time, our efforts to accelerate fragile X research have succeeded dramatically. A few examples:

- FRAXA's efforts have resulted in a special five-year research initiative funded jointly by the National Institute of Child Health and Human Services (\$5 million over 5 years), National Institute of Mental Health (\$1 million over 5 years) and FRAXA (\$1 million over 5 years).
- The Children's Health Act became law, authorizing at least 3 fragile X research centers
- Two Nobel Laureates, James D. Watson and Eric Kandel, joined FRAXA's Scientific Advisory Board
- In 1994, FRAXA funded one grant for \$17,800. In the year 2000, FRAXA supported 27 research teams around the world, for a total of \$1,458,531. This year, additional top researchers have joined the fragile X field, and more grant applications are waiting to be funded, **if** we can raise the funds.

There are many, many ways families and friends can help accelerate research. Foremost is helping to find the funds to support the projects described here and the other projects now waiting for funding. You might consider gathering a group of family and friends to raise funds for a specific project, like the Fragile X Alliance of Ohio, the family and friends of Tyler Gruzin in Maryland, and the Preiser family and friends in New York. You may wish to participate in studies or to become a tissue donor. You might choose to devote your efforts to political advocacy (see the Report from Washington by David and Mary Beth Busby) or to help raise awareness of fragile X. All of this is important and all these efforts will build upon each other to enable us to reach our goals: effective treatments and ultimately a cure for fragile X.

The following articles and announcements are included to suggest ways in which each and every person can help to make an enormous difference. Now that so much exciting research is underway, it is more important than ever to grow our team and move forward even faster than before.



Above: Megan Massey, parent and FRAXA Director, **Sopranos** star Vince Curatola, (a.k.a. gangster Johnnie Sack), Katie Clapp, and **Sopranos** star Dan Grimaldi, who plays henchman Patsy Parisi. Below: Parent Marilyn Therrel and Mary Higgins Clark



by Mary Beth Busby

Those of you who were fortunate enough to attend the glorious event that Mary Jane Clark and her sister, Margaret Ann Behrends, chaired in May still likely have visions of flowers, twinkling lights and romantic Japanese lanterns dancing in your heads. Actually, what

dances in my head most of all was a little pre-dinner talk by Dr. Eric Kandel, our Nobel Laureate researcher. His message was one of inspiration and can-do optimism. In fact, he pointed out that only ten months after he first became involved with FRAXA and fragile X research, he won his Nobel Prize! Dr. Kandel, along with Mary Higgins Clark, sent us all out into the night with renewed enthusiasm for our work.

It may not seem so, but it's time to get out your calendar and mark the date for next year's gala. It will be back in Washington next April 29th, 2002, at the Four Seasons Hotel in Georgetown. That will be a Monday night, so plan to make a long weekend of it. For you political types, we plan to have another Lobby Day on Tuesday, April 30th, starting with a breakfast at a downtown hotel and then fanning out over the Hill for appointments with Congressional staffers and — who knows? — maybe even some Members and Senators. So do please mark your calendars, Gala: Monday, April 29, 2002 and Lobby Day: Tuesday, April 30, 2002.

AUSTIN GALA



Sam's Club in Austin, TX presents a check for FRAXA to Claudia Burnett, Katie Clapp, and Mary Higgins Clark, in honor of Mrs. Clark

May was gala month for FRAXA this year! On May 18th, hundreds of people gathered at The Four Seasons Hotel in Austin Texas for a wonderful evening of dinner and dancing. Guest of honor Mary Higgins Clark thrilled our Texas troups when she spoke of her determination to solve the mystery of fragile X. Mrs. Clark's grandson David is affected with fragile X.

Claudia and Michael Burnett and their friends Jill and Bryan Stevenson organized the event, including a very successful silent auction. The following evening, Mary Higgins Clark joined the Burnett family and their friends at their home to celebrate the event's success. We hope this will be the first of many FRAXA events in Texas.

Stone Pony Party in Asbury Park

Denise Sabo will hold a benefit for FRAXA on Sunday, October 14th at the Stone Pony in Asbury Park, New Jersey. Bring all your friends to enjoy music by the Soul Engines, two comedians, and an Elvis impersonator! Bruce Springstein first became famous at the Stone Pony (www.stoneponyonline.com); he still shows up often, and we have high hopes that he will join us! 3pm until whenever; cash bar and food available, entertainment not suitable for children. Tickets are \$20 and will be available through Ticketmaster, at the door, or from Denise Sabo (phone: 201-804-6110; email: dolphi4752@aol.com)

Patrick's Pals Win Again!

We wish that each and every one of you could be present at one of our annual Patrick's Pals fundraisers because it is impossible to adequately describe to you the immense feelings of success, hope, gratitude and love that is generated by the participants of these events. In June, in Cambridge, MA, our fifth annual Patrick's Pals 3-on-3 Basketball Tournament raised more than \$25,000 for FRAXA!

The wonderful thing is that over 100 people played in the basketball tournament and more than 200 others who could not be there made generous cash donations. Additional individuals and companies demonstrated their support with donations of prizes, auction items (we had our first ever silent auction of sports memorabilia at the tournament), t-shirts, lunches, arts & crafts materials for the children, printing services and more.

The tournament grew this year in more ways than one. The silent auction was a lot of fun and instigated some



Patrick's Pals Organizers: Jim Marks, Bill Rome, Scott Katz, Honorary Pal Steve Burton, Steve Savarese, Jon Pressman, Jimmy Vershbow Not pictured: Pamela Vershbow

serious competition of its own! Everyone enjoyed the addition of local sports newscaster Steve Burton as our "Honorary Patrick's Pal" to kick off the day's events. And, the basketball played rose to new levels, and we now have a new first place 'team to beat' for next year: Kevin Maloney, Chuck Trapani, Chris Feeney, and Andrew Solitro.

We want all of the fragile X families reading this to know that we have found a world of good people out there ready and willing to help our children and that we are sure you can too! To all of Patrick's Pals, thank you for another great year!

— Pamela & Jimmy Vershbow

FRAXA POSTDOCTORAL FELLOWSHIPS REQUEST FOR GRANT APPLICATIONS

**Upcoming Deadlines: December 1, 2001 and
May 1, 2002**

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. Applications are accepted twice each year. Information is available at www.fraxa.org or by contacting FRAXA.



*Mary Higgins Clark Gala
in New York City*

FRAXA

45 Pleasant Street
Newburyport
Massachusetts 01950

RESEARCH
FOUNDATION

FRAXA UPDATE

EDITOR: Katherine Clapp, M.S.

CONTRIBUTORS: Leslie Bagdasarian
David and Mary Beth Busby
Justin Fallon, Ph.D.
Lisa Kowal
Martha Mathews
Mina Johnson-Glenberg, Ph.D.
Alan Tartakoff, Ph.D.
Michael Tranfaglia, M.D.
Pamela and Jimmy Vershbow
Julius Zhu, Ph.D.

DESIGN: Mary Lou Supple

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FRAXA would like to thank Network of Newburyport, MA for hosting the FRAXA website and email. Network has donated this important resource for the past 6 years

PLEASE HELP FRAXA

in supporting research aimed
at treatment for fragile X RESEARCH
FOUNDATION

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

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