



Get Informed FAST

Newsletter for the Foundation for Angelman Syndrome Therapeutics Australia

Volume 1, Issue 1

July 2010

Special points of interest:

- Ube3a loss across the brain (Pg2)
- Running for Angels (Pg4)
- Want to help out? (Pg5)

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Australian Launch

Hope. A small word. The ever resourceful Wikipedia tells us - "**Hope** is a belief in a positive outcome related to events and circumstances in one's life. Hope is the feeling that what is wanted can be had or that events will turn out for the best". This is almost certainly an emotion we all hold dear, not only for ourselves and our families, but for all of those affected by Angelman Syndrome.

Research into Angelman Syndrome (AS) is reaching new heights and has provided a strong base upon which to pursue a cure for individuals with Angelman Syndrome, a reason for hope. This research sparked the formation of the Foundation for Angelman Syndrome Therapeutics (FAST) in the United States in 2008 and the subsequent formation of FAST Australia in 2010.

Despite International interest in the syndrome, research into Angelman Syndrome in Australia is scant at best. Funding research and clinical trials are extremely expensive and because AS is categorised as a rare disorder, access to funding is even more difficult due to the lack of a national approach to rare diseases in Australia.

With a population of over 22 million spread across 7.6 million square kilometers, cases of Angelman Syndrome are sparse. Together with the Angelman Syndrome Association of Australia, our immediate task is to raise the profile of the syndrome. This will pave the way for both fundraising and research.

FAST Australia is an all volunteer, not for profit Australian Company.

Our mission is that of our parent organisation FAST US, and We are currently finalising a memorandum of understanding (MOU) that will define how we will work together to achieve our goals. At FAST Australia we will continue to utilise the fantastic resources and references that are already available from the US, such as branding and reference articles.

One of our most invaluable shared resources is that of the Scientific Advisory Board (SAB). The sixteen professionals that make up the SAB have a breadth of knowledge including, but not limited to; Molecular and Human Genetics, Neurosciences, Cell Biology, Learning and memory, Synaptic Plasticity and developmental disabilities. We hope that by engaging Australian researchers and professionals we can also add one or more Australian professionals to this team.

Although it seems conception of FAST Australia was some time ago, be assured that a dedicated team have been

working tirelessly behind the scenes to ensure that we will very soon receive classification as a Health Promotional Charity. We are an official Australian company, Limited by Guarantee. The Foundation is also now endorsed as a Deductible Gift Recipient as of April 30, 2010.

As with FAST US, our goal at FAST Australia is to secure funding from corporate Australia, large donor contributions and through media awareness and fundraising.

Working closely with our US counterparts we share our excitement, drive, energy and commitment. With the assistance of families and friends to our Australian "angels", together we will change the lives of all of those touched by Angelman Syndrome. FAST Australia is dedicated to pursuing every initiative that will advance the science and research of Angelman Syndrome and to that end; we welcome any and all feedback.

Meagan Cross, Chair, FAST Australia.

Australian AS Research into Anti-epileptic Medications

Darwin based researcher, Dr Mark Naunton (BPharm (Hons), PhD, AACPA) recently published a paper on "Angelman Syndrome and Withdrawal of Anti-epileptic Medications".

Dr Naunton is keen to work with the Foundation in collating information to assist research into this important topic, with a particular interest in challenges with medications in Angelman Syndrome.

*Published in Dec 2009 Australian Pharmacist."



Paula & Ainsley Evans

“findings suggest that neuronal function throughout the brain is compromised”

Welcome

The launch of FAST Australia is a monumental and critical step in the pursuit of a treatment for Angelman Syndrome (AS).

Not long ago, when a parent received the diagnosis of Angelman Syndrome, they were sent home with the advice of getting their child into the appropriate therapies and were told to hope for the best. I was one of those parents and hope was about the last thing I was feeling when I received my child's diagnosis. Then, approximately three years ago, something unbelievable happened. Angelman Syndrome was **cured** in the mouse model – the ‘genetic rescue’. This research was so profound that it was named the “Scientific Highlight of the Year”.

This event not only completely changed the way scientists and researchers view AS, it has forever changed the way parents would feel about the disorder as well. Now we parents and caregivers have hope, real

hope.

The amount of research into AS that has come forth in the last three years is almost unheard of. Typically, in the world of scientific research, researchers pursue areas that are well funded such as Alzheimer's disease and Parkinson's disease. This is very understandable. AS, ironically, has become a very hot area of research despite the fact there is very little funding to go around. This means only one thing: with Angelman Syndrome, researchers are chasing the science, not the money. This is terribly exciting and may help to explain why just three years after the genetic rescue in the mouse model, and in contrast to the typical time frame of scientific research, there is now a potential AS therapeutic in the pipeline.

As exciting as this momentum is, the researchers will quickly approach a point in time where the money will be integral to

advance the research. For example, if the novel therapeutic CN2097 proves significant, many more millions of dollars will be necessary before it could be available to our children. This is how and why the creation of FAST Australia plays a critical role in the pursuit of a viable AS therapeutic. FAST Australia will be working tirelessly and aggressively to raise awareness and much needed funding for this disorder we now know is treatable.

I am absolutely ecstatic to reach across the globe and have FAST USA join forces with FAST Australia to accomplish the mission our children are counting on us to do. The Australian team is a formidable one and we are confident that working together, we will change lives.

Sincerely, Paula Evans Chairperson, FAST USA

Angelman Syndrome Researcher visiting Sydney

FAST Scientific Advisory Board member & UC Davis Genome Centre Associate Professor David Segal PhD will be visiting Australia in August this year.

Dr Segal's lab are using zinc finger-based artificial transcription factors to activate the epigenetically silenced genes in both Angelman and Rett Syndromes.

“Almost every disease has a genetic component. Often this information is used only to

determine how condemned a person is to develop disease. We would like to use the genetic information to fix the disease. A guiding principle for our work has been to study how nature does what it does, then attempt to use that knowledge to make useful tools to improve public health, either through increased knowledge or therapeutic intervention.

Specific research foci in the Segal Lab revolve around engineering custom zinc finger

DNA-binding proteins for specific applications.”

“We are trying to turn on the turned-off copy of UBE3A. The approach we are using is very experimental. It involves introducing an engineered gene regulatory protein into the brain.” – David Segal

Register as a FAST supporter on our website to receive details on the upcoming workshop in Sydney.

Recently Published

As eluded to in Dr Weebers visit to Australia last year, the long awaited paper on ube3a distribution in the brain was published last month. Contrary to popular belief that ube3a is only required in the cerebellum & hippocampus the published research reveals mouse models have “a marked loss of Ube3a protein in hippocampus, hypothalamus, olfactory bulb, cerebral cortex, striatum, thalamus, midbrain, and cerebellum”. Researchers are working to verify those results in the human brain. Each new understanding into Angelman Syndrome brings us closer to our goal! - <http://www.ncbi.nlm.nih.gov/pubmed/20423730>

Research—Insights & Updates (By Edwin J. Weeber, Ph.D.)

Scientific research is a painstaking, meticulous exercise whereby researchers train for years in order to learn to design a sound approach, implement the experiment and interpret the data collected in a critical way. Presentation of the data in a scientific journal represents a long peer-review publication process that may take months. These activities represent the mechanics of research and this scientific machine is similar across all disciplines. Another level of complexity is added when scientific research addresses a human condition. The quantity of resources allocated for research on specific human conditions often dictates the number of researchers, the time spent, and the advancements that are made in that particular field. I use the word 'often' because these three specific aspects of research that are tied to availability of resources are not mutually exclusive. For example, an exorbitant amount of money has been given for Alzheimer's disease (AD) research resulting in thousands of researchers worldwide, yet there has been very little advancement in the treatment for AD in the past 10 years. In contrast, Angelman Syndrome, considered a rare disorder with relatively little resources dedicated to it, is the beneficiary of major scientific advancement and there is a bright outlook for future discovery.

What makes AS research different?

A good analogy for understanding how hundreds of laboratories around the world conduct their respective research is the tale of the three blind men examining different parts of an elephant and trying to describe to others what they think it is. In many ways this is what we do in science; each researcher looks at a different aspect of the condition and tries to see how their findings fit in the larger context. However, even if

you fill the room with blind men, no consensus will ever be reached if there is a lack of open communication between the observers. This is why collaboration, synergy, and sometimes serendipity are paramount for quick advancement of a field of study. In 1998 Dr. Arthur Beaudet developed a mouse model for AS. This represented an expensive endeavor both in time and money. Can you imagine the stifling consequence to scientific discovery and the progression of AS research if Dr. Beaudet had kept this mouse model solely for his own research? Instead these animals were openly shared with whoever wanted to investigate them. I believe the collaborative spirit among the community of AS researchers today is a direct result of Dr Beaudet's decision to share his valuable resources with other colleagues. This spirit is evident in the authorship of many AS-related scientific papers that list scientists from multiple academic institutions world-wide. Today, the community of AS researchers has remained in close communication and is continually growing.

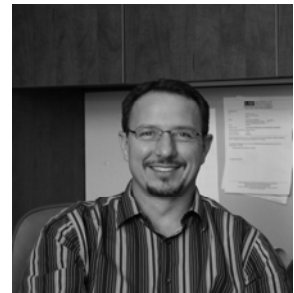
Where is AS research now?

There have been a number of major advancements in the past year. Use of the mouse model has revealed structural changes in the cells of the brain. Changes have been identified in mitochondria, the energy suppliers of cell, and in the spines of neurons where synapses are formed and maintained (1,2). These studies suggest that structural changes outside cell level play a role in the overall change in synaptic function. In two independent studies, changes in synaptic strength are seen in a specific area of the sensory cortex (3,4). These changes indicate that the dysfunction in how synaptic connections are maintained and strengthened during sensory inputs is more wide-spread

throughout the brain than was previously believed. This is supported by the discovery that the AS gene product appears to be absent throughout the brain in the AS mouse model. Recent genetic research has shown that another gene mutation in the TC4 gene located on chromosome 18 were found in a small number of patients clinically diagnosed with AS, but with no identifiable genetic alteration in UBE3A (5). These identifications are important for two basic reasons. First, individuals with a clinical, but not genetic diagnosis represent approximately 12 % of all individuals diagnosed with AS. Identification of additional genetic mutations also associated with AS symptomology will reduce this percentage of unknowns. Second, identification of genetic disruption that results in AS symptoms may shed light on molecular mechanisms and down-stream biological consequences of UBE3A maternal deficiency. Finally, a recent study identified several new targets of the AS gene product, Ube3a (6). One of these targets is a protein called Arc. This protein regulates receptors at the synapse and is known to be involved in the processes that underlie the strengthening of synaptic connections and memory formation. The culmination of the studies listed above, and those not discussed due to brevity, will serve to help shape ongoing and future research.

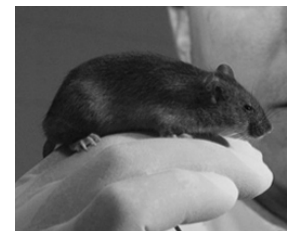
What is the future of Angelman Syndrome research?

This may be an opportune time to talk briefly about the terms "cure" and "therapeutic". A cure is defined as a method or course of medical treatment used to restore health completely. In essence to make a person healthy as if no malady had ever occurred. For example, a "cure" in the context of AS may represent a medical intervention after birth, or in utero, that would be given before the onset of symptoms.



Edwin J. Weeber, Ph.D.

"The past year has seen impressive progress of AS-related research across multiple disciplines"



...Continued Page 5



*"Raising
Awareness
without
saying a
word"*



Billys older brother Max

Save the Date—Official Launch of FAST Australia

On the heels of last year's successful workshop with Dr Weeber, Queensland Angelman Association will be holding another workshop in Brisbane on Challenging Behaviours in Angelman Syndrome (<http://www.angelmansyndromeqld.org/index.php?id=events>).

Taking advantage of a number of families in one place, we plan to hold the official launch for the Foundation! The event will have a short information session about Angelman Syndrome followed by drinks and canapés. Please save the date as follows;

Sunday Sept 26 approx 6-9pm at the Diana Plaza Hotel Brisbane—<http://www.dianaplaza.com.au/>.

More Details to come

Running for Angels

On **July 18th** this year some very dedicated Victorian Angelman Syndrome supporters are showing their support by entering a half marathon event in "Run Melbourne" - 21.1kms! <http://www.runmelbourne.com.au/home.php>

Inspired by their commitment to our cause some Queensland families and supporters are in training for the much shorter Bridge to Brisbane fun run (10km) on **August 29**—<http://www.bridgetobrisbane.com.au/>. Please contact Jen Kyriacou if you are interested in participating—jen@angelmansyndromeqld.org (Walkers, prams and wheelchairs welcome!)

FAST is securing funding agreements with Everyday Hero to enable the team to put up an official fundraising page where others can pledge their support for these two amazing teams and assist in raising funds for Angelman Syndrome.

SpeakOut4AS in Australia

Sparked by one child's desire to hear her friend speak one day, the idea for our SpeakOut4AS was launched in the United States. To date a number of extremely successful events have been held.

SpeakOut4AS is a campaign of no words. It's an acceptance event, in which participants are challenged to remain silent for a set period of time.

Through the silence of these events participants can demonstrate their power to help make a difference for the thousands of individuals left without a voice.

Earlier this month, kids from the **Montrose Primary School** took part in the first Australian SpeakOut4AS event.

The event began with an introduction of four year old Billy Davis, a member of the local Montrose community and an interactive session about Angelman Syndrome.

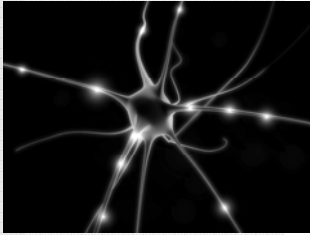
The kids asked some amazing questions and showed incredible understanding and acceptance, some of the kids shared their knowledge and experiences of other people in their lives with disabilities. This part of the session finished up a beautiful and unexpected rendition of the song 'I can sing a rainbow' in sign language!

The next part of the event was the 'silent time' where the kids went back to their classrooms and drew pictures of Angels on fabric which will be sewn together to make a patchwork

quilt to be raffled at the official Foundation launch later this year. Kids were encouraged to communicate using alternate methods and although there was the odd whisper, the kids did an excellent job in staying silent.

Overall, this was very rewarding for my family and also for the kids and teachers involved. Fun and interactive, awareness will continue to spread through the kids, staff, local media and the beautiful quilt.

I would really like to thank The Principal and staff at Montrose for being so supportive of this, we hope to make it a yearly event with new and innovative ideas to enhance and continue its success for years to come. *Jo Davis (Billy's Mum)*



“There is a deliberate and relentless march forward toward a better understanding, and one day a treatment for, Angelman syndrome.”

How can I help?

The aim of the Foundation is to fund aggressive research, education, and advocacy into Angelman Syndrome. It is not our intention to ask already overburdened parents to raise this money. We intend to target grants, corporate sponsors and entice research institutes in Australia to be part of this journey.

The Foundation now holds Deductible Gift Recipient Status (DGR) enabling donors to claim income tax deductions in their income tax returns

To date money in our bank account comes from media fees, Rare Disease Day & a very successful Trivia night! Any contribution, large or small is greatly appreciated.

If you would like to help out with the Foundation, please sign up to our volunteer page on our website.

If you have an idea or would like to raise money for the Foundation please **contact us**.

Research—Insights & Updates (cont from Page 3)

The “cure” in this definition for individuals with a current diagnosis of AS is extremely doubtful. With that said, the development of a therapeutic, defined as a treatment of a disease or disorder, is reasonable. However, the efficacy of therapeutics tends to be only as good as their targets. Thus, a “magic bullet” treatment for all of the symptoms associated with AS is easy to imagine given the one gene etiology, but may be more difficult to realize. This should not discount that the development of therapeutics to treat specific aspects of AS have the potential to profoundly impact individuals with a current diagnosis of AS. The development of novel drugs is an expensive and risky endeavor, but clearly not an impossible task.

Are there new drugs on the horizon?

An interesting development in new drugs for AS is the investigation of a novel compound developed by Ardane Thera-

peutics (www.ardanetherapeutics.com)

. Their new drug called CN 2097 is currently in a Phase I feasibility study for the potential use as a therapeutic to treat the cognitive impairment in AS. This novel drug targets a sub-type of neuronal receptor that is well known to be involved in learning and memory. In fact, a mouse genetically designed to produce more of these receptors was found to be ‘smarter’ than genetically unaltered mice. This ‘smart’ mouse was termed “the Doogie Mouse” with deference to the 80’s TV child prodigy, Doogie Howser M.D. CN 2097 is shown to reduce the threshold for synaptic plasticity; a measurable defect found to exist in the AS mouse model. While these studies are in the first stages of drug development, it indicates that these types of drugs are becoming of interest to the business-minded pharmaceutical development companies.

Conclusions?

The past year has seen impressive progress of AS-related research across multiple disciplines. Increased awareness of AS in the scientific community and high profile scientific publications will continue to attract more basic and clinical scientists. The recipe for this is simple and often underappreciated. For example, there were nearly 2000 scientific publications associated with Arc research in the past 2 years. The study mentioned above will introduce a multitude of new scientists to AS and will likely persuade some of those researchers to include Angelman Syndrome in their respective research programs. As I mentioned earlier, scientific research is a painstaking and slow progression, but a progression nonetheless. There is a deliberate and relentless march forward toward a better understanding, and one day a treatment for, Angelman syndrome.

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2. Su, H., Fan, W., Coskun, P. E., Vesa, J., Gold, J. A., Jiang, Y. H., Potluri, P., Procaccio, V., Acab, A., Weiss, J. H., Wallace, D. C., and Kimonis, V. E. (2009) *Neurosci Lett*
3. Sato, M., and Stryker, M. P. *Proc Natl Acad Sci U S A* **107**, 5611-5616
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**Raising Hope Through Research
Changing Lives Together**



The Foundation for Angelman Syndrome Therapeutics Australia (or FAST Australia) is an organization of families and professionals dedicated to finding a cure for Angelman Syndrome and related disorders through the funding of an aggressive research agenda, education, and advocacy. The Foundation is committed to assisting individuals living with Angelman Syndrome to realize their full potential and quality of life. We are confident that our goals are now within reach and together, with your help, we will change lives.

www.cureangelman.org.au

Research News

[Tissue-specific variation of Ube3a protein expression in rodents and in a mouse model of Angelman syndrome](#)

[The ketogenic diet in childhood epilepsy: where are we now?](#)

[Clinical and genetic aspects of Angelman syndrome \(Updated\)](#)

[UBE3A Gene sequencing now in Australia](#)

[Angelman Syndrome and Withdrawal of Anti-epileptic Medications](#)

Thankyou

There is a huge amount of work behind the scenes to allow the Foundation to reach this point. Although this work continues, we would like to thank the people and businesses who have so generously donated time and services.

FAST for our shared resources, branding and knowledge meaning that we have more time to get to the more important tasks at hand!

MacDonnells Law for their continued legal support and advice, **Anderson-Vidray Chartered Accountants** for financial advice and support & **Fuel Creative Design** for artwork and marketing expertise.

