FRAXA UPDATE

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"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

Katie Clapp, Mary Beth Busby, and (former) President Bill Clinton

FRAXA Invited to The White House

CELEBRATING THE CHILDREN'S HEALTH ACT

On short notice, Katie Clapp and Mary Beth and David Busby hurried to attend the January 4 White House ceremony celebrating the bipartisan enactment of the Children's Health Act of 2000, which boosts federal funding of research on children's diseases, including fragile X. This was a rare, unforgettable opportunity to meet both (now, former) President and Senator Clinton in "The Blue Room," along with several members of Congress and 30 or so other advocates for children's and women's health issues. We were thrilled that Senator Clinton mentioned fragile X in her short speech. Former President Clinton ended his remarks with this memorable statement: "And to all of you who are focusing on genetic research, let me just say that the best stuff is still out there. So, go get it!" Hearing those encouraging words, surrounded by White House holiday decorations, and stirred by music by a Marine Corps orchestra, we felt optimistic that fragile X research will, one day soon, get the attention that it deserves. We all need to renew our efforts to raise fragile X in the consciousness of the Congress and the new administration. Perhaps, while The White House is occupied with replacing "W" keys on computer keyboards, we should offer to send them our golden "X" keys as well!

NEW RESEARCH FUNDED

This issue of our newsletter is double-dipped in research news. Every six months and as funds become available, FRAXA awards grants and fellowships for innovative research that will move us along the path toward finding effective treatments and a cure for fragile X. We place a premium on jump-starting new investigators in the fragile X field, so that they will be able to develop their ideas and preliminary data and compete successfully for other sources of funding. The first set of projects described on page 2 is fully funded by FRAXA.

In addition, nine grants have just been awarded under the special initiative **Neurobiology and Genetics of Fragile X Syndrome.** As we have previously reported, this initiative was funded by the National Institute of Child Health and

New Research Continued on page 2

Also in this issue:

- Research Funded Jointly by NICHD/NIMH/FRAXA
- 5 Annual Banbury Research Meetings Funded
- Upcoming Galas in NY and Texas!

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.

New Research – continued from page 1

research

Human Development (NICHD), National Institute of Mental Health (NIMH), and FRAXA. NICHD has committed $5 million dollars to this project over five years, and NIMH and FRAXA have each committed $1 million dollars. This is an enormous amount of money for a grass-roots foundation like FRAXA to raise, and yet it will fund only a fraction of the deserving proposals received from researchers around the world. See more on page 6. For information on all current FRAXA-funded research and our overall strategy, visit www.fraxa.org or call Katie Clapp at (978) 462-1866.

FRAXA Grants and Fellowships

Funded January 2001

Altered mRNA localization to growth cones, filopodia and spines assessed in hippocampal cultures from FMR1 knockout mice

GARY BASSELL, PH.D. AND LAURA ANTAR, PH.D.

Albert Einstein College of Medicine, The Bronx, NY

Renewal/Extension, $30,000

by Katie Clapp

Nerve cells have two types of long processes called axons and dendrites. During brain development, these processes extend for long distances and interact with other nerve cells and form connections (synapses). The ability of neuronal processes to grow correctly and form appropriate connections depends on the presence of specialized structures, called filopodia, which project from the surface of neuronal processes and growth cones.

Dr. Bassell's team has developed powerful molecular genetic techniques to visualize the movements of RNAs and proteins along these tiny structures. They can track FMR1 mRNAs and FMRP particles as they move through the growth cones, dendritic filopodia, and spines of hippocampal neurons in FMR1 knockout mice and normal controls. This work further indicates an important role for FMRP in normal development of neurons. Comparing fragile X mice with normal mice will enable them to explain which proteins and mRNAs are affected when FMRP is lacking, and how these differences affect the normal structure and development of nerve cells.

Studies on FMR1 gene therapy delivery using viral vectors

DAVID C. BLOOM, PH.D.

University of Miami

Renewal, $52,000

WILLIAM GREENOUGH, PH.D.

University of Illinois at Urbana-Champaign, Renewal $32,000

by David Bloom

The primary cause of fragile X Syndrome is a genetic defect that results in the lack of a protein, FMRP. FMR1 knockout mice, which lack the ability to produce normal FMRP, show a number of central nervous system defects which may be similar to those present in the disease in humans.

We have been using a gene therapy approach to deliver a functional copy of the FMR1 gene into the brains of the FMR1 knockout mice and to determine if this will repair the observed defects in their central nervous system. One tool we have been developing to deliver the FMR1 gene is a vector based on the Herpes Simplex Virus, which causes cold sores or fever blisters. This virus is a common inhabitant of our nervous systems and can be modified to deliver a gene to brain cells. During the past year, we have also been preparing a second vector based on adeno associated virus, a harmless virus associated with the common cold, which has great promise for use in gene therapy. The use of these two vectors together will increase the likelihood of successfully delivering the FMR1 gene to as many brain cells as possible. The construction of the first of these vectors is nearing completion, and initial tests in mice will soon begin.

This study will allow us to determine if delivering the FMR1 gene to the brain is a possible therapeutic approach for the treatment of fragile X Syndrome. This study will also allow us to learn more about how the FMR protein works, which may lead to the development of other types of therapies.

FRAXA first funded this collaborative project in January 2000. Construction of the viral vectors is underway at David Bloom's lab, and, once gene therapy tests have been performed on the fragile X knockout mice, testing of molecular and synaptic functioning of rescued knockout mouse neurons will be done at Bill Greenough's lab.

update:

Startle and Startle modification by prepulses in males with Fragile X Syndrome

ELISABETH DYKENS, PH.D.

EDWARD ORNITZ, PH.D.

UCLA, $37,720

by Katie Clapp and Elisabeth Dykens

Startle is a quick motor response to a loud noise; this is a normal response to a jarring, unexpected noise. If the loud noise is preceded by a much quieter sound, or prepulse, then the startle response is normally inhibited; this is called prepulse inhibition. It is thought that disturbances of prepulse inhibition reflect disruptions of pre-attentional mechanisms which underlie information and sensory processing. Prepulse inhibition is reduced in a number of mental disorders including schizophrenia, obsessive compulsive disorder, nocturnal enuresis (bed-wetting), and Tourette's syndrome, and attention deficit hyperactivity disorder when it occurs with enuresis or Tourette's syndrome.

In general, prepulse inhibition of startle measures sensory gating, that is, how the nervous system "gates" or modulates motor responses to strong stimuli so as not to interfere with the processing of preceding stimuli.

Interestingly, preliminary studies suggest that the fragile X knockout mice have a marked increase in prepulse inhibition. Dr. Dykens and Dr. Ornitz plan to test these responses in children who have fragile X, to see if they show similar responses. If so, then prepulse inhibition will be a target symptom in the knockout mice which can be used to evaluate potential genetic or pharmacological treatments. If fragile X boys show excessive prepulse inhibition, this might be related to the working memory deficit reported in these subjects. Attentional resources, locked to the stimuli such as the prepulse, would not be available for normal storage and retrieval of information.

FMR1 repression and the signals to chromatin

ASSAM EL-OSTA, PH.D.
PETER JONES, PH.D.

Peter MacCallum Cancer Inst., Melbourne, Australia, $35,000

by Michael Tranfaglia

This group is studying mechanisms of methylation-dependent silencing of FMR1, as well as regulation by histone acetylation/deacetylation. They have previously worked with MeCP2, the gene that causes Rett Syndrome, and present interesting pilot studies of the regulatory interactions of the Rett Syndrome gene with FMR1. They plan to extend these findings by studying other members of the methyl-CpG binding family with FMR1. This study is important because understanding the mechanism of transcriptional repression of FMR1 may point to ways to reactivate the gene so that it can function normally.

Restoring FMRP expression in cells from Fragile X patients

ANDRE HOOGEVEEN, PH.D.

Erasmus University, Netherlands, Renewal, $30,000

by Katie Clapp

In people with fragile X Syndrome, a mutation in the FMR1 gene shuts down the gene, so that no gene product, FMRP, is produced. Methylation is the chemical switch which shuts down the gene: several different sites on the promoter region of the gene are methylated. One possible strategy for the treatment of fragile X is to reverse the methylation of the gene, in order to restore FMRP production.

These studies are aimed at removing or preventing methylation in cells from fragile X patients by using antisense strategies. One promising antisense strategy is to use PNAs, artificial molecules that can be constructed to bind to a specific stretch of DNA. The result of this binding can be to alter the function of a gene. PNAs are particularly useful because they are relatively stable and not easily neutralized

GLOSSARY

Neuron brain cell

Synapse junction where a neuron communicates with another neuron or with a muscle cell; correct synaptic development (growth, strengthening, pruning, etc) is key to proper brain development, especially learning and memory.

Axon long arm that serves as a neuron's input from other neurons

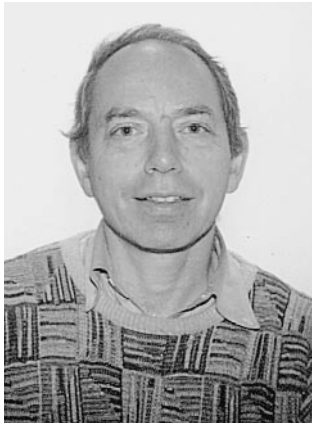
Dendrite long branching arms through which a neuron sends output signals to other neurons or muscle cells

In vitro in a test tube or lab dish; not using live tissue

by a cell's natural housekeeping mechanisms which defend against viruses and other foreign bodies. PNAs have been shown to have the ability to pry apart the strands of inactivated, methylated DNA and actually cause demethylation, which in turn, in the case of the fragile X gene, could restore its normal function.

Work is well underway on this project. Dr. Hoogeveen and his team have produced a panel of PNAs, each directed at a specific site in the FMR1 gene. They have demonstrated that these PNAs can cross the blood brain barrier to reach brain cells. Now they are testing the various PNAs to see which ones can effectively reverse methylation of the gene. The timing of expression and the targeting to the brain will be major challenges. This is a time-consuming process because multiple sites of the FMR1 gene are methylated and no one knows which one(s) must be reversed in order to reactivate the gene so that it can produce protein. Over the coming year, they will produce new PNAs and test the effectiveness of each one.

Monoclonal Antibodies to Distinguish Between and Investigate FMRP, FXR1 and FXR2



ALAN TARTAKOFF, PH.D.

Case Western Reserve University; $30,000 renewal

by Alan Tartakoff

The fragile X research field has been plagued by an absence of antibodies which cleanly discriminate between FMRP and two closely related proteins, FXR1 and FXR2. For example, only a single, non-discriminatory antibody is commercially available. We have therefore undertaken the production of a panel of discriminatory antibodies which will be made public. They should be valuable both for diagnosis and for investigation of the fundamental biology of the fragile X Syndrome.

In the first year of work on this project, we have used fragments of FMRP to raise antibodies. The approach is promising and some antibodies are already available. We are now concentrating on the production of antibodies which cleanly discriminate between FMRP and the two related proteins. This involves further rounds of immunization using segments of all three of the proteins.

Cell Growth and the Fragile X Syndrome

DEVIN ZARKOWSKY

Middlebury College, Vermont; $1000 materials grant

by Devin Zarkowsky

Observing dermal fibroblast (immature skin cells) growth is an unusual, yet promising, tack in fragile X research. Transgenic mouse cell lines exhibit diminished growth rates in comparison to their wild-type counterparts. We hypothesize that the fragile X gene may indirectly regulate a cell's life cycle. We will introduce a working fragile X gene into affected cells to, hopefully, induce growth similar to wild-type cells. If so, we will investigate whether an additional copy of the gene might spur increased proliferation.

Devin is an undergraduate at Middlebury College, who received funding from Howard Hughes Medical Institute last summer to conduct his research on fragile X. FRAXA is pleased to provide supplemental funds to allow Devin to complete this extraordinary project.

Patterns of Protein Expression in Fragile X Syndrome

WALTER KAUFMANN, PH.D.

Johns Hopkins University School of Medicine; $41,000

by Katie Clapp

Dr. Kaufmann will identify proteins which have abnormal levels and/or patterns of expression in males with fragile X syndrome. He will use a powerful technology, 2D PAGE, which will enable him to distinguish proteins from each other. He will correlate specific changes in protein levels with behavioral indicators, such as degree of autism or anxiety or cognitive impairment, in order to better understand what causes these symptoms and how they might be treatable.

Several studies investigate an important new model of fragile X Syndrome, the common fruit fly, scientifically known as drosophila. Although it may seem remarkable that fruit flies can shed light on a complex human disorder, fruit flies have a gene, known as dFMR1, which is quite similar to the human FMR1, FXR1 and FXR2 genes. Early studies show that "fragile X fruit flies" - which have been developed to lack the gene dFMR1 - have some behavioral, learning, and motor deficits, suggesting that this is a promising new line of research.

Neurological Function of Fragile X Gene in Drosophila

KENDAL BROADIE, PH.D. AND

YONG ZHANG, PH.D.

University of Utah; renewal, small bridge grant

By Yong Zhang and Kendal Broadie

One of the most compelling challenges in fragile X research is to understand how lack of the affected protein (FMRP) gives rise to mental impairment and associated behavioral abnormalities. A potentially fruitful approach is to assay FRAXA gene (FMR1) function within a simple, well-characterized genetic model organism such as the fruitfly, Drosophila melanogaster. Drosophila has a long and distinguished history as a genetic system to assay underlying causes of inherited human genetic diseases. In the last few years, Drosophila has contributed enormously to our understanding of a number of common neurodegenerative diseases including Alzheimer's and Parkinson's disease. We anticipate a similar revolution in our understanding of fragile X through developing a Drosophila model.

Last year, we identified and characterized a Drosophila FMR1 gene homologue (i.e. highly similar gene) which is now named dFMR1. Like its human counterpart, the dFMR1 protein product is highly expressed in most, if not all, nerve cells of the central nervous system, from embryogenesis to adulthood. Like human patients, when dFMR1 is completely removed from the fly genome (i.e. null mutants), the mutant fly is fully viable and morphologically normal, but exhibits uncoordinated movement behaviors. Microscopic assays of these mutants show that neuronal synapses (where a neuron communicates with another neuron or with a muscle cell) develop abnormally, resulting in clear structural defects. When dFMR1 is over-expressed in transgenic flies, making excess protein, an opposite structural change is observed. These results show that the level of dFMR1 protein directly dictates the level of synaptic structural development. Similarly, electrophysiological assays of synaptic function in both mutants and transgenic flies show that neurotransmission is abnormal, in agreement with the severity of the structural defects. These phenotypes, together with complementary human and mouse studies, strongly suggest that fragile X Syndrome may result from synaptic defects.

This year, we will focus on looking for dFMR1 interacting partners by employing powerful genetic interaction screens available only in Drosophila. We will mutate the entire fruit fly genome while screening for genes which can ameliorate fragile X symptoms in flies. Identifying and characterizing genes which interact with dFMR1 will help us understand the mechanism by which the fragile X gene and its protein product perform their normal function — and what goes wrong in the absence of the protein. We intend to use this information to develop treatments for fragile X.

This grant was approved by FRAXA's Directors for a second year of funding, but, happily, it will be funded at a higher level by the NIH/FRAXA initiative described below. A small bridge grant was awarded until the NIH funding takes over.

Using flies to Study FMR1 in Learning and Memory

JERRY YIN, PH.D., CARLA MARGULIES, PH.D.

Cold Spring Harbor Laboratory, $38,000

By Carla Margulies

We know that fragile X syndrome results from mutations in the gene encoding the FMR1 protein, but we do not understand the role of FMR1 protein in the central nervous system or how it is regulated. In addition, we do not know when, during a life-time, a person requires FMR1 protein. These questions are relevant in designing a therapy for fragile X syndrome and determining when therapy can be administered.

To answer these questions, we will take advantage of the sophisticated genetic tools developed in Drosophila, commonly known as fruit flies. Because flies have a very short generation time compared to mice, flies are an ideal system to investigate how FMR1 is regulated and to identify proteins that FMR1 protein regulates. Identifying these proteins will provide drug targets and gene therapies. Recently, the FMR1 gene and its protein were identified in Drosophila. This fly protein has the same biochemical properties as the mouse and human fragile X proteins. Mutations in the fly gene cause abnormal morphology (shape and structure) of neurons similar to the neuronal morphology seen in fragile X patients and FMR1 mutant mice.

Our first experiment will be to determine whether FMR1 mutant flies have learning and memory defects similar to FMR1 mutant mice. We will use a paradigm that involves exposing flies to one odor in the presence of an electrical shock. Then the flies are exposed to a second odor without shock. Later, the flies are given a choice between the first and second odor. If the flies remember, they will go to the second odor.

Then, we will use genetically modified flies to test whether the FMR1 protein plays a role in memory. We will construct a genetically modified fly with an extra copy of a FMR1 gene that will "turn off" FMR1 protein production in an adult fly brain. We will test this fly for memory. Later, we will determine whether "turning on" FMR1 protein expression will ameliorate the symptoms of FMR1 mutations in adults.

Proteins/mRNA Interactors of FMRP

JEAN-LOUIS MANDEL, PH.D.

CNRS, INSERM, IGBMC, Strasbourg, France

by Michael Tranfaglia

This project is aimed at pinpointing the function of the fragile X protein, FMRP. The team headed by Dr. Mandel, one of the seminal researchers working on fragile X, has recently discovered four novel proteins that interact with FMRP. This team of investigators will analyze the functions of these new proteins, and how they modulate FMRP functions. They have joined forces with another group in Strasbourg that is expert in analyzing RNA-protein interactions, and together, they will identify the mRNAs binding specifically to FMRP and the target RNA sequences/structures that are responsible for that binding. They will construct mutations affecting the binding site on the mRNA or the KH2 domain of FMRP and study the effect of their interaction on FMR1 mRNA export, stability, and translatability in cell culture. Further, they will analyze the role of these protein and mRNA interactions in model systems, such as cells in culture, Drosophila mutants, and transgenic mice, using a unique in vivo approach.

Over the past year, FRAXA awarded a postdoctoral fellowship to Dr. Barbara Bardoni, an investigator in Dr. Mandel's lab. This project will be funded through the NIH/FRAXA initiative, and FRAXA is providing a small bridge grant until the NIH funding takes effect.

Drosophila as a model to study FMRP function

THOMAS A. JONGENS, PH.D., AND THOMAS DOCKENDORFF, PH.D.

Univ. of PA School of Medicine, $35,000

by Katie Clapp

This group is developing mutant fruit flies which lack FMRP. They have begun to assess this loss of function, with particular emphasis on embryological and electrophysiological studies. They will look for other genes that are involved in the same pathway as dFMR1, in order to identify potential targets of dFMR1 activity. They will also investigate aspects of learning and memory through behavioral paradigms based on the courtship behavior of fruit flies. Fruit fly flirtation is a relatively complex behavior which depends on the ability to learn and remember. This team will compare the courtship of normal flies with that of fragile X fruit flies. Together these studies will help to define the role of the FMR1 protein in flies, which will also shed light on the function of the human FMR1 protein.

Two more grants were approved by FRAXA's Board for a second year of funding, for the laboratories of Dr. Kendal Broadie and Dr. Jean-Louis Mandel. Happily, these two teams have been generously funded under the NICHD/NIMH/FRAXA RFA, and so FRAXA is providing small bridge grants to fund the projects until the RFA funding takes over.

Back row: Dr. Felix de la Cruz, George Gaines, and Dr. Mary-Lou Oster-Granite, all of NICHD Front row: David Busby and Katie Clapp, FRAXA, and Dr. Duane Alexander, Chief, NICHD

Research funded jointly by NICHD, NIMH and FRAXA

Nine grants have been funded under the special initiative "Neurobiology and Genetics of fragile X Syndrome" by the National Institute of Child Health and Human Development (NICHD), with help from the National Institute of Mental Health (NIMH), and FRAXA.

The top five laboratories funded under this initiative have, over the past year, received direct funding from FRAXA for their fragile X work. One of our strategies in funding research is to select and support promising projects in their early stages, to enable the investigators to develop their ideas and gather preliminary data in order to

successfully compete for NIH funding. We think that this strategy works! Some risk-taking is required, but thanks to excellent guidance from FRAXA's Scientific Advisory Committee, we've made good choices.

FRAXA would not be able to function without our Scientific Advisors, who give their time and expertise in order to guide us and, most importantly, to evaluate grant proposals. This is no small task, as we now receive dozens of applications every six months. Thank you, Dr.s W. Ted Brown, Robert Bauchwitz, Seymour Cohen, Linda Crnic, Robert Darnell, John Donoghue, William Greenough, David Gwynne, Randi Hagerman, Eric Kandel, Herbert Lubs, Pamela Mellon, David Nelson, Owen Rennert, Stephen Warren, and James D. Watson.

This new initiative will fund two types of grants: Project Grants, with a direct cost budget up to $200,000 per year for up to five years, and Small Grants, with a direct cost budget of up to $50,000 per year for two years. Indirect costs for university expenses are paid as well, but only the direct annual costs are listed here.

Neurological Function of Fragile X Gene in Drosophila

KENDAL BROADIE, PH.D.

University of Utah, $200,000

This grant will be funded by funds from FRAXA to NICHD, by NICHD, and by NIMH

Fragile X Protein and Synaptic Receptor Deficiencies

IVAN JEANNE WEILER, PH.D.

University of Illinois at Champaign-Urbana $50,000

This grant is funded solely by NIMH. FRAXA has provided continuous funding since 1995 for fragile X research at the University of Illinois under Dr.s IJ Weiler and Bill Greenough.

The remaining grants will be funded jointly by funds from FRAXA to NICHD and NICHD. Dollar amounts are direct yearly costs.

Identification of FMRP Target RNAs

JENNIFER DARNELL, PH.D.

Rockefeller University, $175,000

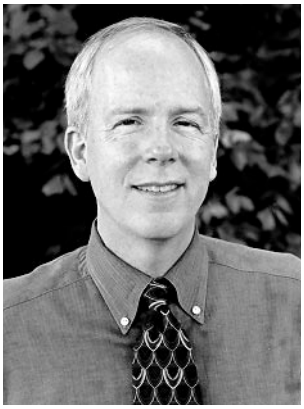
Dr. Jennifer Darnell received a FRAXA postdoctoral fellowship in 1999.

Proteins/mRNA Interactors of FMRP

JEAN-LOUIS MANDEL, PH.D.

CNRS, INSERM, IGBMC, Strasbourg, France; $125,000

Over the past year, FRAXA awarded a postdoctoral fellowship to Dr. Barbara Bardoni, an investigator in Dr. Mandel's lab.



Attention, Memory, and Executive Function in Fragile X

DONALD B. BAILEY, PH.D.

University of North Carolina at Chapel Hill; $200,000

FRAXA provided $30,000 in interim funding for this team over the past year and previously funded a two-year fellowship for Dr. Jane Roberts, a fellow in Dr. Bailey's lab.

Phenotype Consequence of High Repeat FMR1 Alleles

STEPHANIE SHERMAN, PH.D.

Emory University; $50,000

Phenotypic Markers in Females with Fragile X Premutation

AVE M. LACHIEWICZ, PH.D.

Duke University School of Medicine; $50,000

Gene Repression in Fragile X Syndrome

HOWARD CEDAR, PH.D.

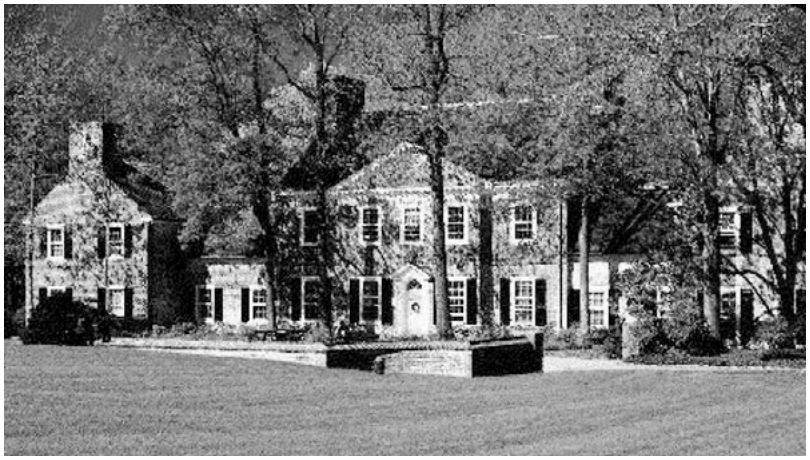
Hebrew University Medical School, Jerusalem, Israel; $100,000

Hearing and Speech in Young Males with Fragile X Syndrome

JOANNE E. ROBERTS, PH.D.

University of North Carolina at Chapel Hill; $50,000

Banbury Meetings



Last April, 39 scientists converged upon Cold Spring Harbor Laboratory's famous Banbury Center to discuss new findings and explore research strategies aimed at understanding and treating fragile X. The Banbury Center is known for small, focused, intense research meetings, where scientists share ideas openly and forge new collaborations. Last year's meeting, funded by the National Institutes of Health and FRAXA, was so fruitful that we decided to hold annual research meetings. We are very, very pleased to report that the National Institute of Mental Health (NIMH) will fund the next five years of Banbury meetings on fragile X, with a generous contribution from the National Institute for Child Health and Human Development (NICHD) and supplemental funding by FRAXA. We thank Dr. Bill Greenough for writing a successful grant proposal to secure NIH funding and Dr.s Bill Greenough, David Nelson, and Don Bailey for organizing the 2001 meeting. In addition, we thank Dr. James D. Watson, Dr. Bruce Stillman, and Dr. Jan Witkowski at Cold Spring Harbor Laboratory for offering to waive conference registration fees for the coming five years.

The program for this year's meeting, Understanding the Neural Basis of fragile X, held March 4-7th, is available from the Banbury Center (www.cshl.org/banbury) or FRAXA.

An impossible challenge in organizing research meetings is to include everyone who should be included and yet keep the meetings small enough to facilitate productive, open communication. Banbury imposes severe discipline because accommodations are limited. As new investigators join the fragile X field, the need for additional targeted research meetings grows. Banbury is a wonderful beginning, and we will continue to work to expand opportunities for collaborative research to blossom.

Fragile X Researchers are in need . . .

Human tissue donated at the time of surgery or death by people of all ages, especially those who have a developmental disorder like Fragile X, is a precious resource on which researchers depend.

The Brain and Tissue Bank for Developmental Disorders at the University of Maryland in Baltimore is one of two tissue repositories that is funded by the National Institute of Child Health and Human Development for the study of childhood disorders. The second bank is located at the University of Miami. The purpose of the Banks is to make human tissue available for research. Tissue donations are needed both from people with developmental disorders and their relatives, people of all ages and either sex.

The Banks provide information to anyone having questions about tissue donations and maintain a registry of individuals who wish to donate tissue either at time of surgery or at time of death. There is no cost to families who donate tissues. Currently a number of families with Fragile X are registered as potential tissue donors with the Bank at the University of Maryland. However, since this is not a fatal disorder, it is necessary to have a large pool of registrants to assure that the few isolated deaths may benefit the vast number of affected individuals both living now and those that will be born in the future. It is especially important that families with older members diagnosed with Fragile X consider registration for tissue donation. Also, families that have established an in utero diagnosis of Fragile X, and have made the decision to terminate the pregnancy, can make an important contribution by donating aborted tissue for research. Contact with the Bank several days before the procedure will enhance our chance of obtaining tissue that is of maximum value for research.

For more information or to receive a registration form, please call or write: Brain and Tissue Bank for Developmental Disorders, University of Maryland,
655 W. Baltimore St., 10-035 BRB,
Baltimore, MD 21201-1559 1-800-847-1539
Attn: Patricia L.W. Nash, PA-C, Project Coordinator.

National Fragile X Foundation Update

By Robert Miller

By the time you read this, or shortly thereafter, our new website will have premiered. The site has been completely reworked and you can be sure that the site has been designed with you, the parent or professional, in mind. The site not only features a great deal of new content, but also a layout designed to make the search for and comprehension of material much easier. Information about specific topics within Fragile X is now more self-contained, while the extensive use of hyperlinks allow you to easily jump to related topics.

Also of note is our new database containing all of our resources, including the excellent FRAXA materials carried by the NFXF. By contacting us you will be able to learn the location of any Fragile X related topic within the almost 20 titles we carry. That includes all of our books, newsletters, videos, audiotapes, CD's, and our website. If, for example, you're seeking to learn more about preparing students with Fragile X for the work-world, we'll do a database search for "employment," "pre-vocational," "vocational," and similar keywords. The results of that search will allow us to direct you to each title that contains information about those subjects.

These are just some of the ways the National Fragile X Foundation is committed to assisting families and professionals in the Fragile X community. As quickly as new information about Fragile X intervention, treatment and therapy becomes available we will add it to our resource list and database. As always, I can be reached at 1-800-688-8765, or at NATLFX@sprintmail.com. You can find us on the web at www.FragileX.org and, of course, you can always write us at PO Box 190488 / San Francisco, CA 94119.

Best Buddies

Best Buddies International, a nonprofit organization, aims to enhance the lives of people with mental impairment by providing opportunities for one-to-one friendships and integrated employment. Best Buddies works with high schools and middle schools to set up friendships between students with and without mental impairment. They currently have offices in about one dozen states. To find out more, visit www.bestbuddies.org or call 1-800-89-BUDDY.

Best Buddies' newest program, e-Buddies, builds e-mail friendships between people with and without mental retardation. People twelve years or older are eligible. All e-Buddies participants complete the same online application found at www.ebuddies.org. After the application is submitted, all prospective e-Buddies are screened before matching. e-Buddies agree to e-mail each other once a week for one year, or more often if they wish.

Some people with mental retardation may need assistance in typing or reading their e-mail messages, according to Lisa Derx, e-Buddies Director. "e-Buddies creates friendships," Derx said. "Friendship can occur even if one party needs help reading an e-mail or has to dictate a response to someone else for typing."

Derx said that special education teachers have found that e-Buddies helps motivate students to want to improve their keyboard skills, as well as reading and writing. "Getting a regular message from a friend is a powerful motivator," Derx said. You can reach Lisa Derx, e-Buddies Director at 202-266-2295 or EbestBuddies@aol.com.

Bridge Over Troubled Waters

by John May

The years since our child was diagnosed with Fragile X and the subsequent founding of FRAXA have slipped by with ever increasing speed. Some of the years have been hard and hurtful while others have filled us with joy and hope.

The development of FRAXA, much like the development of our child, has been wondrous to behold, far exceeding our expectations. FRAXA has grown into an ever more powerful and influential force in its drive to increase awareness, funding and research for a cure to the common disease that unites us.

Reading about the research being done in the many grants being financed by FRAXA, gives us hope for a future where our child may not be limited in his options, dreams and experiences because of a genetic fluke. Plank by plank, FRAXA is building a bridge to the future that can do much to still the troubled waters of our past.

John May's wife Kathy was one of the original founders of FRAXA in 1994 and has served on its Board of Directors ever since. For all of the energy, the brainstorms, and most of all, for all of the hundreds of phone calls, Kathy, thank you! May there be many more phone calls over the coming years.

FRAXA EVENTS

Fundraising for FRAXA

Have you ever read the newsletter and wondered where all the grant money our researchers receive comes from? It comes from YOU! None of this would be possible without the people who are dedicated to helping raise funds for FRAXA. So if you have any idea for a fundraiser in your community - big or small — FRAXA would be grateful for the help. Even a few hundred dollars is meaningful! Anything is possible — from a garage sale to a dressy dinner party to a letter to family and friends, asking that they donate to FRAXA instead of giving you that new tie or scarf at holiday time. Anything goes!

With so many research projects now underway and dependent on our support, FRAXA needs to build consistent, longterm funding sources. Most serious research projects are multi-year endeavors which require commitments of funds over several years. FRAXA depends entirely on donations and fundraising. In 1999, a single, million dollar donation raised our income dramatically. If we knew we could raise this kind of money every year, we could commit more funds to research NOW, thus speeding up progress towards a cure.

You can help. One possibility is to call or write us to pledge a monthly credit card donation. This is easy to start and just as easy to stop or change with a phone call or a letter. If you would like to talk about your ideas, or if you would like to see brochures, invitations, and other materials that others have used successfully, call Debbie Stevenson at 212-828-1883, email dstevenson@pop.net, or Katie Clapp at 978-462-1866, email kclapp@fraxa.org .

Texas Fragile X Gala

With Honored Guest Mary Higgins Clark
May 18, 2001
7:00 – Cocktails & Silent Auction
8:00 –Dinner
At The Four Seasons Hotel, Austin, Texas
Music by The Beamers

The tickets are $125. The sponsorship levels are as follows:

Friends of FRAXA - $1000	Patron - $2500
Bronze Sponsor - $5000	Silver Sponsor - $10000
Gold Sponsor - $15000	Platinum Sponsor - $20000

Contact: Claudia & Michael Burnett: (512) 453-4210 or 453-4806, wilburne@aol.com

Patrick's Pals V

by Jon Pressman, Steve Savarese, Bill Rome, Scott Katz, and Jimmy Marks

We proudly and enthusiastically announce our annual Patrick's Pal's Three on Three Basketball Tournament to be held on June 2, 2001 in Cambridge, MA. Patrick's Pals V represents our fifth year of organizing the event to raise awareness and funds for the research of Fragile X.

We emphasize the word proud for a number of reasons. When you set out to try and make a difference in the world of medicine and someone's life, there are numerous hurdles. The relatively modest hurdles that we have overcome in organizing this tournament for five years have shown each of us how difficult the hurdles must be for those with Fragile X or any serious condition. Accordingly, we once again honor Patrick, his parents Pamela and James, our boyhood friend, with Patrick Pal's V. 100% of the funds that we raise will go to FRAXA to further scientific research, so that each of you who plays, makes a donation, or lends your time to the tournament will contribute to the cause.

This year there will, of course, be the traditional three-on-three double elimination tournament, shooting contests and games (including prizes) for the younger hoopsters, an art table, lunch for all attendees, and, for the first time, a silent auction of sports memorabilia. As day turns to night, join us for more fun and friendship at our Patrick's' Pals annual barbeque and softball game. No one will leave hungry! For an invitation or more information, call Katie Clapp at FRAXA.

The flowers will be bursting into bloom again, signaling another rebirth of our efforts to find treatments and a cure for Fragile X Syndrome. The site of the 2001 Gala is truly an appropriate place to renew our fundraising quest. The Tavern on the Green in May is arguably the prettiest spot in New York. Distinguished journalist Roger Mudd has graciously agreed to guide us through the evening as we unite in our cause. Mark your calendars now for a beautiful evening of cocktails, dinner and entertainment along with, most importantly, an update on the state of our progress in solving the mystery of Fragile X.

Individual ticket: $350
Individual table sponsor: $3500
Individual table benefactor: $5000
Corporate sponsor: $5,000
Corporate Patron: $10,000
Corporate Benefactor: $25,000

YOU CAN HELP: In order for the Gala to be the biggest success possible, ***We must have corporate sponsorships***. Please let us know if you have any suggestions, connections, or ability to help with this. ***It's crucial!*** For more information contact Katie Clapp at 978-462-1866 or email Mary Jane Clark at maryjane.b.clark@worldnet.att.net.

EVERY SINGLE BIT HELPS

If you'd like to do something to help with FRAXA fundraising, how about running a raffle? The prize: Two tickets to the Mary Higgins Clark Gala on May 3, 2001 at NYC's Tavern on the Green? One sister of a Fragile X boy is doing just that, selling tickets at her high school for a dollar a piece. Think about doing it in your neighborhood, at your club or community center. Sell the raffle tickets for whatever seems best to you . . . one, five or ten dollars...you need to raise at least $700 to cover the cost of the tickets. We want to broaden our FRAXA base and get the word out to more people. This is a great way of doing it.

Philadelphia Fundraiser

by Cristy and Mitchell Hollin

On October 19th, 2000 over three hundred people gathered at Green Valley Country Club, just outside Philadelphia, to support our Third Fragile X Fundraiser. The event was chaired by our dear friends, Nicole and Todd Kendall, Jamie and Warren Klein, and Marla and Robert Friedman, who worked tirelessly to help us raise over $120,000 for fragile X research. The theme of the evening was "team spirit…being part of a winning team."

After being greeted by an energetic and beautiful squad of cheerleaders, guests were free to roam around our boutiques, which were set up by local stores donating 20% of the proceeds to our charity. Guests could also bid on an impressive and lavish display of auction items including jewelry, trips, and sports memorabilia generously donated by wonderful retailers . One of our most popular items was an autographed picture of Britney Spears. We also had a cruise and a trip to Aspen Colorado with a stay at the Aspen Club Lodge.

Our evening then kicked off with a team spirit cheer led by local entertainer, Reggie Williams. Reggie's cheer was followed by a moving speech from Jonathan Doring, a twenty year old who is affected by fragile X. Jonathan flew in from Florida to tell us what it's like to live with fragile X. He shared his failures, hopes and dreams with us leading us into the world of fragile X. After Jonathan's speech, we all cried for the person he'll never be due to fragile X, while rejoicing in the remarkable person he is. Jonathan's speech was followed by a video featuring our eight year old son, Matthew Hollin, who is also affected by fragile X. Following that, Bill Parker, father of two children with fragile X, spoke of his experience with fragile X and then live auctioned tickets to a Flyer's hockey game and introduce some of the past and present professional players.

Finally, after a full course, sit down dinner, we were all treated to a fabulous fashion show by Saks Fifth Avenue. To say that we were awed and overwhelmed by the tremendous show of support we received from our family and friends would be an understatement. What a night! We chose to divide the proceeds of the evening between Fraxa Research Foundation and Conquer Fragile X Foundation with the hopes that a cure or treatment will be found for fragile X.

FRAXA POSTDOCTORAL FELLOWSHIPS REQUEST FOR GRANT APPLICATIONS

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

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.

FRAXA's Katie Clapp, Mary Beth and David Busby and Senator Hillary Clinton at The White House

FRAXA UPDATE

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PLEASE HELP

FRAXA RESEARCH FOUNDATION

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

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

FRAXA RESEARCH FOUNDATION

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