Historic milestones – 25th conference!
10-years since the gene discovery!

Registration is now open! This is absolutely a conference not to be missed.

- Unparalleled sessions on communication, education, life planning issues, medical care, and research updates from Rett syndrome experts such as the Kennedy Krieger Institute at Johns Hopkins University
- *Very* special guests to commemorate our historic milestones
- Special pricing for IRSF Partners and early registration before April 15th
- Sponsorship and Exhibitor opportunities available now

Visit the website or call us at 1.800.818.RETT for details and to register

Attend in person or in spirit
Write a touching message to your loved one or submit an advertisement for all to see in the Helping Hands Keepsake Program! Tell grandparents, family members, friends, co-workers, doctors, teachers and therapists about this opportunity to write a poem, share a loving thought, a message of hope, feature a scanned photo or piece of school/artwork, and/or advertise a business - ideas are endless!
See website for details.

IRSF would like to thank all of our generous supporters.

The Rett Gazette – a publication of the International Rett Syndrome Foundation © 2009 IRSF. All rights reserved.

www.rettsyndrome.org

Winter 2/09

IRSF
INTERNATIONAL RETT SYNDROME FOUNDATION
4600 Devitt Drive
Cincinnati, Ohio 45246

CHARITY NAVIGATOR
Four Star Charity

NON-PROFIT
US POSTAGE
PAID
CINCINNATI OHIO
PERMIT NO 8093

FPO

Mr. & Mrs. J. Doe
123 Any Street
Anytown
01234

Winter 2009

IRSF
INTERNATIONAL RETT SYNDROME FOUNDATION

RETT GAZETTE

CHARITY NAVIGATOR
Four Star Charity

Volume 2, Issue 1

Inside This Issue

Research Updates
Page 1, 5, 6, 7, 8, 9, 10, 11

Family Advisory Board News
Page 2, 3

Letter from IRSF Board Chair
Page 4

Family Support
Page 12, 13, 14, 15, 16

Sibling Stories
Page 17

Connecting Grandparents
Page 18, 19

Partnership Program
Page 20

Regional Representative Program
Page 21

Advocacy and Awareness
Page 22, 23, 24

In Other News
Page 25, 26

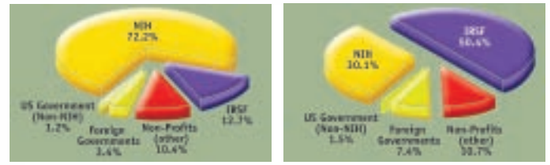
Events and Fundraising
Page 27, 28, 29, 30

In Memory of Angels
Page 31

IRSF Invests in Most Advanced Rett Syndrome Treatments to Date!

Over $15 million dollars invested!

Since the identification of the *MECP2* gene in 1999, research on Rett syndrome has made some important advances. Today, we have a gained a greater understanding of the molecular mechanisms underlying Rett syndrome which arise as a result of MeCP2 dysfunction. Numerous target genes have been identified that are regulated by MeCP2 and valuable animal models have been developed that effectively reproduce the disease and demonstrate the potential reversibility of the disease. International Rett Syndrome Foundation (IRSF) has played a critical role in driving this progress forward through funding, having now awarded over $15M in direct support of research grants since 1998. This funding has primarily supported innovative basic and pre-clinical research focusing on understanding the mechanisms that contribute to Rett syndrome and its associated complications.



Government agencies collectively provided 77% of the funding for Rett research (left). IRSF collectively administered >50% of the total number of grants awarded (right) (period of survey 1998-2008).

In order to expand upon this valuable research, the IRSF recently completed a comprehensive survey of previously funded research programs, providing a careful review of the past ten years of funding in the Rett syndrome field. This survey took a detailed look at research along a "bench-to-bedside" pathway. To accomplish this, IRSF funding was evaluated alongside that provided by a number of other sources including the National Institutes of Health (NIH), other US Government funders and several private foundations. This survey was carried out using publicly available information and with detailed records obtained from individual private foundations based in the US and overseas. The overarching purpose of the analysis was to assess progress in the field to date and to identify areas of unmet need along the bench-to-bedside path of therapy development.

This information will position IRSF to strategically allocate funding to areas of greatest impact and areas of need.

Government agencies collectively provided 77% of the funding for Rett research (left). IRSF collectively administered >50% of the total number of grants awarded (right) (period of survey 1998-2008).

Government agencies collectively provided 77% of the funding for Rett research (left). IRSF collectively administered >50% of the total number of grants awarded (right) (period of survey 1998-2008).

The survey collected information on the overall number of grants awarded and the level of funding provided by 15 governmental agencies (10 US, 5 foreign) and 5 private funders (3 US, 2 foreign). This represents a total sum of $107.5m. Of the private funding agencies for which data was available, a total sum of $25m, was collectively contributed towards Rett syndrome research between 1998-2008. IRSF administered more than 50% of all grant awards during the period surveyed. The total funds awarded by IRSF since 1998 amounts to $15.2m (including 2008 grants).

In December of 2008, IRSF convened a strategic advisory panel which brought leading investigators in the Rett syndrome field (including researchers Huda Zoghbi, and David Katz, plus clinicians Alan Percy and Walter Kaufmann) together with a number of senior advisors from NIH, industry and other individuals with extensive experience in drug discovery and development. This panel was brought together to discuss the progress that has been made to date towards developing therapies for Rett syndrome and their clinical evaluation. The advisory panel also discussed the most achievable near-term goals and potential treatment strategies for Rett syndrome.

This is not to underestimate the challenges still remaining. At the December advisory meeting a number of critical obstacles were highlighted, which underscored the difficulty of developing new therapies for Rett syndrome. Due to the complex biology of MeCP2 and its role as a regulator of many downstream target genes, continued work

continued on page 5

The Rett Gazette is published periodically by The International Rett Syndrome Foundation (IRSF), a non-profit 501c3 organization. IRSF's mission is to find treatments and a cure for Rett syndrome (RTT) while improving the day-to-day lives of those living with RTT.

Officers:
Kathryn Kissam, *Chair*
Steve Gallucci, *Vice Chair*
John Corpus, *Treasurer*
Gordy Rich, *Secretary*

Board of Directors:
Dr. Rick Altschuler
Ed Draves
Michael Joyce
Sean Lebson
Christian McMahan
Karen Nussle
Barry Rinehart
Jeff Stelmach

Staff:
Chuck Curley, *Executive Director*
Jennifer Endres, *Family Resource Manager*
Jennifer Grammer, *Special Events Program Manager*
Mary Joyce Griffin, *Administrative Officer*
Lisa Hayden, *Family Support Coordinator*
Antony Horton, PhD, *Chief Scientific Officer*
Cara Leighton, *Administrative Assistant*
Paige Nues, *Director of Family Support*

About Rett Syndrome (RTT)
Rett syndrome (RTT) is a devastating neurological developmental disorder that occurs almost exclusively in females. It is usually caused by a mutation of the MECP2 *gene on the X chromosome. Rett syndrome is found in all racial and ethnic groups throughout the world, and in every socioeconomic class. RTT affects 1 in 10,000-15,000 live female births. Early developmental milestones appear normal, but between 6–18 months of age, there is a delay or regression in development, particularly affecting speech, hand skills, and coordination. A hallmark of Rett syndrome is repetitive hand movements that may become almost constant while awake. Other features may include seizures, irregular breathing, swallowing difficulties, deceleration of head circumference with age, and curvature of the spine. Many individuals with Rett syndrome live well into adulthood. There is currently no cure.*

All material in the IRSF newsletter is copyrighted and most may be reproduced with permission. Call 1-800-818-RETT. Back issues are available for $2 per copy.

All submissions and correspondence regarding the newsletter, information and partnerships should be directed to:

IRSF
4600 Devitt Drive, Cincinnati, OH 45246
1.800.818.RETT or 513.874.3020
admin@rettsyndrome.org
Fax Number: 513.874.2520
EIN Number: 31-1682518

Policy Statement
In an effort to improve the quality of life for those with Rett syndrome we welcome ideas from our readers on various techniques of management and care, general and educational suggestions that individuals have investigated and/or found beneficial. This exchange of ideas is welcome. Parents and others have the opportunity to decide if they want to follow through with the suggestions. As a foundation, we do not support or endorse any particular treatment, therapy or medication. We encourage parents to support one another with suggestions and to contact their child's physician for final approval.

© 2009 IRSF. All rights reserved.

New Members Join the 2009 IRSF Strategic Family Advisory Board

FAB members work with IRSF and it's Board of Directors on strategy regarding all Family Support matters, especially in the areas of Communication and Information; Support Programs and Services; Fundraising; Advocacy and Awareness. We welcome our 4 newest members and look forward to great collaborations in 2009!

CLIFFORD FRY

Clifford L. Fry is the father of Ashley Fry, a 28 year old beauty with Rett Syndrome. Clifford and his wife, Judy, and Ashley attended the first IRSA conference. Clifford was on the first board of IRSA, and was a board member for about five years. During this time he and Judy and Dr. Alan Percy sponsored the Houston IRSA conference for parents, combining medical information with fun events, that set the pattern for many subsequent conferences. Clifford and Judy were Texas representatives for many years, during which time they talked with many parents and got Ashley involved in several research studies at the Rett Center in Houston. Clifford helped get then Governor George Bush to declare October as Rett Syndrome Awareness month in Texas, the first state to so designate such a proclamation, and he advised those in other states about how to obtain their state proclamations. Clifford recently nominated Dr. Huda Zogbhi for the Texas Women's Hall of Fame, a rare award given only every other year, resulting in her acceptance and recent induction. Clifford has a Ph.D. in Economics from Texas A&M University and has been a professor at the University of Houston, Washington State University, and Texas A&M University. Clifford has also worked in commercial banking and at the Federal Reserve Bank of Dallas. Clifford currently co-owns an economics consulting business called RRC,Inc. Clifford, Judy, and Ashley reside in College Station, TX. Clifford is enthusiastic about the formation of IRSF and the opportunities that it provides for all of those involved with Rett Syndrome!

SHIRLEY HURLBURT

My name is Shirley Hurlburt and I live in Liverpool, NY with my husband Paul, my daughter Kaila MacLaury who is 7, and we are expecting our 2nd child, a girl, due any minute at the time of writing this. Kaila was diagnosed with Rett Syndrome August 6, 2004 when she was 3 years old. It was after Kaila was first diagnosed with Autism that I became involved with advocacy. I joined a parent group that was just starting out called Families for Effective Autism Treatment of Central New York (F.E.A.T. of CNY). I have been a part of that group since 2004 and I have held officer positions and served as a board member. I have been able to be a part of a wonderful group that has grown by leaps and bounds and is making a difference in the lives of children who have Autism each and everyday. I decided in 2006 to begin working as a Medicaid Service Coordinator because I wanted to help other families with advocacy, services, and supports. I also attended and graduated from Partners in Policymaking; a leadership training program that is offered in many states for individuals who have a disability, parents, and family members. This training provides knowledge about issues and policies related to disability, and develops participants competencies to become more effective in influencing policy development at all levels. I enjoy helping families learn about services and supports and I hope I can make those connections for families who live with Rett Syndrome by working with the other members of the FAB.

SHAWN MANSFIELD

My name is Shawn Mansfield and my wife, Shelley, and I live with our three daughters in Washington D.C. I am currently working in the Homeland Defense Branch of Headquarters Marine Corps at the Pentagon. Our youngest daughter Lauren, age 4, was diagnosed with Rett Syndrome in July 2006. Within a month of Lauren's diagnosis we attended a strollathon in Fairfax, VA. This emotionally powerful event convinced us to host our own strollathon in Wilmington, NC. With enormous help and support from family and friends, we are entering the third year of this event. Shelley also serves as the Virginia Regional Representative for family support. As a family, we believe that God has given us Lauren to not only bless our lives but also inspire everyone around

continued on page 3

continued from page 2

her. In the past two years we have seen more people receive blessings because of her than we could have ever imagined. Through Lauren, our world has expanded to include wonderful people like her teachers, therapists, awesome volunteers and business partners that support the strollathon, and most importantly, other Rett families. Our world has expanded, our friends have multiplied, and our purpose in life has become even clearer. As I'm sure all of you can relate, our girls have a magic about them in their smiles, their eyes, and their touch that moves people down to their souls. I consider it an honor to serve the families of these special girls and women. As a FAB member, I will strive to help provide information and advocate for the resources that Rett families need to experience the unique joy and blessings that their daughters can bring to the family and the community. Shawn and Shelley's email is sman1119@yahoo.com

MARYANN SABO

My husband Steve and I live in Edgewater, MD (outside Annapolis). We have 4 children: Nick (21), Katie (18), Christopher (14) and Zachary (9). Nick has cerebral palsy and my Katie was diagnosed with Rett Syndrome at age 5. From the day we learned that Katie had Rett, our world changed; that is when I devoted my life to help Katie and others with Rett Syndrome. I started my first fundraiser that year and have done one every year since. Since having two children with disabilities, I have learned so much and know we have a lot of work to do for much needed changes in society as far as children/ young adults with disabilities are concerned. I have been a state representative for Rett Syndrome for over 10 years. I am on the parent advisory board for Uniform Services University (Military Medical School) in Bethesda, MD. As part of this program we host first and third year medical students to orient them on understanding medical care and the impact disabilities have on families. I also serve on the Commission for Persons with Disabilities in Anne Arundel County. I have worked at Sato Travel for over 18 years and will always be here to serve those who need assistance in traveling to and from conferences or taking your family on a vacation. I look forward to being on the Parent Advisory Board.

Meet John Corpus: IRSF Board of Directors Treasurer

John Corpus is married to Kathy Corpus, and resides in Alamo, CA. Their daughter, Samantha Corpus, was diagnosed with Rett syndrome at age 3.

Since Samantha's diagnosis, John and Kathy have been on a crusade to help find a cure for their beautiful baby girl who is now 9 years old. Samantha is the middle sister to 2 brothers, Julian (age 12) and Jacob (age 7). When John is not along side his family, he is actively fundraising for the Rett syndrome cause and advocating for increased Rett syndrome research. For the past 3 years, John and his family have hosted the Samantha Corpus Golf Tournament at the Blackhawk Country Club in Blackhawk, California along with other fundraising efforts to help increase public awareness and fund research. Through John's tireless fundraising ventures, he and his family, friends and supporters have raised over $450,000.00! Samantha is John's inspiration that keeps him persevering to ultimately find a cure.

John is the Senior Vice President and Chief Information Officer of Mervyn's LLC. John says, "It is a privilege to serve IRSF as Treasurer. For me, accelerating treatments and cures of RTT is personal. The power of Samantha's smile is overpowering. Many of our girls have smiles that melt our hearts, captivate us and motivate us. My daughter's smile has given me strength I never knew I had before. I want to use this new found strength to help support the IRSF mission and provide the continued awareness that will allow IRSF to reach new heights in fundraising, providing research support and family support services. The involvement of our family, friends and community is a must. As a united force, we can achieve the IRSF mission and provide our girls with continued care and hope for a cure. From the smile in Samantha to the strength in me... together with IRSF we will find new hope to keep the smiles of our daughters endless."

John Corpus and daughter Samantha

FamilyMatters

The Family Advisory Board of IRSF recently introduced "Family Matters" emails to RettNet. These emails were developed as a tool to tap into the vast knowledge and expertise of the many RettNet subscribers. All individuals and families touched by Rett Syndrome deal with many of the same issues, concerns and dilemmas and are always looking for answers. Each posting will focus on a particular topic and a member of the FAB will share a personal story to get the ball rolling. The first two topics were "Searching For Caregivers" and "How Much Therapy?". Responses to each topic will be gathered and summarized then posted on the IRSF website in the Forums section. This way, families, caregivers, professionals and others will be able to review the responses at any time and the Forum will allow members to continue to add responses to a particular topic. The FAB hopes that you all find this helpful. Please look for the next posting and send us your replies. Feel free to contact us with any questions or input.

"IRSF Family/Caregiver Survey"

The Family Advisory Board is happy to announce the IRSF Survey will be rolled out in early 2009. The goal of this survey is to find out what is important to those we serve and to ensure that we are doing our best to meet your needs. We will let you know by email and regular mail when the survey is complete. You will have the option to have the survey mailed to you, to take it online or even by phone. We hope you will participate and help us continue to grow and improve. We're looking forward to hearing from you!

continued from front page

readthrough drugs could be moved into clinical trials as a possible treatment for a subset of Rett syndrome patients with non-sense mutations.

Development and Testing of Therapeutics Targeting Brain Derived Neurotrophic Factor:

Brain Derived Neurotrophic Factor (BDNF) is known to play a role in various brain functions which are affected in Rett syndrome and the *Bdnf* gene is known target of MeCP2. Drugs called Ampakines are known to increase BDNF levels in *Mecp2* mutant mice and these drugs improve respiratory function (see article on BDNF & Brain Functions by David Katz this issue). This presents a strong rationale to pursue

Several therapeutic candidates targeting BDNF are currently in development

BDNF based therapies as potential disease modifying agents for treating nervous system dysfunction in Rett syndrome. Several therapeutic candidates targeting BDNF are currently in development which work via increasing BDNF levels or by directly activating its receptor or downstream signaling mechanisms. Since these therapeutic candidates are in pre-clinical drug development, it will be necessary to assess a number of these in parallel to compare their effectiveness side-by-side and increase the probability that one or more will reach the clinic. IRSF seeks to validate these promising drug candidates in animal models of Rett syndrome. .

Facilitating Experimental Medicine:

The testing of new therapies in clinical trials (experimental medicine) requires the careful selection of patients who meet the specific entry criteria of the trial. Given that Rett syndrome is a rare disease with a relatively small population of affected individuals, identifying and recruiting a sufficient number of patients for clinical trials may ultimately require conducting multi-center clinical trials. IRSF will direct funding towards critical resources and infrastructure that facilitates patient recruitment and support for experimental medicine. An important goal here is to foster the development of robust clinical trial outcome measures that are standardized for use across multiple clinical trial sites and are accepted by regulatory authorities (in the case of a new drug). A related priority is the development of biomarkers that can be used as guideposts to monitor the action of drugs in clinical

IRSF is currently working with leading clinicians and clinical trials specialists

testing. IRSF is currently working with leading clinicians and clinical trials specialists to better harmonize clinical research and experimental medicine. Working to best position these clinical teams to carry out multi-center trials with new treatments is a high-priority.

Developing Resources for Drug Discovery & Development

Basic research studies focused on gaining a greater understanding of the disease through physiological and molecular mechanisms are critical for the identification of new drug targets and pathways. A critical area of need to help facilitate drug discovery is the development of cellular assays as resources for study of MeCP2 function and for the identification and further testing of small molecules. A key component will be to develop functional readouts in these assays that reliably measure aspects of MeCP2 function and can be used as endpoints in small molecule drug screening. There are a number of different resource requirements that could facilitate this process enabling the research community to develop reliable cell-based assays for drug screening. IRSF will shortly launch a new grant-funding mechanism which seeks to provide seed funding to help cultivate this area. Future funding may follow on directly from successful efforts in this area.

BDNF & Brain Functions

More is being learned about the importance of BDNF for brain functions affected in Rett syndrome.

Work in the laboratory of David Katz at Case Western Reserve University previously revealed that loss of Mecp2 in mice results in a dramatic reduction of Brain Derived Neurotrophic Factor (BDNF), a protein that is critical for nervous system development and function. BDNF is important for many brain functions affected in Rett syndrome, including development of breathing, motor function, cognitive and emotional behavior. Dr. Katz's laboratory found that a drug belonging to a class of compounds called ampakines can increase BDNF levels in Mecp2 mutant mice and improve respiratory function. In addition, during the past year, Dr. Katz's research group has identified specific synaptic defects associated with loss of BDNF in brainstem areas involved in respiratory and autonomic control. Based on these findings, Dr. Katz's laboratory is now screening different classes of ampakines and other drugs in order to find ways to restore normal BDNF function in the Mecp2 mutant mouse. One aim of this work is to determine whether or not BDNF-targeted therapies that improve respiratory function can also prolong lifespan and improve autonomic, motor, cognitive and behavioral function in Mecp2 null mice. The long-term goal is to develop and test BDNF-based therapies for the treatment of Rett syndrome. "Many genes are affected by the loss of Mecp2 function," says Dr. Katz. "Therefore, one challenge facing researchers is to determine which Mecp2 targets are most likely to be promising candidates for development of potential therapies. Because BDNF is important for development and function of so many neural systems that appear to be affected in Rett syndrome, we believe it is a potentially high value therapeutic target."

Research Updates

Society for Neuroscience Annual Meeting

The Society for Neuroscience's 38th annual meeting was held from November 15th to 19th in Washington, DC. The meeting provides a forum for researchers to exchange ideas and share cutting-edge research findings in the field of neuroscience. This year, there were over 31,000 attendees from around the world present at the conference. IRSF hosted a booth to disseminate information on Rett syndrome and to provide researchers with details on upcoming meetings and funding initiatives. Current research on Rett syndrome was highlighted at the meeting in slide and poster sessions. Selected highlights of IRSF funded research presented at the meeting are shown below.

Localized deletion of MeCP2 in basolateral amygdala is sufficient to recapitulate anxiety and cue-dependent fear conditioning deficits
M. ADACHI, H. E. COVINGTON, III, A. E. AUTRY, L. M. MONTEGGIA; U. Texas Southwestern Med. Cn, Dallas, TX

In previous work, the authors demonstrated that mice in which MeCP2 was deleted in a broad region of the forebrain (cortex, hippocampus, striatum, and amygdala) recapitulated behavioral abnormalities observed in RTT patients, including hindlimb clasping, impaired motor coordination, elevated anxiety, impaired cue-dependent fear conditioning and deficits in social interaction. The group aimed to determine whether these behavioral phenotypes could be attributed to a particular brain region. MeCP2 in a region of the brain called the basolateral amygdala (BLA). The study used molecular techniques to selectively eliminate MeCP2 in the BLA region, showing that loss of MeCP2 in the BLA resulted in deficits in anxiety related behaviors. However, motor coordination or social interactions in these mice were unchanged. These results suggest that MeCP2 plays an essential role in mediating certain behavioral effects linked to RTT. This work was supported by an IRSF Postdoctoral Fellowship to Dr. Megumi Adachi.

Auditory evoked related potentials in mice heterozygote for null-MeCP2 mutation
*Authors: *W.-L. LIAO, T. B. HALENE, R. S. EHRLICHMANN, S. J. SIEGEL, G. C. CARLSON; (Univ. of Pennsylvania, Philadelphia, PA, Inst. Neurosci, Natl. Yang-Ming Univ Taiwan;)*

Amongst other symptoms, girls with Rett syndrome often lose speech, present with autistic features and develop abnormal EEGs patterns that often lead to seizures. As a potential source of the language disorder, girls with RTT appear to have difficulty with some auditory tasks yet appear to have near normal hearing. This has led to studies that show abnormal auditory responses and processing in girls with RTT. This study used a technique called auditory evoked potentials (AEP) where electrical potentials are recorded from a mouse following presentation of an auditory stimulus. The study was conducted to determine if AEPs are abnormal in a mouse model of RTT. The results of this work suggested that these mice may model the auditory abnormalities found in the girls with RTT. Further work will be conducted to determine if auditory processing is also perturbed in these mice, and to determine if these abnormalities cross into other modalities similar studies are planned using a visual stimulus. This work was supported by IRSF funding provided to Dr. Greg Carlson, U. Penn

Effect of Mecp2 mutation on X-Chromosome inactivation in a novel mouse model of Rett syndrome
*Authors: *R. D. SMRT, R. L. PFEIFFER, X. ZHAO; Neurosciences, Univ. New Mexico, Albuquerque, NM*

In Rett syndrome (RTT), the brains of females are mosaic in their deficiency of MeCP2, due to the random process of X Chromosome Inactivation (XCI). Observations in RTT patients and in Mecp2 mouse models, have shown that this mosaicism produces an unusual effect - MeCP2 protein levels are decreased in the normal nerve cells surrounding Mecp2 deficient nerve cells. This surprising discovery suggests that Mecp2 mutant neurons may affect the development of neurons in their near vicinity in the mosaic brain. There is also a difference in the ratio of normal versus Mecp2 deficient nerve cells suggesting that the normal cells have a survival advantage compared to the Mecp2 deficient cells. Given the critical function of MeCP2 in brain development,

it is important to determine whether MeCP2 mutation affects XCI or neuronal survival. The focus of this study was to determine if Mecp2 leads to changes in nerve cell survival rather than skewed XCI. To address this question, the group developed a novel Mecp2 mosaic mouse model, in which the normal nerve cells expressed Mecp2 coupled with a fluorescent marker protein, while the Mecp2 deficient nerve cells did not possess the GFP marker. Due to random XCI, the female mosaic mice have a combination of both fluorescent and non-fluorescent Mecp2 deficient nerve cells which can be distinguished by fluorescence microscopy. Using this mouse model the group observed a decreased ratio of normal versus mutant nerve cells at 6 months of age in a specific population of cells in the hippocampal region of the brain. The study will continue to examine early embryonic stages through adulthood as wells as in multiple brain regions will unveil whether Mecp2 mutation affect the survival of WT neurons or XCI in heterozygote brains. This study was supported by IRSF funding to Dr. Smrt.

Loss of MeCP2 in forebrain GABAergic neurons results in impaired motor coordination
Authors: H.-T. CHAO, R. C. SAMACO, M. CHAHROUR, J. L. NEUL, H. CHEN, M. EKKER, J. L. R. RUBENSTEIN, C. ROSENMUND, H. Y. ZOGHBI; (Baylor Col. of Med.; Univ. of Ottawa, Canada; UCSF, CA

This study was carried out to determine the contribution of inhibitory (GABAergic) nerve cells to the neurological impairments observed in RTT patients. The investigators used molecular techniques to generate a novel mouse model with selective loss of MeCP2 from inhibitory GABAergic nerve cells in the forebrain. These mice displayed impairments in motor coordination, suggesting that inhibitory GABAergic neurons play a critical role in the motor impairments seen in RTT patients. IRSF support for this study was acknowledged by the authors.

Grants Awarded in 2008

In October 2008, IRSF provided $1.5M to fund new research grant proposals and post-doctoral fellowships. A number these grants will be provided to investigators who seek to test potential therapeutics in animal models of Rett syndrome (RTT). A breakdown of these awards is listed below.

Research Grant Awards

Nathalie Berube, Ph.D. (University of Western Ontario)
Proposal Title: Epigenetic Regulation of Gene Expression by MeCP2 in the Mouse Brain

Dr. Nathalie Berube will examine the role of MeCP2 in epigenetic control of downstream genes using mouse models of RTT. She seeks to understand the relationship between MeCP2 and ATRX, a protein linked with other neurodevelopmental disorders. ATRX was recently demonstrated to bind directly to MeCP2 potentially co-regulating the expression of other genes. Dr. Berube will examine whether MeCP2 and ATRX bind and regulate common genes and how this might relate to abnormal DNA structure and brain function.

John Bissonette, M.D., (Oregon Health and Science University)
Title: Insufficient GABA inhibition underlies respiratory disorders in Mecp2 deficient mice

Dr. John Bissonnette seeks to understand the mechanisms underlying respiratory deficits in RTT. The inhibitory neurotransmitter GABA is known to be dysregulated in RTT and this defect may contribute to respiratory dysfunction. Dr. Bissonette will study individual inspiratory neurons using an investigational drug that enhances GABA receptors without causing side effects in order to rectify respiratory dysfunction.

Qiang Chang, Ph.D., (University of Wisconsin)
Proposal Title: Administering novel small molecules that have been shown to specifically activate TrkB in MeCP2 mutant mice to evaluate the therapeutic potential of BDNF.

Dr. Chang's group has created mouse models to study how the disruption of the *Mecp2* gene leads to RTT-like symptoms. Loss of Mecp2 results in a decrease in the level of brain derived neurotrophic factor (BDNF) which in turn may lead to respiratory dysfunction in RTT. Dr. Chang plans to test whether BDNF can be replaced with custom designed small molecule compounds that have the same biological properties (behaving as functional replacements of BDNF). If successful, this research could provide new BDNF-targeting therapeutics for patients with RTT.

Kerry Delaney, Ph.D., (University of Victoria)
Title: Systematic Evaluation of Cortical Neuronal Morphology in a Rett Syndrome Mouse Model

Dr. Delaney proposes a unique study that will conduct a detailed examination of neuronal structure. She will conduct a series of experiments using cell staining techniques to examine neuronal structure in the mouse cortex. She will next use the approach to study neuronal branching patterns to assess phenotype following administration of gene therapy vectors to replace Mecp2 in the RTT mouse brain. This study offers a valuable new technique for assessing reversal of RTT in animal models.

Aristea Galanopoulou, M.D., Ph.D. (Albert Einstein School of Medicine)
Proposal Title: Restoring GABAA signaling in Rett syndrome

Dr. Aristea Galanopoulou will examine an area of the brain called the substantia nigra pars compacta (SNC) which manifests signaling defects in the inhibitory neurotransmitter GABA in RTT. In this study, Dr. Galanopoulou will examine whether targeted interventions that aim to correct this abnormal GABA signaling, can be used as a new therapeutic strategy for restoring function in RTT mice.

David Ravine, M.D., Ph.D. (University of Western Australia)
Proposal Title: Microtubule instability is a feature of Mecp2 deficiency.

Dr. David Ravine has conducted preliminary studies which suggest that *Mecp2* mutations known to cause RTT result in functional changes in microtubules. Microtubules are stabilizing structures within nerve cells which form a scaffold and function as an internal cellular transport system. Microtubules are large aggregations of ordered proteins formed from smaller subunits. Destabilization of microtubules is known to be a causative mechanism which contributes to certain neurodegenerative diseases. In this project Dr. Ravine's lab seeks to understand if microtubules are subject to destabilization as a result of MeCP2 deficiency. If MeCP2 mutations actually result in destabilization of neuronal microtubules, this could present a new angle on treatment, since there are now a number of microtubule stabilizing agents in pre-clinical development for the treatment of other neurologic diseases.

Dag Yasui, Ph.D., (UC Davis)
Proposal Title: The role of MeCP2e1 in brain development and function

MeCP2 is known to exist in two different subtypes (isoforms) called MeCP2e1 and MeCP2e2. Dr. Yasui's research project aims to study the specific role of the MeCP2e1 isoform which is the most abundant form of MeCP2 in the central nervous system. Preliminary results suggest that MeCP2e1 may have a different effect on neuronal target gene expression than the other isoform MeCP2e2. The goal of this proposal is to determine the role of the MeCP2e1isoform in regulation of MeCP2 target genes *in vivo*. The project will examine if specific gene expression and behavioral defects are caused by loss of MeCP2e1 by comparing them with their normal littermates and will provide new information on the defects underlying RTT.

Post-Doctoral Fellowships

Bruno Blanchi, Ph.D., (UCLA); Mentor: Yi (Eve) Sun
Proposal Title: Gene and microRNA expression analysis in MeCP2 deficient human neuronal cultures. Dr. Blanchi received a post-doctoral fellowship to conduct a gene expression analysis to identify modulators of synaptic function which are abnormally expressed in MeCP2 deficient neurons. The aim of this part of the study will be the identification of novel targets to treat RTT. Following this he will manipulate the expression of the most relevant candidate genes in cultured neuronal cells to ascertain whether they can reverse the synaptic defects caused by MeCP2 deficiency

Gaston Calfa, Ph.D., (UAB); Mentor: Lucas Pozzo-Miller Ph.D.
Title: Hippocampal network excitability in MeCP2 deficient mice; a voltage sensitive dye study

Dr. Calfa aims to investigate the cellular basis of recurrent seizures that occur in RTT using a well-established mouse model of RTT. Using new imaging techniques, Dr. Calfa will examine hyperexcitable neuronal networks in the hippocampus. He will determine if this phenomenon is caused by too much synaptic excitation, too little synaptic inhibition, or a combination of both and will test whether the antiepileptic action of adenosine can reduce hippocampal hyperexcitability in RTT mouse models.

Michael Gonzales, Ph.D. (UC Davis), Mentor: Janine LaSalle Ph.D.
Proposal Title: Post-translational modifications of MeCP2

Dr. Michael Gonzales at UC Davis will receive a post-doctoral fellowship to study 'post-translational modifications' of MeCP2. Post-translational modifications are changes to a protein resulting from the addition and subtraction of small molecules that can subtly change the function of a protein. They can act as molecular switches for proteins which cells use to turn certain activities of proteins on and off, direct them to specific sites within cells, and regulate specific interactions between proteins. Identifying these modifications and determining their effects on MeCP2 function will provide a more nuanced understanding of mechanisms by which MeCP2 functions.

Ying Lin, Ph.D. (Cold Spring Harbor Laboratory); Mentor: Z. Josh Huang, Ph.D.
Proposal Title: Determine the pathogenic mechanisms of MeCP2 mutations on development and function of the inhibitory circuits in RTT mouse models.

Dr. Ying Lin of the Cold Spring Harbor laboratory will receive a post-doctoral fellowship to work on pathogenic mechanisms caused by MeCP2 mutations and how these impact on development and function of the inhibitory circuits in RTT mouse models. Dr. Lin's hypothesis is that abnormal expression of the protein Gad67, which is caused by MeCP2 mutations, affects inhibitory transmission and the maturation and plasticity of inhibitory circuits which underlies the pathologies observed in RTT. Dr. Lin will examine the precise morphological and physiological consequences of MeCP2 mutations on inhibitory neurons and circuits.

Severine Durand, Ph.D. (Children's Hospital Boston); Mentor: Michela Fagiolini Ph.D.
Title: Role of MeCP2 in experience-dependent development and plasticity of cortical circuits.

The complexity of neurodevelopmental disorders may lie in the formation of excitatory/inhibitory circuit imbalance during critical periods of development. In this study, Dr. Durand proposes to test the hypothesis that neuronal activity creates an optimal excitatory/inhibitory circuit balance during critical periods of development. Circuit disruption leads to the complex behavioral phenotype of neurodevelopmental disorders such as RTT. Using systems physiology, she aims to inquire about the functional development of cortical circuits in animal models of RTT.

Li Yong, Ph.D. (University of Alabama, Birmingham); Mentor: Lucas Pozzo-Miller Ph.D.
Title: The consequences of genetic deletion on MeCP2 in BDNF-induced membrane currents in hippocampal neurons.

Dr. Yong Li seeks to understand the role of BDNF in hippocampal neurons, a region of the brain involved in memory formation. The main aim of the project is to understand the role of BDNF and its effects on activity-dependent neuronal and synaptic functions. By use of specific recording techniques, Dr. Li will measure membrane currents in a specific group neurons that release BDNF from presynaptic terminals, these experiments will address the apparent discrepancy between the total BDNF levels versus the releasable BDNF content. These experiments seek to address an apparent discrepancy between the total levels of BDNF versus the releasable BDNF content in neurons from a mouse model lacking Mecp2. Dr. Li will conduct experiments to measure membrane currents in specific neurons from the hippocampal region of the brain which demonstrate the release of BDNF from terminals.

Jing Han, Ph.D., (Baylor College of Medicine); Mentor: Huda Y. Zoghbi M.D.
Title: Investigating the Role of the Neuroendocrine-Hypothalamic System in Rett Syndrome.

The hypothalamus is a circumscribed region of the brain that is dysfunctional in RTT. A post-doctoral fellowship award to Dr. Jing Han will allow her to examine specific neuronal cell types within the hypothalamus to better understand the role of this brain region in RTT. Dr. Han will use genetic techniques to eliminate MeCP2 from many of the cell-types within the hypothalamus and will then assess the behavioral and physiological changes that result in these mice. In parallel she will conduct studies on signaling molecules, called neuropeptides that are released by the hypothalamus to regulate activity in the central and peripheral nervous systems. Dr. Han will then genetically normalize the altered function caused by increased neuropeptide levels to seek a potential rescue of some RTT phenotypes providing potentially novel therapeutic targets for RTT.

Research Updates

Introducing Mr. Jim Keller, IRSF Grants and Research Manager

My name is Jim Keller and I am IRSF's new Grants and Research Manager. I began working with the foundation in November 2008 and have four years experience in Grants Administration. Most recently I was the Grants Manager for the Alzheimer's Drug Discovery Foundation where I managed a diverse portfolio comprised of academic, industry and conference grants. Prior to that I held a similar position at the Juvenile Diabetes Research Foundation.

My first experience after joining IRSF was to attend the Society for Neuroscience Annual conference in Washington, D.C. I staffed our booth and spoke with scientists about the upcoming changes to our grant program. I was also afforded the opportunity to meet some of our funded investigators as well as some longtime collaborators in the field of Rett Syndrome.

Jim Keller

I am very excited about this opportunity to work with our Chief Scientific Officer, Dr. Tony Horton. One of my first tasks working with Dr. Horton will be to implement a new streamlined grant submission process that will enable investigators to apply more efficiently to our existing and future grants initiatives.

InterRett

InterRett is the largest congruent dataset of phenotypic data in the world on Rett syndrome. Funded by ISRF, there are 1,722 unique cases documented in InterRett since data collection began in 2003. Ironically, only a fraction have been submitted by U.S. families. Put your hard-earned research dollars to real use by adding your child's data to this internationally accessible genotype-phenotype database. More families means more meaningful trend results! You too can access this data and create output graphs of interest to you, such as "Age at first steps unaided" as reported by mutation types. For more details about how to participate, go here: http://interrett.ichr.uwa.edu.au

IRSF Secures Government Grant

Through intense advocacy efforts IRSF secured a government grant in the amount of $143,000 in September 2008. This grant is directed towards four critical components in the education and awareness of patients, health professionals, and the public regarding Rett syndrome (RTT).

Since 95% of the funding raised by IRSF is directed toward program services with 90% of those funds directed toward research. This leaves precious little funding available for building an effective, nationwide organization for the girls and women suffering from this disability, their parents, doctors, caregivers and friends. The grant was provided to aid IRSF in funding specific activities in education and awareness. The funds were provided towards the continued support of several databases containing valuable clinical information on RTT genotype and phenotype; traveling clinics which send groups of expert clinicians to educate patients, parents and health professionals and who are enrolling RTT patients into a longitudinal Natural History study; support several researchers to present their findings at the World Rett Syndrome Congress in October 2008 and to develop a booth and printed materials for education and awareness of RTT for display at public and professional meetings.

Research Updates

Rett Syndrome Program

The Rett Syndrome Program in the Department of Neurology at Children's Hospital Boston provides multi-disciplinary, specialist-coordinated clinical care for children and women with Rett syndrome. Patients in this Program have access to expert providers in fourteen fields: neurology, epilepsy, genetics, developmental medicine, gastroenterology, orthopedics, physiatry, cardiology, gynecology, sleep medicine, nutrition, dentistry, endocrinology and pulmonology; in addition, the Program provides continuous access to nursing and social work support. Established in 2006 and designed in close consultation with parents, the Program continues to be guided by an advisory body comprised of parents and scientists. Important collaborations have been forged between the Program and basic scientists, other Rett specialist programs, and, crucially, with parent and family support groups. Fellows, residents and medical students both at Children's Hospital and Harvard Medical School receive part of their education in the Program. As the only specialist Rett syndrome program in New England, the Program has seen over 200 patients and enrolls an average of 6 new patients per month. Omar Khwaja, MD, PhD, is Director of the Rett Syndrome Program and a member of the Children's Hospital Department of Neurology. He studied medicine and human molecular genetics at the University of Cambridge in the UK. Following residency and fellowship in pediatrics and newborn medicine in Cambridge and London, he trained in clinical genetics in Melbourne before moving to Boston to train in pediatric neurology. His specific interest is the development of clinical trials for Rett syndrome; in collaboration with colleagues at MIT, Dr. Khwaja is leading the effort to study a novel approach to treatment of Rett syndrome using Insulin-like growth factor type 1. Children's Hospital Boston is the primary pediatric center for Harvard Medical School and is home to the world's largest and most active research enterprise at a pediatric center. The Hospital is a major pediatric tertiary care facility of 347 beds and serves as the largest referral center pediatric center in New England. The proximity of Children's Hospital to Harvard Medical School and the Harvard School of Public Health contributes to its rich research environment. The Department of Neurology at Children's Hospital currently includes 68 clinical and research faculty. Basic neuroscience programs focus on molecular neuroscience and systems neurobiology; clinical neuroscience efforts focus on epilepsy, developmental disorders, neuro-oncology, fetal/neonatal disorders, neuromuscular disorders and disorders of behavior and cognition. In addition to the Rett Syndrome Program, the Department is home to 13 other subspecialty programs for the diagnosis and treatment of epilepsy, learning and other developmental disabilities, attention deficit disorders, sleep disorders, neuromuscular disorders, brain tumors, neurogenetic disorders, neonatal neurology, mental retardation and cerebral palsy, mitochondrial disorders, tuberous sclerosis, and autism. The Department's support staff including nurses, social workers, and an autism specialist ensures that patients receive the highest level of care.

Dr. Omar Khwaja

Tell Congress to Approve 2009 Funding for IRSF!

In the coming weeks, members of the House and Senate will finalize the FY2009 Labor–HHS-Education Appropriations bill. In that bill, IRSF has funding from the Center of Disease Control and Prevention to support education, awareness and outreach for patients, health professionals and the public regarding Rett syndrome (RTT). This funding will also help us establish the foundation required to accelerate treatments of this debilitating brain disorder that is often misdiagnosed.

We need you! It is critical that we show widespread advocacy across the nation supporting this request.

In the House of Representatives, Congressman David Obey (D-WI) and Congressman Steny Hoyer (D–MD) are critical to ensuring our funding. In the Senate, our key supporters are Senator Tom Harkin (D–IA) and Senator Ted Kennedy (D-MA).

Please help us make sure that the House of Representatives and the Senate support our request for funding so that we can position ourselves for critical translational and clinical research on the horizon.

Visit www.rettsyndromeadvocacy.org to enroll in our new Rett syndrome advocacy website. We have a turnkey approach with sample letters and tips on setting up face-to-face meetings with your representatives. For more information, email Kathryn Kissam at kkissam@rettsyndrome.org

Rett Syndrome Clients and Good Nutrition:

Learning Nutrition Principles to Promote Growth and Well Being and When and How to Seek Assistance

By Suzanne Geerts, MS, RD
Registered Dietitian, UAB Rett Syndrome Clinic and Civitan-Sparks Clinics, University of Alabama at Birmingham

In the clinic and research setting, parents often described their client with Rett syndrome (RS) as having "excellent appetites" and eating many of their waking hours. Although each story is different, it is sometimes hard for parents to believe the client is not growing as expected. Many families and therapists have developed excellent feeding strategies to boost intake. Multiple RS publication and education material are available to help guide parents in this area. It is always beneficial to recall the basic principles of good nutrition and "short cuts" to encourage good intake. Some RS clients also have feeding problems that place them at risk for not growing well. Once the problems are defined, appropriate feeding programs can be put into place at home and at school. Those with severe problems must seek help by locating a medical team trained in nutrition support/feeding therapy. The feeding team should consist of the care giver and possibly several specialists. Establishing good communication is one important key to success. Realizing that children are growing and medical condition/needs can vary greatly; developing a dynamic plan of nutrition care with periodic review is needed. Many of these specialty feeding services are provided in pediatric hospital/clinic settings or state children's rehabilitation programs. A proactive approach to feeding will result in less family stress, better growth, save money, and avoid hospitalizations. Then attentions can be turned to positive family dynamics, learning and other beneficial therapies.

Basics of Good Nutrition

The principles of good nutrition for typical children have been well defined for many years. It is simply defined as eating a good variety of healthy foods in the correct amounts needed for growth and health. Variety of intake will provide all the protein, carbohydrate, fat and vitamins and minerals one needs. These days there is much emphasis on low fat, low salt and high fiber intake which may protect against heart disease and possibly certain types of cancers. Drinking 6 - 8 glasses of fluids (preferably water) is still the recommendation to promote hydration and good gastrointestinal/urinary function. Doesn't forget-vigorous exercise several times per week go hand in hand with healthy food intake.

Good nutrition for clients with RS is identical with several areas of special emphasis. Research and clinical experience continue to indicate the RS clients need more protein and calories for growth than typical children although the reason for this remains a topic for needed research. Adequate sources of calcium and vitamin D are necessary to promote good bone mineral density. Abnormal breathing patterns and feeding and Gastrointestinal problems may interfere with eating. Ambulation as tolerated and physical therapy sessions replace vigorous exercise. Providing for special nutrition needs is a major focus for the growth years of your child. As I tell my clinic clients "approximately 14 years of attention to feedings and growth." Do not feel overwhelmed by this but get proactive and seek help!! Needs will usually decrease dramatically when the growth of puberty has ceased and adult size is determined. The focus then turns to healthy eating habits and portion control to avoid obesity and aide mobility or transfers.

In general and if your child is on a normal diet and is still in growing years and trying to gain weight, basic nutrition rules to remember for home and school.

- Eat a wide variety of healthy foods-modify texture as needed to make it easy/enjoyable to eat
- Push protein/calories for growth-extra portions and adding protein foods and fats are essential
- Offer several feedings per day-3 meals and 2 to 3 snacks
- Provide dairy foods (milk, yogurt, cheese) 3 to 4 servings for children and 3 to 4 for teens and adult women) to help strengthen bones
- A multivitamin may be necessary several days per week if variety of intake is not obtainable or possible
- Encourage fluids throughout the day
- A variety of nutrition supplements or feeding tube maybe indicated if growth is not progressing or as medical complication(s) dictate.

A good source for additional hints is the K. Hunter, Rett Syndrome Handbook, 2007, Nutrition and Feeding, page 259.

Realities of Feeding in RS Clients

Many of the RS clients experience feeding difficulties. In the clinic setting, we interview and screen for these difficulties so early recognition can lead to early/ongoing interventions.

Questions/Comments we often hear in clinic

Parents often report "but my doctor or dietitian doesn't know Rett Syndrome!" They can contact the resources persons listed below for guidance.

Q: How do I find a feeding/nutrition specialist?

A: Your pediatrician, gastroenterologist, or neurologist may have suggestions. Call the nearest pediatric hospital/clinic-most have doctors, registered dietitians, OT and speech therapists on staff. Call state rehabilitation services to see if feeding therapists are on staff

Q: Why do I have to see/follow up with a dietitian?

A: In general, clients with RS are short of stature and small for age although this varies from one situation to the next. Just because the child is small does not indicate they are underweight or malnourished. Although in a clinic setting, we do see incidences of calorie malnutrition. Determination of good body mass is best done by evaluating height and weight on standard NHS pediatric growth charts and doing the skin fold test (arm and sub scapular area) with calipers. Adequate skin folds, healthy appearance skin and shining hair and nails are good indications of proper nutrition not just the weight or height on a growth chart.

Common Nutrition Risk Factors Seen in UAB RS Clinic

- Poor oral/motor function including weak or no chewing and poor swallowing of foods or liquids
- Failure to grow as seen on pediatric growth curves
- Food allergies/intolerances or food aversions
- Picky eaters for extended periods of time
- Reflux-can result in pain and discomfort and lack of desire to eat
- Constipation-decreased appetite; pain and impaction many necessitate emergency treatment
- Medications that cause sleepiness or poor appetite
- Underweight or overweight conditions
- Recent weight loss or gain-unexplained or greater than 2 pounds
- Poor dental health
- Financial restrictions to food/supplement supply
- Preoperative needs to prepare for surgery- ie scoliosis
- Other chronic health conditions

If these conditions are recognized, it is best to seek the help of your primary medical doctor, gastrointestinal specialist, and other members of the health care team involved in feeding and nutrition support (pediatric registered dietitian, OT, and speech therapist). Remember the most important member of the feeding team is the parent! These practitioners can evaluate your child and develop a feeding care plan that is specific to their needs. Planning should include long and short term goals. They can also make suggestions for nutrition supplements appropriate you're your child and seek financial assistance to purchase them if needed. Feeding needs may resolve and care can be lessened from time to time. But should problems arise, the team can regroup and make additional recommendations with past knowledge to support efforts.

Q: My health care plan will not cover the services of a dietitian.

A: If you need to see a registered dietitian, you need to ask if her services are covered by your health care plan and if preauthorization is needed. You may need a referral or letter if medical necessity from your doctor. Ask what the fees are? In our clinic setting, initial fees are reasonable and follow up fees are greatly reduced. Follow-up visits and progress checks can often be done by phone at no cost.

Q: Does my child need a vitamin/mineral supplement?

A: Generally, consuming a good variety of foods including adequate dairy foods and ample fluids ensures adequate nutrient intake. But children with medical complications, food allergies/intolerances or "picky"/monotonous eating habits can indicate a need for supplements. Be sure they consume adequate amounts of calcium and vitamin D for age. Ask your health care providers for assistance with product selection.

Q: How can my child be malnourished when she eats all the time?

A: The classic textbook definition of malnutrition includes two types-protein malnutrition and calorie malnutrition. Most of the girls eat well so protein malnutrition is unlikely unless feeding difficulties severely limit intake. Some clients are very thin from time to time with low body mass index and poor fat stores. Adequate fat mass is necessary to maintain body temperature and protect fragile bones and joints during an occasional fall or bump. Calorie malnutrition will respond over a few months to increase of nutrient intake by mouth or by feeding tube if needed.

Q: What are the indications for a feeding tube and what is the best type to get?

A: Each situation is different and this decision is best made after much thought and discussion and if feeding support has failed. Some are for temporary use and some are permanent and require surgery for placement. Always consult an experienced pediatrics gastroenterologist or surgeon to explore what is appropriate for your child. And learn all that you can about the procedure and care of the tube so you will feel comfortable with your decision. Know that there are many types of feeding tubes and the doctor will dictate what equipment is used. Overall, feeding tubes are much more sophisticated than they used to be and one can be very successful with their use with the correct guidance and care.

General Indications for a Feeding Tube

- Growth failure for 6 to 12 month period
- Very low BMI (body mass index)
- Unable to chew or swallow efficiently Reflux with recurrent aspiration pneumonia
- Urgent need for weight gain or nutrition supplements to prepare for surgery Refusal of needed medications or failure to drink enough fluids to maintain health

RS Resource centers Available for Assistance

IRSF www.rettsyndrome.org

Hunter, K. Rett Syndrome Handbook, second Edition, IRSA press, 2007.

UAB Rett Syndrome Clinic
Civitan International Research Center
University of Alabama in Birmingham
www.circ/uab.edu (Sparks Clinics link)
(205) 996-6406 or (205) 934-1064

The Blue Bird Circle Rett Center
Baylor College of Medicine
The Texas Children's Hospital,
Houston, Texas
http://bluebirdrett.bcm.edu
(832) 822-1781

Caring for an Adult: Our Special Gift

by Lamar Beaty

Sandy was born in Gulfport, Mississippi in 1967, and like most Rett girls experienced normal development for the next 18 months. It was at that age that things began to change rapidly. We were first told that she suffered from a hearing loss. Next came a diagnosis of autism. Shortly before her fifth birthday we moved to Houston, Texas, so she could enter a program for autistic children. Over the next five or six years her diagnosis changed several times until we were finally told that the doctors really didn't know what Sandy's problem was. She was in several different programs during that time.

Needless to say, this was a very difficult time in our lives. We were far from our families. We were trying to cope with the fact that we might never know what happened to our beautiful little girl, and we also felt very alone because we had come to the conclusion that there was no other child in the world like Sandy. It wasn't until after Sandy's 20th birthday that we were told she had Rett Syndrome. Although little was known at that time about Rett, we were relieved to at least have a diagnosis and to know that we were not alone on this journey. Had it not been for two very special people in Houston, Texas, Drs. Danny Williamson and Alan Percy, this diagnosis might have never been made.

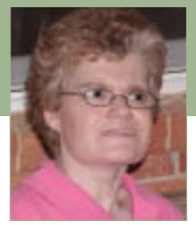
When Sandy was 30 years old, Sally and I retired, and, along with Sandy, moved back to our hometown of Houston, Mississippi. Our other child, a son who is four years older than Sandy, remains in Texas today with his wife.

Naturally, Sandy is a big part of our lives. We live on a small farm and we try to involve Sandy in everything we do. When we travel Sandy always goes with us. We recently purchased a pontoon boat and although we have only taken it out one time, Sandy loved riding around the lake with the wind in her face. We have a Kawasaki Mule and we like to take Sandy riding in it as much as we possibly can. There are several hundred of acres of land around our house that we can ride on. Sandy loves riding in the woods as well as the open fields. Sometimes it seems that the faster we go the better she likes it. We have a pond on our place and sometimes she goes fishing with us. She will sit in the Mule and watch as Sally and I fish.

Both Sally and I have family living near us and we get together every month to celebrate birthdays. Sandy loves being around everyone and acts as though each birthday party is being held especially for her. If weather permits we take her to festivals in our town.

As much as we enjoy including Sandy in our activities, it is important that Sally and I have time to spend together. We have a wonderful sitter that is available to stay

Sandy in 1977



Sandy at age 40

with Sandy when we call on her. I would encourage parents to take advantage of respite services in their community or find someone that can care for their daughter. Time for yourself and spouse is important.

I would not be truthful if I said the journey to this point has been easy, because it has not. But it has gotten easier as Sandy has aged, and it has certainly had its rewards. All too often we hear of divorce in families with a special child. Sally and I are closer today because of Sandy. We do so many things together that other couples do not. We are friends as well as husband and wife. Sandy is an inspiration to us as well as our families and friends. Her silent stare and beautiful smile has touched many lives over the course of her life. We consider it an honor that God chose us to raise and care for such a beautiful girl. Because of Sandy we have a different outlook on life. She causes us to love and cherish the little things in life that otherwise might be taken for granted. When she looks up at me with those telling eyes and smiles and then rests her head on my chest, it makes so many things in this world seem insignificant.

Lamar & Sally Beaty are the parents of Sandra (Sandy) Beaty. They also serve as the Special Representatives for Adult Population for the IRSF.

Finding the Right Van for our Family

By Joyce Opinsky

After years of lifting Lilly and her wheelchair into and out of the car, my husband and I decided it was time for a wheelchair van. We both had already switched to vehicles that could accommodate her wheelchair, but the lifting was just getting too hard for us and uncomfortable for Lilly. How many times I bumped her poor head getting her into the car!

We visited our local mobility dealer to check out the options. We quickly decided a lowered floor minivan was the best vehicle for us, but were not sure about a side-entry ramp versus rear-entry ramp. We rented both types of minivans for a weekend each. Actually using the van for a weekend was a huge help for us in making a decision – running errands, going grocery shopping, parking at home and out and about. In the end, decided on a rear-entry model with a manual ramp. We bought a slightly used Chrysler van from a local car dealer and then took it to the mobility dealer for the conversion. This was less expensive than buying a new modified van from the mobility dealer.

Both the side and rear ramps had pros and cons, but the Vision rear-entry van was the best choice for us. I also have a 5-year old son and the rear-entry had the most "family" feel to it. Lilly's wheelchair fits between two captain chairs that were remounted to sit closer to the doors so there is room for the wheelchair in the middle. In the side-entry van, Lilly was all by herself in the center of the van and then my son was in the rear bench seat by himself. I joke that I'll regret this layout in a few years, but for now I like have the kids next to each other and being able to reach them both from the driver's seat. Another nice feature of this layout is that someone can sit in one of the captain's seats next to Lilly in case she needs a snack, drink, etc.

Another major decision was manual ramp v. power ramp. With the power ramp, the van "kneels" to lower the vehicle so the ramp incline is not too steep. Since Lilly will always have someone pushing her chair into the van rather than propelling it herself, the steepness of the manual ramp was not a problem. The manual ramp was less expensive than the power ramp and also should require less service and maintenance over time.

Parking and getting into and out the van is really easy with the rear-entry model. I don't necessarily need an accessible parking spot and don't need the extra space on the side for the ramp. Parallel parking is problematic, however. Also, I couldn't get Lilly into and out of the side-entry van in my garage as there wasn't enough room for the ramp and the required turning radius.

We are thrilled with "Lilly's" new van. From quick errands to a summer roadtrip, the van has changed our lives and made it much easier to include Lilly in all our outings.

Grief to Growth Part II

by Diane Ross, MS, LCPC

Part Two: The Growth

In Part One of this article: The Grief, we learned that we all experience grief, when we learn that our child has a disability. Letting go of the 'normal child' and accepting the child with the disability is a process. People experience five stages of grief when they experience such a loss. Those stages identified by Dr. Elizabeth Kubler-Ross are denial, anger, bargaining, depression and acceptance. People may also experience extreme sadness, stress, confusion, disappointment, powerlessness and a sense of rejection for themselves and their child. How does one deal with these feelings and learn to grow from their grief and pain?

First and foremost, it is important to know that you are not alone. Enlist the help and support of others. Express and talk about your feelings - all of them. Don't be afraid to ask for what you need. Seek out support from your spouse, your parents, other family members, your friends, clergy and professionals. One of the greatest resources you will find are other parents. Not just parents of girls with Rett syndrome, but parents of children with other disabilities as well. One of the best things for parents is other parents.

Initially after diagnosis and at other times along your process of grieving it is important to take one day at a time. There may be times when you will have to take things one hour or one moment at a time. Don't expect too much of yourself. Set small, realistic and achievable goals for you and your family. When in crisis stick with your normal routine, to help create stability.

While talking about your grief is extremely important it is equally important to take breaks from your grief and talk about everything but your grief and Rett syndrome. Another effective vehicle for dealing with your feelings is writing about them. Keep a journal of how you feel. Try to write two to three times a week. Crying things out is a way of cleansing yourself of all the hurt and pain that you are experiencing. Laughter is also good for the heart and soul.

Learn as much as you can about Rett syndrome and every aspect of it, that impacts your child. Learn all the terminology that goes along with Rett syndrome and special education. Be sure to request doctors, teachers, therapists and other professionals to stop and explain anything that you don't understand. Knowledge at times can be painful, but it can also be a powerful tool. Seek out programs for your child and support groups for yourself. Ask your child's school to start a parent's support group if they do not have one.

Taking care of yourself is crucial to being available for your child. Take time for yourself, by engaging in physical activity, reading, listening to music, doing crafts or projects and engaging in hobbies or anything else that you enjoy. Take time to recharge your parental battery by taking time away from your child. If you can't separate yourself from your child occasionally you will wear yourself out. Restore, refresh and revitalize with respite. If you don't have any family or friends who are available to care for your child for brief periods of time, contact your local respite agency and get on their waiting list.

One of my personal favorite things to do when I'm having one of those Rett syndrome days that we all have, is to go and do something fun with Lindsey. Sometimes it is going for a walk, watching a movie, cuddling on the couch, reading a book, swimming or anything that is fun and enjoyable for us.

Keep in mind that time does heal. However, the hurt and pain never goes completely away, but it does get better. Always remember that just because your child's development is different, that doesn't make your child less valuable, less important or less in need of your love and parenting. Everyone, including your child has strengths, gifts and abilities to share with others. Your child may very well become your life's greatest teacher.

The International Rett Syndrome Foundation is here for you any time that you need us for information, awareness and support. We are dedicated to helping you meet your needs.

Diane and Mick live in Schaumburg, IL. They have four children; Kristi, 24, Lindsey 22, Andy, 19 and Corey, 13. Diane is a Licensed Clinical Professional Counselor in private practice. She has served as a source of support for hundreds of families of children with disabilities.

IRSF Welcomes Jane Lane, RN

Jane Lane, RN

IRSF is pleased to announce the appointment of Jane Lane, RN, BSN to the IRSF team as Family Support Program Manager starting January of 2009. Jane will work part-time with IRSF, while continuing her valuable work with Rett syndrome families at the Civitan International Research Center at the University of Alabama at Birmingham. Her real world experience of delivering medical care and coordinating research programs for those diagnosed with Rett syndrome makes her an excellent addition to the IRSF team. She will be available to consult directly with families that come to IRSF searching for help with complex medical issues and concerns. Jane will help to expand our current circle of Professional Advisors, and will regularly write about common health issues and their assessment in Rett syndrome. These articles will be published in IRSF newsletters, on the website, and developed into guides for the general medical community.

Jane Lane, under the tutelage of Alan Percy, MD has more than sixteen years experience as a research coordinator and manager in child neurology and the Civitan International Research Center at the University of Alabama at Birmingham, specifically related to the study of epilepsy in neonates and movement disorders including Tourette syndrome, Huntington disease, and Rett syndrome. Jane received a BS in Microbiology from Mississippi University for Women and a BS in Nursing from the University of Alabama. During the past six years she has worked exclusively with Rett syndrome, serving as Project Manager for the Angelman, Rett, and Prader-Willi syndromes consortium of the Rare Disease Clinical Research Network. The Natural History study of Rett syndrome and MECP2 mutations alone has enrolled nearly 700 females and males with the disorder. She has co-authored over 25 publications, many pertaining to Rett syndrome.

Jane serves as a member of the RettSearch

continued on page 19

IRSF Partnership Program

Partnership Pride

By Lisa Hayden

With the pressure of the economy tightening our belts, it may not seem like a good time to spend a little extra money. However, by becoming a Partner you receive quite a few benefits that will help lessen the strain on your wallet.

Gas prices are finally working their way down and now so can the price of the items you purchase at IRSF's online store. All Partners, of any paid level, receive a 10% discount off all IRSF merchandise.

If that isn't enough to peak your interest here are some of the other perks of becoming an IRSF Partner! The website, as informative as it is in its original state, has much more to offer. With your IRSF Partnership you gain access to extra information that the regular site visitor does not see. All that is needed from you is an email address and you instantly become a Corresponding Partner.

There are five levels of the Partnership Program. A Corresponding Partner costs you nothing and you will receive timely E-news alerts and have your contact information added to our private database to enroll you as a member of our community.

Our paid Partnerships vary in price as well as benefits:

Active Partner: $40.00

- Your own personalized International Rett Syndrome Foundation Partnerships Card
- A full year of timely news in the Foundation Newsletter
- Discounts on all foundation merchandise, materials, conferences and educational programs
- Timely E-news alerts
- Special announcements about self help and education programs
- Special Rett syndrome Research updates
- Invitations to local clinics, events and program activities in your area
- Special access to the partners only section of the website

Organizational Partnership: $125.00

- Partnership benefits for 5 individuals within the same organization
- Personalized International Rett Syndrome Foundation Partnerships Card
- A full year of timely news in the Foundation Newsletter
- Discounts on all foundation merchandise, materials, conferences and educational programs
- Timely E-news alerts

Lifetime Partner: $500.00

- Partnership benefits for 2 family members
- Personalized International Rett Syndrome Foundation Partnerships Card
- Personalized Certificate of Appreciation
- A complimentary copy of The RS Handbook, 2nd edition and the Raindrops and Sunshine
- Special recognition during the annual IRSF conference Tribute Dinner
- A full year of timely news in the Foundation Newsletter
- Special announcements about self help and education programs
- Special Rett syndrome Research updates
- Invitations to local clinics, events and program activities in your area
- Special access to the partners only section of the website

International Partner: $50.00

- Your own personalized International Rett Syndrome Foundation Partnerships Card
- A full year of timely news in the Foundation Newsletter
- Discounts on all foundation merchandise, materials, conferences and educational programs
- Timely E-news alerts
- Special announcements about self help and education programs
- Special Rett syndrome Research updates
- Invitations to local clinics, events and program activities in your area
- Special access to the partners only section of the website

Our Partnership Program not only includes the obvious tangible benefits; it also helps us keep the most accurate documentation of our girls within our database. We have perfected the database and are now able to track many different attributes of our girls such as age, mutation, location and more! This makes it easier for us to connect you with other families sharing the same experiences or living in your area.

Join our Partnership Program by visiting our website at www.rettsyndrome.org or by calling the office a 513.874.3020.

IRSF Receives 4-Star Charity Rating

On September 30th, the International Rett Syndrome Foundation was officially notified that we have received a 4-star rating from Charity Navigator, America's largest independent evaluator of charities. Receiving four out of a possible four stars indicates that our organization excels, as compared to other charities in America, in successfully managing the finances of our organization in an efficient and effective manner. The letter saluting our accomplishment noted that this rise in our rating "is an exceptional feat, especially given the economic challenges many charities have had to face in the last year." To learn more about Charity Navigator and IRSF's charitable efforts, please visit www.CharityNavigator.org. A special thank you to our many donors, sponsors, and in-kind volunteers who have helped us earn this prestigious ranking.

Regional Representative Program

Our Regional Representatives have been busy this fall gathering families together and raising funds for IRSF's mission! On behalf of all families, we THANK YOU for all you do to support the families in your region. You are all amazing.

Regional Rep Activities Around the Country

Awareness Day in NJ

Robin Turner, aunt of Danielle (RTT), worked with Leslie Greenfield (Regional Rep for NJ) in getting Governor Jon Corzine to sign a bill in 2007 designating the third Tuesday of every October as Rett Syndrome Awareness Day in New Jersey. The girls and families

were invited to the NJ State General Assembly meeting for a formal resolution. Leslie spoke to the Assembly men and women about Rett syndrome and how important awareness is for helping to find a cure. Diane Gruskowski spoke about her daughter, Danielle (RTT), who passed away. Abigail Genzlinger, 14 years old and diagnosed with Rett syndrome, spoke to the Assembly using her voice output device. She thanked them for listening to their pleas and asked them to "raise their voice" to help all affected by Rett syndrome. Way to go families in NJ!

Dinner at the Ronald McDonald House

Thank you to the family of Alexis Cisneros who hosted a dinner at the Ronald McDonald House in Amarillo, TX in honor of Rett Syndrome Awareness Month! Alexis is pictured with her great grandparents, great aunt, three cousins, one brother and her parents. Way to spread awareness in Texas!

Utah Family Picnic

The Rett Syndrome Families of Utah held their 1st Annual Family Picnic on September 13th. Eight special girls, along with their families, attended. Grandparents and caregivers also joined the group. The girls were stars of the day as they enjoyed bubbles, having their nails done and meeting each other. This group is already excited about their next picnic planned for September 12, 2009.

Swim Party in Missouri!

Enjoying some fun, sun and friendship in MO!

Southern California Picnic

In late October Southern California Rett Families, along with relatives, friends and professionals gathered for the 6th Annual IRSF Family Picnic and Fundraiser. There were over 200 people in attendance which was an all time high! There were approximately 30 girls with Rett syndrome participating that day! After lunch attendees were able to participate in all the fun! Guest could choose from taking part in an arts and crafts activity, games, a bouncer, face painting...and more! The day ended with the annual Angel Auction. This wonderful day brought in over $10,000! Congrats to all involved!

Interested in becoming a Regional Representative?

IRSF is looking for motivated, dedicated and passionate people to become Regional Reps in the vacant states mentioned below. Reps are not always parents of a daughter diagnosed with Rett syndrome. IRSF has grandparents, Godparents and older siblings appointed as Regional Reps country-wide.

IRSF is currently accepting applications in the following states. To apply please contact jendres@rettsyndrome.org

- Alaska
- Arkansas
- Delaware
- Hawaii
- Nebraska
- New Hampshire
- North Dakota
- South Dakota
- Tennessee
- Vermont
- West Virginia
- Wyoming