Foundation for Angelman Syndrome Therapeutics
Raising Hope Through Research
Changing Lives Together
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Designed by Makiko Kanzaki

You had me at hello

by Debbie Guagliardo *Vice-Chairperson for FAST*

I became involved with the FAST organization nearly 3 years ago during the planning of the first FAST gala. FAST had just formed and I was excited to help with the event. At that point, Ainsley Evans was the only individual with Angelman Syndrome (AS) I had met, the Evans's were the only AS family I knew and I didn't really know much about the science, except that Dr. Weeber's research had recently rescued AS deficits in the mouse model. Things would change on December 6, 2008.

Many people have asked me why I volunteer so passionately for FAST and my reasons are threefold.

I don't know anyone with half a heart that can meet an individual with AS and not be affected. The challenges they face on a daily basis are hard to comprehend. They have to work so hard to accomplish things that would be second nature for a typical child. Their accomplishments, no matter how big or small, are truly inspirational.

Deep down, I am an entrepreneur at heart. The opportunity to help build something in its infancy and watch it grow was very appealing. While there are always risks with a "start up", after learning more about the science, I believe in FAST's mission and that its goals are attainable. I believe in its Board of Directors and Scientific Advisory Board members. It's amazing how far we've come in a short time. This is truly an exciting time in AS research and I'm thrilled to be a part of it!

At that first gala, I met several more AS families and was really touched and inspired. I've shared this story before, but at the first gala, Paula called me up to accept an award on behalf of all of the volunteers from LexisNexis, my employer at the time. Shortly afterward, Mike Brockie came up to me and asked if I was with LexisNexis. I said, "yes." He threw his arms around me, gave me a big hug and said, "You have no idea how much this means to my wife and me. We travelled four hours from Michigan to be here and you've given us hope!" I guess you can say Mike had me at "hello"!

Over the past three years I've had an opportunity to meet many of you in person or electronically and what strikes me most and draws

me in is the sense of community. You all have your battle scars and most have been to hell and back. But what is clearly evident is that you always make time to offer advice or to reach out to the person who is struggling with a day or week or year that really hasn't gone so well. The AS community I've met is strong and formidable and they will stop at nothing to do the best for their children, grandchildren, nieces, nephews, siblings, neighbors, and friends. This could not have been more evident in the Vivint Gives Back Project. The AS community is taking the fate of their loved ones into their own hands and making things happen! You are a huge reason why FAST has accomplished what it has in a short time and you can be proud of that!

I am proud to count myself as a member of your community and I look forward to seeing many of you again at this year's gala and to meeting many of you that I only know electronically. And if you can't join us, know that you are with us in spirit and that you are truly a part of something great! ◆

Approaching clinical trials... "What a long, strange trip it's been"

by Edwin J. Weeber, Ph.D.

For those of you who are new to FAST and haven't read previous articles, and/or listened to my anecdotes about my involvement in Angelman Syndrome (AS) research, I would like to walk you down the "short path" of where we were a few years ago, and how a basic science approach has forged an unexpected path to our first upcoming clinical trial to test a therapeutic for AS. My sincere hope is that you will see, as I did, the logical progression the research has taken, how it intersected and very much walked hand-in-hand with the mission of FAST. Our progress has allowed us to form a unique perspective for the future of Angelman Syndrome research and hope for Angels everywhere.

Front Row: **Tricia Ramgoolie, Jennifer Voegler Maggie Dorsey, Daniela Aguirre Raigoza**
Back Row: **Kelly Psilos, Justin Rodgers, Jennifer Daily Erika Donaldson, Joseph Grieco, Edwin Weeber**
From Left to Right

An important turning point for Angelman Syndrome research in general was the paper Dr. Elgersma and I authored in 2007 entitled "Rescue of neurological deficits in a mouse model for Angelman Syndrome by reduction of alpha-CaMKII inhibitory phosphorylation." This paper contained interesting data generated in two different laboratories separated by the Atlantic. However, beyond the face value of the data we presented, was the fact that an enzyme not directly associated with the AS gene (*Ube3a*) was capable of removing all of the major symptoms in the mouse model of Angelman Syndrome. Following the strict definition of a cure (a means of correcting or relieving anything that is troublesome or detrimental), this was a genuine genetic cure of the animal model. This particular method of a cure could never be used for humans with AS, simply because the genetic changes that led to the cure of the mouse model occurred literally before conception. Simply put, the rescued AS mice developed and were born with both the mutation in *Ube3a* and a mutation in a different gene, *CaMKII*, which allowed these mice to be born and mature without the symptoms of AS. What this didn't tell us, is whether or not modifying CaMKII in an individual that already had AS would be of benefit so long after the brain had formed and developed. However, it is believed that this enzyme (CaMKII) is not significantly expressed in the human brain until after birth, so the rescue we saw in the mouse model could represent a "cure" after the development of the brain. It is probable that the developmental processes that form the brain in individuals with AS are unaffected and only after birth does the dysfunction begin to manifest. It is important to note that the term "Developmental Disorders" is used for most cognitive childhood disorders, i.e. Fragile X, Rett Syndrome and Autism, and proposes

that the disorder is linked with the in utero development of the individual. Think about this: the brain is made up of 100 billion neurons making 3–5 quadrillion synaptic connections in order to function. A genetic or environmental insult to that incredible complexity in connections during the formation of the brain is devastating and irreversible. In other words, there is simply no way to rewire a brain that has been wired incorrectly during development. However, if Angelman Syndrome was not a developmental disorder, and the brain formed correctly, then an effective therapy may be possible.

The identification of C-3 has not made us complacent. With the help of FAST, we are continuing to look for other readily available drugs and compounds that can be "FAST-tracked" for use as a therapeutic.

This revelation is not unique to AS researchers. In fact other laboratories studying Fragile X, Rett Syndrome and Neurofibromotosis-1 were reaching the same conclusions with their own unique mouse models; human disorders associated with cognitive disruption were not necessarily due to developmental disruption in the formation of the brain. Our thoughts in the context of this revelation then turned to a very basic question: Could you rescue the cognitive defects in an adult AS mouse, one that has shown the symptoms of AS throughout life, by simply giving it back the ability to make UBE3A? We recently answered this question. To do this we utilized a viral mediated gene therapy strategy. We made an Adeno-Associated viral (AAV) particle containing the *Ube3a* gene. By allowing the viral particles to infect regions within the hippocampus and surrounding brain, we were able to deliver the *Ube3a* gene to hundreds of thousands of neurons in mice with AS. (The hippocampus is a brain structure well known to be involved in learning and memory). After a few weeks we tested the AS mice and found that their ability to learn and remember specific behavioral tests increased dramatically. In fact, we found that the function of the synapses in the hippocampus were almost equal to that of typical mice. The ability to use AAV particles in humans is currently not available and certainly would involve an incredibly invasive procedure. However, as a proof of concept, this research showed convincingly that treatment in the adult mouse model could improve the symptoms of AS. Thus, it should be possible to do the same with human AS patients, and importantly this improvement should be obtainable regardless of age.

This leads us to Compound Three (C-3). The idea for testing FDA approved drugs in the AS mouse was born in FAST as a way to bring a potential therapeutic to use with the greatest speed and efficiency. In light of the success with viral-mediated *Ube3a* gene therapy described above, this was an exciting proposition, but was a high risk–high payoff experimental approach. This is because the typical scientific approach would be to first identify the target for a drug, then pick the potential drug that would work on that specific target if one existed. We are still unsure of the exact molecular mechanisms underlying *Ube3a* deficiency and how it causes synaptic disruption. What was working for us is an intimate knowledge of the mouse model, and a collective meeting of some of the best scientific minds associated with FAST to identify compounds that may be useful due to their known mechanisms of action. We also had to determine parameters of duration of treatment, concentrations of the drugs, method of giving the drugs, etc. Most important was that we were confident a change could be detected following rigorous tests of behavior and synaptic function in an effectively treated AS mouse. Each FDA approved drug that was tested was injected into a group of mice for three weeks. We then tested a number of behavioral parameters affected in the AS mouse: activity, motor coordination and motor learning, associative learning and memory, sensory perception, hearing and anxiety. We also tested the ability for creating long-lasting

What's in a name?

Ube3a, *UBE3A*, UBE3A—What's the difference? Is your editor asleep?

Different text formats are used to distinguish between genes and the proteins made from those genes. Each model system has their own rules, so the formatting can provide clues as to which organism the gene or protein comes from.

In mouse, rat or chicken—the gene is referred to as *Ube3a* while the protein is UBE3A.

In humans and non-human primates—the gene is referred to as *UBE3A* while the protein is UBE3A.

In fish—the gene is referred to as *ube3a* and the protein is Ube3a.

synaptic plasticity (our cellular model for learning and memory). We found that in mice treated with C-3 the motor coordination was nearly identical to typical mice and their ability to learn and remember was increased as well. In addition, we found that the synaptic function in the hippocampus of our treated mice was significantly greater then saline injected mice and equal to that of typical mice. In many aspects, these results were more dramatic than those seen with the gene therapy approach described above! Logic again subscribed that these indications were sufficient to move C-3 to a small clinical trial. We can then use this same scientific method and the rigorous tests and evaluation to determine the efficacy of C-3.

Our laboratory is currently investigating the mechanism by which C-3 can so dramatically affect the AS mouse model in a relatively short period of time. This current research may identify novel targets for other FDA approved drugs, or reveal molecular similarities of AS to other disorders for which a treatment is already available. The future will tell us how effective C-3 is, but the identification of this drug has not made us complacent. With the help of FAST, we are continuing to look for other readily available drugs and compounds that can be "FAST-tracked" for use as a therapeutic. And the long, strange trip continues… ◆

Questions regarding the potential clinical trial

by Rebecca D. Burdine, Ph.D. *Chief Science Officer for FAST*

As you are now aware, Dr. Weeber's group is in the process of gaining approval to conduct a small clinical trial to assess the efficacy of Compound 3 (C-3) as a therapeutic for the symptoms associated with Angelman Syndrome (AS). This has raised excitement and many questions in our community and I hope to answer some of those here, as well as provide other important information you should know.

1. What is a clinical trial?

A clinical trial is a health-related study on human beings. The current clinical trial would be considered an interventional study to see if C-3 has any benefit for relieving symptoms associated with AS. A fantastic website for definitions about clinical trials and other important information is http://clinicaltrials.gov/ct2/info/understand

2. What type of trial will it be?

The exact details of how the trials will be conducted can't be made available to us until the trial has been approved by the IRB (see below). As soon as these details can be released to FAST, we will make them available.

3. What are the different phases of clinical trials?

There are four phases of clinical trials. In Phase I, researchers test a drug or treatment for the first time and determine safe dosages and identify side effects. In Phase II, the experimental treatment is given to a larger group to see if it is effective. In Phase III, the trial expands to large groups of people to confirm its effectiveness and monitor for side effects. Phase IV trials are post marketing studies to obtain additional information. Please see http://clinicaltrials.gov/ct2/info/understand

4. What phase of clinical trial are we in for C-3?

Since C-3 is an FDA approved compound, Phase I has already been completed. The trial that Dr. Weeber plans to conduct would be a Phase II trial. If results from this trial are positive, a Phase III trial will likely be conducted.

5. Where is this trial taking place?

The upcoming Phase II trial will take place at the University of South Florida and Tampa General Hospital. If positive results are obtained, the trial will hopefully expand to other locations in the US as well as other countries.

6. When is this going to happen?

Dr. Weeber and his team hope to start this clinical trial as soon as possible. A team has been established including a neurologist, a psychologist, and a clinical coordinator. The protocol for the trial has been sub-

mitted to the regulatory and ethics authorities (IRB) at the University of South Florida for approval. Once the protocol is approved, they will begin recruiting for the trial.

7. What is an IRB and why do we need their approval?

The Institutional Review Board (IRB) is a group designated by an Institution or University to review and monitor all research involving human subjects. The IRB will go over the protocol submitted by Dr. Weeber's team to be sure that everything is in place to protect the rights and welfare of people who would participate in these studies. In a nutshell, they make sure the clinical trial makes sense to conduct from a scientific standpoint and is as safe as possible for those who participate. Without IRB approval, the clinical trial cannot take place.

8. Who decides who is allowed to participate? How will individuals be selected for the trial?

The general purpose of a clinical trial is to obtain concrete evidence that a treatment is safe and effective and thus worth promoting for all who might benefit. To do this, it is important to have the research subjects you are comparing being as close to identical as possible. Of course, we all know from meeting others in the community that just because two individuals have Angelman Syndrome, it doesn't mean they are identical in their symptoms or their abilities. So for the purposes of a trial, we need to get a group of individuals together that are as similar as possible to be able to compare them to each other and find differences that are meaningful and quantifiable. Thus, Dr. Weeber and his team have decided on criteria that they feel will best allow them to a) recruit enough individuals for the trial and b) be able to see meaningful changes between the individuals not taking C-3 or taking a placebo and those taking C-3.

9. Do we know anything about the age range or inclusion/exclusion criteria?

Unfortunately, no. Until the IRB approves the protocol, everything is subject to change. What is not likely to change is that to participate you must have a confirmed molecular diagnosis of AS. Additionally, if you are already participating in another clinical trial for a therapeutic compound, you would not be eligible to participate in the trial for C-3.

10. My child is already in a clinical trial, but I want to be in this one. Should I drop out of the current trial we are participating in?

No! First, if you are currently participating in a clinical trial, it is incredibly important that you finish the trial. The only way we will know as a community what does or doesn't work for our loved ones is to have proper clinical trials conducted. We are a small community given our rare disease status and that makes it even more difficult to get enough participants and data to prove that a treatment is working. If you were to drop out of a clinical trial, it would make it harder for that trial to obtain enough information to reach a conclusion that could be instrumental in providing safe and effective treatments for the entire community. Plus, if you were in a recent treatment trial, you would likely be excluded from another one even if you did drop out because they would be too close together and, thus, could influence the results the current C-3 trial might obtain. Additionally, you would need to discuss stopping your participation in a current trial with the investigators of that trial to ensure that the proper procedures are followed since stopping some medications can produce side effects.

11. What is the approximate time frame of a clinical trial?

Clinical trials can take from just a few weeks to years to complete depending upon the treatment, mode of action, and results. In this case, C-3 was shown to provide relief of symptoms in the AS mouse in just three weeks of treatment. Thus participation in this clinical trial will likely last a few months since we expect to see some benefit within weeks or months.

12. Should I move/take out a mortgage/sell my car to participate in this trial?

Absolutely not! We don't yet know if C-3 is going to work. While we need participants for this trial, we do not want anyone to put themselves or their family into financial difficulty to participate. This trial is going to be relatively quick in duration, and Dr. Weeber has agreed that the data they receive will be shared as quickly as possible so that more clinical trial sites can be established. You will not be missing the only opportunity to participate in a clinical trial. If there is true benefit in taking C-3, we will make sure you know about it as soon as possible.

13. If this compound is FDA approved, why should I participate or wait on this trial? Can't I do this on my own?

This is a tough question to answer, but the main reason is that if C-3 works, we want it to be available to ALL individuals with AS all over the world. The only way that will be possible is to have concrete scientific data from a controlled clinical trial to present to the medical field as a whole. While you may have a relationship with your doctor that could allow you to bypass the wait for results, the vast majority of people do not have this available to them. So if you are willing to have your loved one try C-3, we would strongly encourage you to participate in the trial so that the results become available for everyone. Again, if the trial is successful, we would hope to see it expanded to more areas in the US and across the world so more people can participate. Additionally, the trial will also assess any potential negative effects of C-3 which will be most evident in a controlled clinical trial setting. It's hard to say, "Please be patient and help us do this the right way," but that is the only way we will be able to help everyone. Additionally, we don't know the mechanism of action of C-3. We do know that C-3 from one particular company seems to be more potent. You want to have your loved one receive a safe and effective therapy that has been tested and proven. The most beneficial way to get the right compound at the right dose is through the trial.

14. Do we know what C-3 is doing? How will it work?

We don't actually know the mechanism of C-3 at this point. Researchers in Dr. Weeber's lab are working to determine why C-3 rescues the AS mouse. Fortunately, since this compound is FDA approved and has very few side effects, we don't have to know the mechanism before moving forward with a clinical trial.

15. Does it affect methylation or activate the paternal UBE3A gene?

Dr. Weeber's team has looked at this and it does not appear to be working through activation of the paternal UBE3A gene.

16. Will Compound 3 work on all genotypes or is it specific to one?

Since we don't know the mechanism by which C-3 is functioning, we can't say for sure. But since it isn't specifically targeting UBE3A, there is no reason to think it will not be effective for all genotypes and potentially clinical cases.

17. Will Compound 3 help individuals of all ages?

Honestly, we don't know. But there is no reason to think that if C-3 is effective in AS, that it won't be effective in individuals of all ages. Think of it this way. We all know that individuals with AS continue to learn and grow throughout their lives. The potential to learn doesn't end when they become adults. If C-3 allows neuronal functioning to improve such that learning and memory improves, there is no reason to think this won't help everyone with AS at any age.

18. What genotype was the mouse?

The AS mouse model Dr. Weeber uses contains a small deletion specifically in the UBE3A gene. It would be most similar to patients with mutations or small deletions in UBE3A.

19. Were there any apparent side effects to Compound 3? If so, what were they?

We don't have any information on potential side effects at this time.

20. Also, how is the drug going to target the areas in the brain required?

The compound is known to cross the blood-brain barrier, so ingestion of the compound will be enough to allow it access to the brain. Recent work has determined that UBE3A is imprinted throughout the brain, so there is no need to target a specific region. In fact, it will likely be better to have it in all regions.

21. Does any of this fit in with Dr. Weeber's work on CaMKII and Reelin?

So far there is no indication that C-3 is working through CaMKII or Reelin.

22. Is the treatment a one time occurrence or is it ongoing? If more than one treatment is required, what is the frequency of the treatment?

Given that C-3 is a compound, it is likely that a treatment would be ongoing. Likely a daily dose would be required, but this is a question that the clinical trial will help to answer.

23. Once the trial is completed and Dr. Weeber has compiled all his data, what is the typical amount of time for FDA approval for broad usage of the drug?

It depends upon the results from the trial and how compelling they are. If positive results are obtained, then a larger Phase III trial would be initiated. If the results continue to be positive, the company producing C-3 would apply for approval to expand the use of C-3 to Angelman Syndrome. Dr. Weeber has agreed that his team will be as open as possible with the results of the trial so that we can help as many people as quickly as possible.

24. What if C-3 doesn't work as well in humans?

It is important to remember that mice aren't humans. I know that sounds like a ridiculous thing to say, but there have been a number of compounds that look great in the mouse model that do nothing once they progress to human clinical trials. So we use the mouse to give us some indication of whether or not a drug or compound might be effective, but we need the clinical trial to be sure that what helps a mouse brain function better will also help a human brain do the same. But some reasons for optimism include the fact that C-3 has already been shown to have some benefits in other human cognitive disorders. In fact, that is one of the reasons Dr. Weeber was asked to test C-3 in the first place! In addition, C-3 isn't the only compound that Dr. Weeber has tested that has shown benefit in the mouse model. Research presented this summer also indicates that multiple laboratories are identifying compounds that may work in AS. FAST isn't waiting to see if C-3 is going to work, we're already pushing to find other compounds and we won't rest until we have the right one to help everyone with AS.

25. How can I stay informed about clinical trials?

To find active clinical trials you can search at http://clinicaltrials.gov/ct2/home

You can also register at http://rarediseasesnetwork.epi.usf.edu/arpwsc/takeaction/index.htm

Click on Join the Registry.

26. How will I find out about the C-3 trial?

Dr. Weeber's trial will be posted on clinicaltrials.gov when he gets IRB approval and begins recruiting. FAST will also e-mail our membership base, post details on our website, and post announcements on Facebook and the AS listserv. ◆

Becky would like to thank Kristi DeHaai M.S., Steve Skinner M.D., and Ed Weeber Ph.D. for helpful comments on her articles for this newsletter.

Opinion piece—clinically important

by Rebecca D. Burdine, Ph.D. *Chief Science Officer for FAST*

In 1965, Dr. Harry Angelman published his seminal work describing three children with "a superficial resemblance to puppets" due in part to their "jerky movements". This is considered one of the earliest reports of a "behavioral phenotype" based on the recognition that these children shared a happy disposition and easily provoked laughter. Based on these characteristics, researchers in 1967 modified the name to "Happy Puppet" syndrome. But in 1982, Drs. Charles Williams and Jaime Frias proposed the name "Angelman Syndrome" as being more appropriate and respectful.

In 1982, all individuals with Angelman Syndrome (AS) were clinically diagnosed. It wasn't until 1987 that research determined that a deletion on Chromosome 15 was associated with AS. By 1989, it was recognized that deletions associated with AS were on the maternal chromosome and, in 1991, paternal uniparental disomy (UPD) was recognized as a cause of AS. Armed with this information, tests were developed to look for the deletions and other known chromosomal differences that indicated a diagnosis of AS was appropriate.

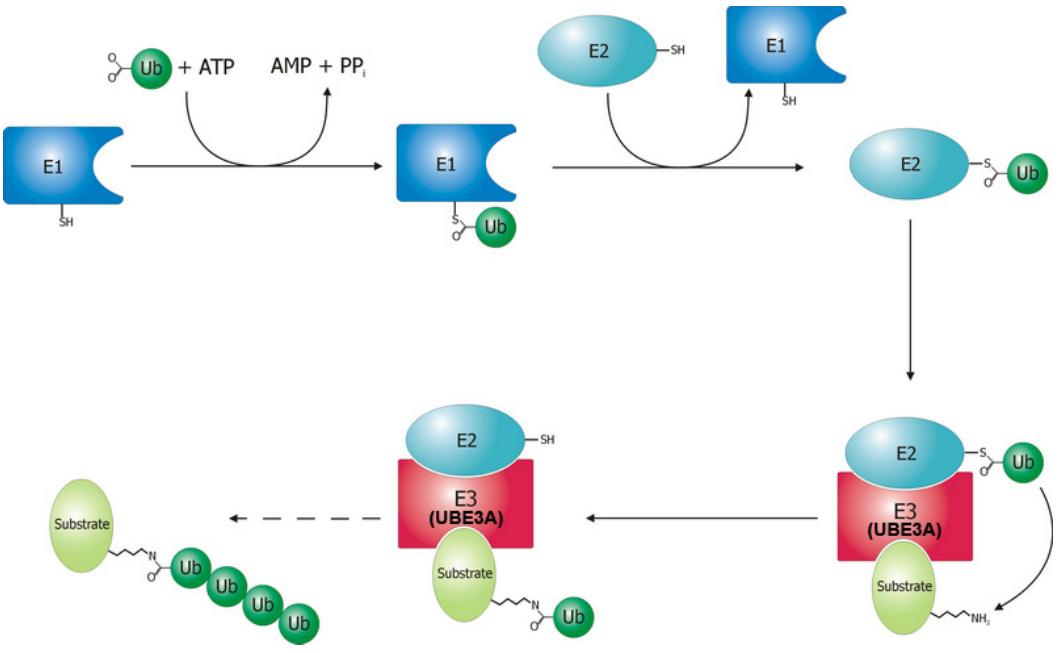
However, this left approximately 17% of the remaining clinically diagnosed individuals at that time, without confirmation that the syndrome they had was indeed caused by defects somewhere on chromosome 15. But these individuals would hold the key to understanding AS at the molecular level and put us on the path to a therapeutic that we are on today. That is because some

of these individuals were carrying mutations specifically in the gene that causes AS. Many of these families were gracious enough to provide samples for researchers to study and, in 1997, several groups reported that mutations in the gene *UBE3A* were underlying Angelman Syndrome. With this knowledge, researchers were able to create the first AS mouse model we use today to study the function of *Ube3a* and to test potential therapeutics. This knowledge allows researchers to target *Ube3a* expression and function in their studies looking for potential therapeutics. The critical results demonstrating that AS could be genetically cured in the mouse model came within a decade of the first reports on *UBE3A* as the gene underlying AS, an astonishingly fast time-frame for basic science research!

Today, there are still individuals with a clinical diagnosis of Angelman Syndrome who do not have identified mutations in *UBE3A* or other known alterations on chromosome 15. I have been asked what the future holds for these individuals in terms of therapeutics we might uncover in our supported research. Are we going to be leaving these individuals with AS behind?

Of course, I don't have a crystal ball so I can't say what the future will hold. But what I can say is that the current compounds tested in Dr. Weeber's lab are not compounds directed at turning on *UBE3A* expression. Thus, there is no reason to think that this compound won't be helpful to anyone with AS. In addition, we don't know if the remaining clinical cases of AS have reduced *UBE3A* expression in their neurons or not. If they do, then strategies aimed at increasing and controlling *UBE3A* expression may be helpful for these cases as well.

Perhaps more academic, it is possible that the current clinically diagnosed individuals hold the key to finding the best therapeutics. Think about the role of UBE3A in cells. UBE3A is a ubiquitin ligase. What this means is that UBE3A recognizes specific proteins in cells that need to be degraded or modified and adds a small protein called ubiquitin onto these targets. You can think of UBE3A as an overseer that looks down a list of specific proteins, finds them, and then adds ubiquitin onto them like a stamp. These ubiquitin stamped proteins are either moved to new locations or taken to the dump and dismantled. UBE3A does its job with other proteins including E1 and E2, but since it is an E3 protein its job is to recognize the specific targets that will be tagged. This is reflected in the name of the protein: UB-ubiqutin, E3-type of protein, and A-to distinguish it from other described E3s of this type (UBE3B and UBE3C). In AS, we assume that there are targets of UBE3A that are not being tagged with ubiquitin, and this may lead to buildup of proteins that should be dismantled, or lack of proteins in the appropriate locations to do their jobs.



E1 and E2 proteins bind ubiquitin (ub) and bring it to an E3 protein. E3 proteins find their targets or substrates and add ub onto them. This typically marks the substrate for disposal by the cell. The protein affected in AS, UBE3A, is an E3 protein and thus recognizes specific targets. We do not know how many targets UBE3A recognizes or how many are important in AS.

The problem is, which targets of UBE3A are the ones that cause the symptoms of AS? All of them? Only a subset of them? Are there one or two targets that are the most critical and thus would be the best proteins to study to find therapeutics? The answer to these questions may lie in the current clinical cases of AS. These individuals may have mutations in the most important targets of

UBE3A. That knowledge could unlock even more doors towards effective therapeutics with the lowest number of side effects. For example, if the important target of UBE3A is protein Y, then maybe we need to focus on controlling protein Y. If protein Y is the most critical, then focusing on protein Y would be the best bet for a complete cure for AS in all affected individuals.

So what should you do if your loved one has a clinical diagnosis? If you haven't explored testing beyond looking for deletions or methylation status to identify UPD or imprinting defects, it may be worth talking to the doctor about what new testing is available and what would be covered through insurance. There are also many syndromes that have all the symptoms of AS, but are actually caused by known mutations in other genes. We are keeping a list of potential differential diagnoses on our website (www.cureangelman.org/what-differential.html). Some of these differential diagnoses have specific health implications for your physician to consider, so it is worth testing for these even if your loved one is an adult to insure the highest quality of care.

For the remainder, it is my hope that research will continue to explore the mechanisms causing AS in our current clinically diagnosed individuals as they could provide the most important information of all in our quest to understand Angelman Syndrome.

(Does your loved one have a clinical diagnosis of AS? We'd love to hear from you so we can keep you informed of research that may be of specific importance to your loved ones.) ◆

For more information on the genetics of Angelman Syndrome please see our Genetics and Testing FAST FAQs and the articles in GeneReviews.

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www.omim.org/entry/105830

Meet our new postdoctoral fellows

The path to running a research group is a long one. Scientists are first trained in graduate school to obtain their doctorate degree in their chosen field. In the U.S. this can typically take four to seven years. After graduation, scientists typically do another three to six years of training beyond their graduate work, called a "postdoc", to expand their skills. Most often, the work conducted during the postdoctoral training time determines the work that scientist will focus on in their own research group. To be competitive for a position to run a research group, the postdoctoral researcher must focus intensely on their project and produce publishable results. To help increase the number of talented and dedicated researchers that will be focusing on Angelman Syndrome research in their careers, FAST is providing fellowship awards that will cover the salary and experimental costs associated with postdoctoral research. These fellowships also provide travel funds to allow the fellows to attend scientific meetings to present their work and learn about the recent advances in the field. By obtaining one of these fellowships, the researcher can focus exclusively on their work and not spend time they could be using for research on writing grants to obtain funding. This will allow these researchers to get a jump on the competition and make them more competitive for research positions in the next few years.

In December of 2010, FAST issued a call for proposals from postdoctoral researchers interested in pursuing careers in Angelman Syndrome research. Applications were reviewed by our Scientific Advisory Board and their recommendations were passed on

to the Board of Directors in May 2011. Awards were made in June to two outstanding individuals whose projects particularly impressed the review panel with their potential and their relevance to the mission of FAST. With these awards, FAST has allocated $200,000 towards furthering the careers of two exceptional scientists.

Please welcome our two newest members of the Angelman Syndrome research team!

Jason Yi, Ph.D.

The Christina Castellana Postdoctoral Fellow
University of North Carolina — Chapel Hill

Mentors: Drs. Klaus M. Hahn and Benjamin D. Philpot

Title: Targeting Upstream Regulators of UBE3A in Angelman Syndrome

1. Where did you do your graduate training and what did you work on?

I completed my graduate work at Duke University under the mentorship of Dr. Michael Ehlers, who is currently the head of Neuroscience for Pfizer global research. My work identified patterns of growth factors in the developing embryonic brain that shape how the brain is wired.

2. What interests you about research into Angelman Syndrome?

From a scientific standpoint, Angelman Syndrome is unique in that a single gene is responsible for the disease. This allows us to focus on UBE3A knowing that we can solve Angelman Syndrome if we can understand enough biology about UBE3A and the enzyme that it encodes. It was clear to me that significant breakthroughs in understanding and treating Angelman Syndrome could be made if we could answer some fundamental questions about the biochemistry of UBE3A in the brain.

3. How will this funding help you to focus on your research?

I am grateful for the award from FAST. Research funds are always scarce, and this generous award solidifies my project for an extended period of time and allows me to devote my full attention toward my research into the root synaptic causes of Angelman Syndrome.

4. How does your funded project help FAST advance towards potential therapeutics for Angelman Syndrome?

My research aims to answer a basic question about the enzyme encoded by the UBE3A gene, namely, how is it turned on and off in neurons. With this knowledge, we can begin to map how UBE3A functions at synapses and understand how its absence or dysfunction changes the molecular composition of synapses. Ultimately, this knowledge will provide various pharmacological targets that may useful for the treatment of Angelman Syndrome.

Justin T. Rogers, Ph.D.

University of South Florida

Mentor: Dr. Edwin J. Weeber

Title: Exploring FDA Approved Therapeutic Strategies for the Treatment of Angelman Syndrome

1. Where did you do your graduate training and what did you work on?

I received my B.S. in chemistry and biology from

Walsh University in Canton, Ohio in 2001. In 2008, I received my Ph.D. from the University of Kentucky. In Kentucky, I concentrated my focus to neuro-pharmacology with a specialty in electrophysiology. Specifically, my focus was on how estrogen affected certain calcium ion channels and cognition in the aging female brain. My research found that estrogen replacement in mid-aged female rats protected them from cognitive impairments associated with aging. Estrogen replacement also prevented the shift in different forms of synaptic plasticity that are related to aging and associated with cognitive impairments in female rats as well. These effects may be directly related to my findings that estrogen directly regulates voltage-gated calcium channels in the hippocampus.

2. What interests you about research into Angelman Syndrome?

Being associated with Dr. Edwin Weeber's lab has given me the opportunity to meet with many of the Angelman children and their families. These experiences, especially interacting directly with the children, really gives you a drive to move forward and try to come up with new ideas and insights that may lead to a future cure, if not, a therapy that leads to improvements in their mental and physical states. What interests me as a scientist is that this condition in mice was genetically rescued through calcium-dependent processes in the brain. With my background in calcium research, this puts me in a unique position to try use my expertise to really advance the field in this area of research.

3. How will this funding help you to focus on your research?

This funding is a huge boost both to my personal research and future career. Research in the Weeber lab is funded through a variety of grants, which I was paid from. As such, I had to complete the work that is scheduled on the grants. This grant allows me to become freer in my research. It allows me not only to focus on a more specific area of Angelman research, but allows me to develop my individual research unique from the Weeber lab. This individual research makes it easier for me to become an independent researcher and eventually become promoted to assistant professor. Also, having my own funding makes the proposition of hiring me for a tenure track more appealing.

4. How does your funded project help FAST advance towards potential therapeutics for Angelman Syndrome?

There is a growing consensus in the scientific community that a treatment for Angelman Syndrome (AS) is not just possible, but very probable. However, the lack of known therapeutic targets at the cellular level that underlies the mechanisms of AS has hampered the development of therapeutic strategies. Couple that with the laborious and timely task of obtaining FDA approval once a therapeutic strategy is found, it quickly becomes evident that a treatment for AS obtained from a novel untested compound or drug is years or maybe even decades away. With these roadblocks in mind, this proposal tries to circumvent both of these deficiencies in regard to successfully and responsibly developing a therapeutic strategy for the treatment of AS. In this regard, this proposal does not focus necessarily on understanding mechanisms of AS, but rather using what is already known about these molecular mechanisms for a strategy to treat AS. Two main concepts were taken into consideration when I developed this proposal, shortening the time to elucidate the underlying mechanisms of AS and shorten the amount of time to have a therapeutic strategy FDA approved. This was accomplished in two ways: 1) use pharmacological agents that are known correlates to counter the molecular or cognitive deficiencies involved with AS; 2) use pharmacological agents that are already FDA approved for use in humans and have an established treatment regimen. The use of these two strategies will significantly reduce the amount of time from experimental testing, to preclinical evaluation to a working and publicly available treatment for AS. To test the validity of these compounds, the AS mouse model will be used and four compounds tested and compared to wild-type mice at the levels of: 1) degree of cognitive enhancement; 2) rectification of biological and genetic abnormalities; 3) increases in neuronal connectivity and neuronal efficiency. It is my hope that one of these compounds will have a positive effect on one or more of these aspects that underlie AS. Furthermore, any and all positive results will prompt a full preclinical evaluation of the compound(s) and could potentially lead to the development of an effective AS therapeutic strategy. ◆

Thoughts on the word "cure"

by Rebecca D. Burdine, Ph.D. *Chief Science Officer for FAST*

"Hope! of all ills that men endure, the only cheap and universal cure."
—Abraham Cowley, poet

We are in exhilarating times, moving forward with research and clinical trials to find a therapeutic to treat Angelman Syndrome. Yet some have asked if we can ever really "cure" Angelman Syndrome (AS) and have claimed that use of the word "cure" is misleading. I'd like to argue that it isn't misleading, and is in fact, very appropriate.

By definition, a cure is:

(1) Restoration of health; recovery from disease.
(2) A method or course of treatment used to restore health.
(3) An agent that restores health; a remedy.
(From the American Heritage Medical Dictionary, 2007)

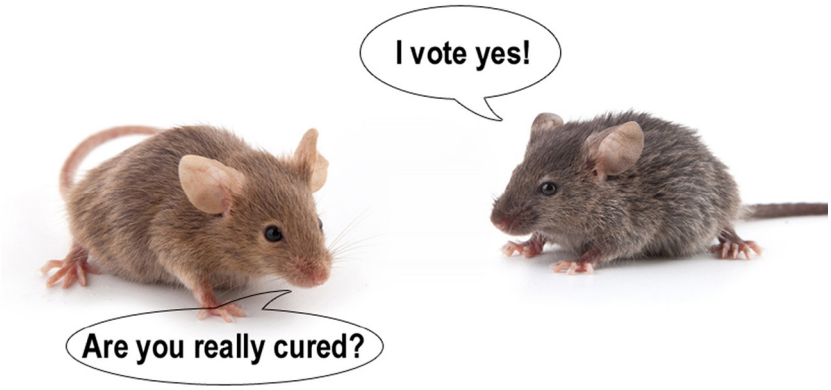
Therefore, if we find a therapeutic that would eliminate seizures, restore proper muscle tone, and allow for proper neuronal functioning in individuals with AS, we would be fulfilling the definition stated above.

I will admit that I have argued in the past that since we can't repair the underlying genetic lesion we can't truly cure AS. But the more I have thought about the issue, the more I realize that cure really should refer to the relief of symptoms as opposed to the correction of chromosome 15 at the DNA level. I think we should all feel comfortable saying that we are looking for a cure, and that we are well on our way to finding one.

Others have argued that the word cure can only refer to the correction of the genetic lesions that cause Angelman Syndrome. If that were possible to accomplish, it would likely produce a restoration of health. But we currently do not have the technology that would allow us to repair the DNA in each and every neuron in the brain of affected individuals. But is this really the only outcome we should be allowed to brand a cure?

I would argue that this shouldn't be the case. First, if researchers are successful in finding methods to reactivate and restore UBE3A levels in the human brain this would likely allow neurons to function correctly. In this scenario, one would hope that individuals would recover from the more devastating symptoms of AS such as seizures. In terms of protein composition and function, the neurons from those with AS in this scenario would be indistinguishable from neurons from those without AS. Yet, the underlying DNA lesion would not be corrected. Still, it should be permissible to call this a cure given that the underlying biochemical issue has been corrected. Second, if the current compounds being studied by Dr. Weeber allow the neurons in individuals without UBE3A to function as well as neurons with UBE3A, this too would also allow for restoration of health and recovery from the symptoms of AS. Again, a correction of neuronal function is by definition, a cure.

What about the argument that the paper from the Elgersma and Weeber laboratories showing that mutations in *CaMKII* could rescue the AS mouse is not a cure? Some argue this isn't really a "cure" because it prevents the symptoms of AS from ever emerging as opposed to recovery from symptoms. While true, the mere fact that altering CaMKII activity could prevent the loss of UBE3A from being deleterious is astounding and pointed us to the idea that the issues in AS are biochemical in nature and not developmental. The new work reported in this newsletter by Dr. Weeber demonstrates that UBE3A delivered to mice *who already exhibit symptoms* can allow them to recover from those symptoms, again underscoring the idea that the defects in AS are biochemical in nature and can be cured with an appropriate method (therapeutic).



But should we be looking for a cure at all? I have had interesting discussions about this point with many people. I think everyone should realize that we aren't looking for a cure because our children or loved ones

are unacceptable the way they are. All of us have experienced the struggle of getting others to recognize the wonder and perfection that our loved ones embody. I am not arguing that my daughter Sophie needs a therapeutic so she can be a more acceptable person. I am searching for a cure because I do not want to stand in another emergency room watching the medical staff trying treatment after treatment to stop her seizures while she is in status. I do not want to read another Facebook post about losing one of our community members to seizures or to illnesses that they were unable to alert their caregivers to.

We already treat the symptoms of AS every day. We give anti-epileptic medicines to control seizures. We engage in therapies to help improve muscle coordination, fine motor skills, and balance. We opt for surgeries to allow our kids to retain their mobility when their spines curve or their tendons tighten to the point of altering their quality of life. Finding a therapeutic would be very similar in that we would hopefully eliminate or severely curtail the symptoms that reduce the quality of life in our loved ones.

But the fact remains that the person I want to have this discussion with is too young and unable to really tell me how she would feel about me seeking a cure for her condition. So I turned to a young woman who could tell me exactly how she feels. Harli is a talented young woman with AS (deletion +). She is able to communicate using her typer and a whiteboard, so I asked her mom Tami to see what she thinks about this issue. Here is what Tami conveyed about that conversation and it is repeated here with permission from Tami and Harli.

"I explained to Harli that some people are afraid that persons with Angelman might feel like we don't think they are good enough the way they are, or that we want to somehow 'fix' them as though they are broken if we try to find a cure or a real treatment. I then said to her 'So Becky and I want to know from you what you think. What do you think about a cure for Angelman? Do you think it's wrong? Does it make you feel bad to hear us talk about curing Angelman or finding a treatment for it?'

She thought about it for an hour or so, I guess, as she just remained very quiet. Eventually she motioned to me she wanted to talk. So I got her typer ready for her an ohhhh you should have seen her rhythm!! She was reallllly into telling me her thoughts on this. At one point she stopped and just looked at me then grabbed me for a hug. I asked her if she had too many words screaming in her head again, and she nodded YES! haha!

Harli says sometimes she has so many things to say and her body will mess up and she can't type as fast as she wants

After about 6 minutes though, she got it all out.

Here is what she said…

'i want to be free on the outside it not mean i dont still be me. tell becky it ok to stop angelman from reaching in my mind. i need to be all of who i am.'"

Harli, I want to say, "Thank you!" for sharing your thoughts with me and everyone. I also want you to know that FAST will not rest until we have done everything we can to help you with your goal. ◆

Jamie Berkley Memorial Tournament

September 23, 2012

On September 23, 2012, Jason and Cindy Berkley will host the first annual Jamie Berkley Memorial Tournament. The tournament will always be held on September 23rd, in order to remember and honor Jamie. We will post additional information on our website as it becomes available. ◆

Jamie & Jason Berkley

The turning point

by Paula M. Evans *Chairman for FAST*

I think the summer of 2011 will forever be remembered in the Angelman Syndrome (AS) community as the summer that changed everything. Not for any one particular reason, but rather a culmination of events.

FAST had funded research earlier in the year and the results of that research had started coming in during the early summer months. It was astounding—Dr. Weeber's research had identified an FDA approved medication that restores cognition and motor function in the AS mouse model!! If we could secure the proper funding, we were looking at a human clinical trial on the first-ever potential treatment of Angelman Syndrome that was shown to be effective in the mouse model. During this same time period, the AS community was in the throes of the most exciting, nerve-racking, and meaningful contest of our lives. Our little known organization stood to win a lot of money for this little known disorder and we were completely crazed by the prospect of winning.

By August, the Angelman community had come together and embraced the unthinkable, envisioned the unattainable and achieved the impossible. We built virtual bridges around the globe, joined hands with our fellow families and came together as one; stronger and more united than ever imagined. We wanted the world to know what we were doing and how formidable we had become, but how? How could we let the world know we were on the brink of something amazing, something powerful, something transformative? The answer was simple; send a text message to our friend Colin Farrell who was walking into a taping of Late Show with David Letterman. "Hey Colin, can you give us a shout-out? We're winning this amazing contest that would pay for a human clinical trial and we want everyone to know about it." The response, "Consider it done." I was thrilled when after the taping Colin messaged me saying he thought it went really well. However, you never know what will be edited out of a show like that until you actually see the finished product. So, on August 4, 2011, the Angelman community sat glued to their televisions at 11:30 PM EST.

Out came Colin, the first guest, and we were on the edge of our seats. He did not wait for an opportunity, he created one. When David Letterman asked about his family, Colin blurted out, "Just a quick shout-out if I can…" It was brilliant. David Letterman asked several

questions allowing Colin to discuss Angelman Syndrome, FAST and Dr. Weeber more so than the movie he was there to promote. And wait a minute, but was that the FAST website address, displayed boldly on the bottom of the television screen? Why yes, it was!!!! You can watch the video of Colin Farrell on Late Show with David Letterman here.

Despite the late hour, as soon as Colin finished speaking about AS and FAST, all three phones in my house started ringing and emails were coming into FAST faster than I could count. The subject line of each email read 'Thank you for your gift to FAST'. Donations!!! Donations coming in every minute—it was amazing. Facebook blew up with posts from parents rejoicing in hearing the words 'Angelman Syndrome' and 'CureAngelman.org' on a major television show. There was no stopping us now and Colin was speaking to me about other publicity opportunities to raise awareness and funding for Angelman Syndrome and FAST.

The community went on to win that contest for FAST and between the Grand Prize and the donation matching period, FAST received just over $290,000.00, more than enough to fund our first-ever human clinical trial for a potential therapeutic. FAST is providing the funding to explore other potential treatments for Angelman Syndrome and FAST continues to maintain relationships with highly recognizable names such as Yahoo!, Colin Farrell, and Hulu as we explore additional opportunities to raise awareness and funding for Angelman Syndrome.

You know when historians look back at a certain moment in time and say that was the time that everything had changed? The Angelman community is actually witnessing such a moment. Yeah, the summer of 2011 was pretty spectacular. Together, we accomplished some amazing feats. But, you know what? FAST and the Angelman community know that the best is yet to come. ◆

What I did this summer

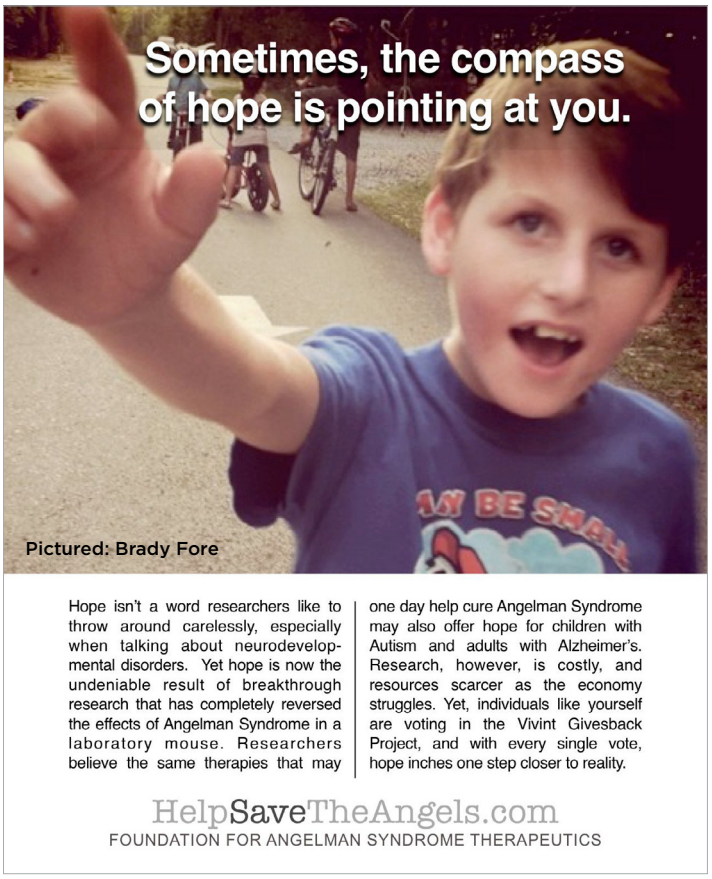
by Tina Thompson

"What did you do this summer?" is a common question. Answers typically include things like fun, family, vacation, friends, laughter, adventure or bonding. My summer contained all of those elements and more. Indeed, it was life-changing.

Really, my "summer" started last spring, on April 27 to be exact. That was the day that Yvonne Hamrick nominated FAST in the Vivint Gives Back Project. The contest consisted of two phases—the top 20 endorsed charities in each region at the end of Phase 1 would move onto Phase 2, at which point the charity with the most votes overall would win $250,000 and the remaining top charity in each region would win $100,000. Throughout Phase 1, FAST steadily gained support and made it through the nomination phase as the Central region's top endorsed charity. However, Debbie Guagliardo was monitoring the numbers at the end of Phase 1, and we realized that our approximate 400 votes per day weren't going to cut it if we wanted to win the grand prize.

On June 12, the day after Phase 1 ended, Yvonne created the Facebook group "Help FAST to win!!!" Phase 2 began on June 14 at midnight Eastern Standard Time. Within minutes, FAST was propelled to the top 10 overall. The "Help FAST to win" page was on fire with all the posts by supporters. By 1 p.m., Pacific Standard Time, FAST had logged 1000 votes and was momentarily in first place. Within a few more hours, Cherubs and Team Sanfilippo Foundation ("SF") from the Eastern region emerged as FAST's main challengers. By the end of the first day, FAST logged 1500 votes. Over the next few days FAST remained in the top three cluster, but tended to drop to third place more often than not. Much of the community became obsessed with constantly checking the numbers, rankings and group message posts, and panicking whenever we dropped within the top three.

On June 15, Marcel Cairo, a friend and supporter of the Angelman community, worried about our collective sanity and offered the following bit of advice in order to keep us from obsessing too much: "Ladies and Gents, I am going to offer an opinion, which on day two, might sound defeatist or negative, but is merely offered to provide some needed sanity and clear thinking here. If the charities in position #1 & #2 can keep up their current pace over the next 7 days, it will be extremely difficult to beat them. At that point, this group should either consider promoting the competition offline (i.e. getting out the vote at church, malls, events), or being happy to win $100,000 as regional champ. I think a few people on here are going to either lose their minds or fall into a deep depression if they try to chase down a leader that can't be caught. Just looking out." A few hours later, possibly realizing that he could not talk us out of obsessing, Marcel decided to join the insanity and help our efforts by creating the website www.helpsavetheangels.com as an easy way to remember where to go to vote. Then he began creating memorable promo ads for us to use to promote the contest to our friends.



Poster by Marcel Cairo

We became a begging, tweeting, pleading, posting, voting machine as FAST, SF and Cherubs broke away from the rest of the pack and remained in the lead. FAST received a boost on June 16 when the Colin Farrell fansite asked its readers to vote for FAST. As of June 19, we received an aggregate of 10,000 votes, surpassing our entire vote total for Phase 1 in less than a week's time. Debbie Guagliardo began posting the

daily number count each evening and checking for the numbers post became a nightly ritual for me and much of the community.

Around this time, I "added" my father, Hardy Zantke, to the "Help FAST to win" group. I had already recruited his support and he was busy roping all of his friends into voting for FAST as well. My father quickly started posting and urging, err, pushing, err, commanding people to not only vote for FAST but to get busy getting their friends and family to vote for FAST as well. If you know my father personally, you know that he has a thick German accent and it is easy to forgive him if he doesn't always choose the most eloquent way of requesting assistance (in fact, my father told me that "requesting" someone to do something is incredibly pushy, as that word sounds like a command, so his knowledge of the intricacies of the English language may not always be accurate). However, online, in black and white text, there was no charming personality behind his demands, so I was a bit scared when I first saw him post online. Fortunately, the community embraced my dad as the whip-cracker that they needed to get out the vote and did not shun my family as a result.

By the middle of June, FAST and SF managed to break away from Cherubs, but SF and FAST continued to change leads, SF often gaining overnight and FAST taking back the lead during the day. One weekend towards the end of June, FAST suddenly made a bigger gain on SF. Throughout the weekend, we speculated and worried whether the lead would slip away again come Monday, but it never happened. The lead continued to vary, sometimes less, sometimes more, but the lead remained. During this time, whenever my father and I saw each other or spoke on the phone we would simply greet each other with a number "172!" for example, and we each understood that whatever number we just reported was FAST's lead over SF. This was also the time that my dad began pushing us to go international by contacting all Angelman Syndrome support groups that we had contact information for worldwide.

On June 27, we managed to crack 3,000 votes in a 24 hour period. Right before the Fourth of July weekend, Michele James, the mother of a young woman with Angelman Syndrome, was part of a news story that aired about Angelman Syndrome and the Vivint contest. Then Debbie Guagliardo, Paula Evans and Linda and Billy Yoakam handed out flyers promoting the Vivint contest at their local Fourth of July parade. In fact, Debbie Guagliardo had been tweeting for votes so much that she was temporarily suspended from twitter. On July 3, the community celebrated online as our lead over SF hit 1,000 votes.

In late July, the community was rocked by the news that young Brady Fore was hospitalized with life-threatening seizures. The community was united even more through Brady's hospitalization as we all continuously checked his status online. Fortunately, Brady pulled through, and as an added bonus the numbers made large gains as well.

August 5 has always been a special day for me, as it happens to be my birthday, but this summer it was a particularly memorable day as Colin Farrell appeared on David Letterman the night before, promoting FAST's website, and on the evening of August 5, the community gathered online to once again virtually party as our lead hit 10,000 votes.

Poster by Marcel Cairo

A week later, on August 12, I was supposed to be packing my things for a two week family vacation to Germany, but instead I was glued to Facebook because some of the other charities in the contest formed alliances to help propel them to the top over FAST. The numbers from that morning showed our lead was slowly dropping. Thankfully, FAST was able to send out an email letting members know that the winnings from the contest would be used to fund a human clinical trial of an FDA approved drug that has been identified to improve cognition and motor impairments in AS mice. This news, along with the news of the alliances, motivated the community to band together and recruit more votes. The alliance effort actually backfired as FAST received a record number of votes that day. Sitting in the airport that evening waiting to board my flight to Germany with my family, I received several text messages saying that John Heinzmann had posted an early glimpse at the evening number wrap up and we had already surpassed 3,000 votes logging almost 800 more votes than SF. The glee on my father's face when I told him the news was priceless, as he had been banging his head against the wall for weeks asking why we couldn't consistently log over 3,000 votes per day. A few days later, on August 15, we managed to crack 4,000 votes in a day. On August 16, many members of the community traveled to a park in Chicago where Vivint filmed FAST and interviewed Paula Evans about the contest. Later that day, we hit a 20,000 vote lead.

For the final week of the contest, Vivint decided to hide the vote tally and on the final day, they also disabled the rankings in order to create some suspense around the announcement of the winners. The final day of the contest, August 27, coincided with our return from Germany. When I first realized that our return from Germany was on the same day as the end of the contest I thought staying up to witness the results was going to be a wonderful way to keep me awake that evening and fight off jetlag. However, once Vivint hid the rankings and vote tallies, there was nothing to watch, or so I thought, so I gave in to jetlag and headed to bed early. The next morning when I checked my phone, I had a text message informing me that I was "missing the party." Turns out, after the contest ended, Vivint accidentally displayed the rankings which indicated that FAST won the grand prize with 217,288 votes, a whopping 40,391 votes more than SF, the Eastern regional winner and 141,409 more than the Central regional winner, CURED Foundation. But then Vivint let us know that the winners were not official and that some of the final tallies posted were not accurate. So while hopeful, we had to wait patiently until the winners were officially announced on September 6, at which point we had a virtual watching party, celebrating wildly as FAST was handed the $250,000 check. To view the inspirational video and check presentation, click here.

So looking back at the last few months—what did I do this summer? I spent a whole lot of time sitting in front of my computer, on the brink of insanity, tuning out the outside world, and at many times my wonderful husband, who resorted to Facebook messaging me to ask simple questions. But, I also helped FAST to win $250,000 for research and in the process made some incredible connections with an amazing community that bonded through heartbreaking lows and celebrated through exhilarating highs. We did it. We all got to be part of this wonderful step for Angelman research. It was an amazing summer. Thank you everyone. I am looking forward to seeing many of you in December. ◆

Ready for my close-up...in the Ville

by Sharon Weil-Chalker M.D. *Science Officer FAST*

On a lovely spring day in May 2011, the Foundation for Angelman Syndrome Therapeutics opened hearts and minds in the Ville of Swarthmore, Pennsylvania. This picturesque college town closed its streets to host the annual Swarthmore Charity Fun Fair, an event which hosts numerous charitable causes supported by local residents. The Creative Living Room (TCLR), a family arts organization located in the center of town, selected FAST as it charity to support with fundraising events during the festival and for the coming year. For many in the community, it was their first opportunity to learn about Angelman Syndrome.

TCLR teamed with a professional photographer, Andy Shelter, who donated his time and equipment and invited individuals and families for free photo sessions and pictures, in exchange for donations to FAST. This Photography Project is designed to allow families to chronicle their lives in pictures, and they are encouraged to return each year. This was incredibly popular as you can imagine! The Creative Living Room was packed with people—little girls in their fanciest party dresses, families dressed in matching jeans and shirts, babes in arms. The comfortable space was decorated with posters created by Fellow Board Member Becky Burdine and myself, spotlighting the beautiful faces of many of our children with Angelman Syndrome. Copies of "Jade and the Walking Stick" by Ryan Tipton were on display, videos from past Galas played continuously, while Becky and I educated anyone who would pause about Angelman Syndrome and FAST. Our children, Ethan and Sophie, were also perfect hosts!

Rebecca Burdine, Marc Schwartz
Donovan Schwartz, Sophie Schwartz
Photographed by Andy Shelter

Outside the storefront, tables staffed by TCLR were piled high with goodies and activities for fair-goers. Home-baked delectables prepared by friends and families of TCLR and angel food cake with strawberries were available for sale, to be washed down with delicious, ice cold lemonade. For a donation to FAST, children could fashion wire-and-ribbon halos, color pictures, or purchase a beaded Angel bookmark. Children could be seen twirling in the streets in sparkling halos with ribbons trailing down their backs. Others sat with chubby hands and intent faces concentrating on coloring pictures of angels. The creative staff of TCLR generously provided their popular music, drama, dance, Spanish, and art classes as silent auction items. TCLR regulars clamored to bid on these coveted prizes, in addition to several donated gift baskets.

Andy Shelter take photos for donations at TCLR.

My son and Ethan's older brother, William, decided on his own to run a booth at the Fair on behalf of FAST. He planned a $1 ball toss to win goldfish, complete with a poster and an intricate cup target design. He wrote a fantas-

Ethan Chalker

William Chalker runs a booth to benefit FAST at the charity fair.

tic letter to local pet shops for donations, and scored a basket of pet supplies and a gift card for the silent auction table. William and his friends manned the booth in front of TCLR, attracting small children and fellow tweens to the challenge. He sold out of goldfish rapidly and moved on to Silly Bands for prizes.

At the registration for the morning fun run at the Fair, we distributed flyers to advertise the running programs that raise funds for FAST, Miles for Smiles miles-for-smiles.org and Angel Runners www.angelrunners.com.

The event was really moving. People were so interested in FAST and AS, and seemed genuinely pleased to recognize a member of their community, Ethan, in the posters. They gave generously, and some, later, became loyal voters in the Vivint contest. ◆

FAST families creatively raise community awareness and announce an upcoming family Concert fundraiser

The Creative Living Room will host its next event for FAST on **November 19, 2011 at 4:30 PM.** The annual Thanks and Giving Family Concert will feature award-winning children's songwriter and entertainer Allison DeSalvo and her World of Song, with her band and her back-up singers, the Singing Moms (including me). Angelman families from PA/NJ/DE are encouraged to attend, enjoy the concert, introduce their children to the community, and thank TCLR for their support.

For more information about the concert, visit www.thecreativelivingroom.com or contact Sharon.Weil@chalker.net.

Scentsy Fundraiser

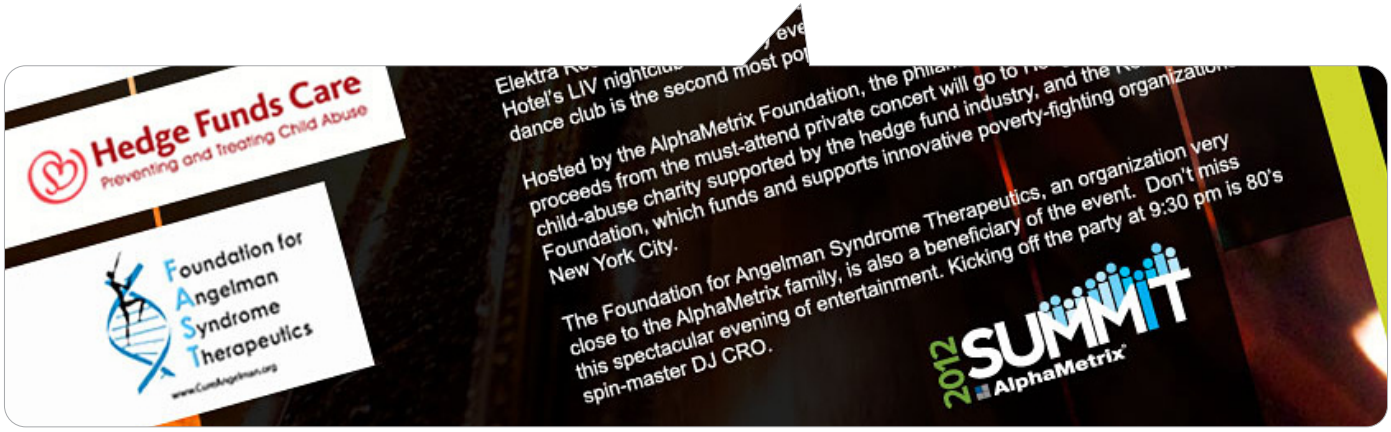
As a representative for Scentsy candles, Michelle Fingold held a fundraiser selling candles with the hope to raise sufficient funds to help sponsor a parent or parents to attend the 2011 FAST Gala. Michelle was successful and with her dedication and hard work, was able to pay for two parents to attend the Gala. Way to go Michelle! ◆

Utah Cycling Event

Mauricio Melendez will be hosting a cycling event on July 28, 2012 in Utah. Mauricio is hosting the event in order to raise awareness for Angelman Syndrome and to raise funds for FAST. The course will travel through one of the most scenic areas of Utah. There will be three options for riders to choose from. Additionally, the event will be tied in with the county fair to help raise awareness for Angelman Syndrome. We will post additional information on our website as it becomes available. ◆

AlphaMetrix 2012 Summit Benefit Concert

FAST is enormously grateful to be a beneficiary of the AlphaMetrix 2012 Summit Benefit Concert starring recording artist Cee Lo Green. This exclusive, private event is attended by the top Hedge Fund Managers and Hedge Fund Investors in the world. In addition to being a beneficiary of the event, AlphaMetrix will be increasing awareness by providing guests with information on Angelman Syndrome and FAST. ◆



FAST is looking very forward to seeing our fellow parents and supporters at the 2011 FAST Gala in Chicago.

Runners Abound

"The miracle isn't that I finished. The miracle is that I had the courage to start." —John Bingham

In a little over a year, runners from Angel Runners and Miles for Smiles have raised well over $50,000 for Angelman Syndrome research. Inspiring, that a concept turned into reality has turned into a phenomena! So much so that on Saturday, December 3rd, 2011, during what is predicted to be, "the worst winter in the nation this season", mere hours before the annual FAST Gala, over 35 parents and friends of individuals living with Angelman Syndrome will don their Santa hats, Santa suits, warm running gear and gloves in order to raise funds and awareness for Angelman Syndrome by participating in the Santa Hustle. Last year, Jason Bernstein and Dawn Ganzhorn ran the Santa Hustle, in the snow, in their Santa gear, raising awareness for Angelman Syndrome. This year, Jason and Dawn will be joined by grandparents, mothers, fathers, friends and relatives to celebrate a year that we refer to as the turning point for the Angelman Syndrome community.

If you would like to join the FAST group in walking or jogging and have not signed up for the Santa Hustle, please visit: www.SantaHustle.com/register.html. If you would like to sponsor the runners, please visit: www.firstgiving.com/fundraiser/jason-bernstein/santahustle. If you would like to turn your walking or running habit into an opportunity to raise awareness please join Angel Runners or Miles for Smiles. Both groups provide helpful advice and support whether you are a seasoned runner or a "couch to a 5K" wanna-be! For more information please see: www.angelrunners.com or miles-for-smiles.org.

We would also like to take this opportunity to recognize all the runners, which at this point have happily become too many to list! Every one of you, whether you walk, run or crawl across that finish line, raises awareness and funds to further research towards finding a cure for Angelman Syndrome. ◆

About the Foundation

FAST is run by an all-volunteer staff and board who dedicate their time and expertise towards finding a cure for Angelman Syndrome. Our goal is to bring practical treatment into current medical practice as quickly as possible. It is our hope that grants we fund will lead to additional research support from government agencies and other funding sources. To make a donation, click here.

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