UPDATE
A-T CHILDREN'S PROJECT®
kids. hope. cure.
April 2008

NEW TOOLS HOLD POTENTIAL TO ACCELERATE A-T RESEARCH

OBJECTIVE WAYS TO MEASURE A-T IN PATIENTS

To review existing neurological measures for ataxia-telangiectasia (A-T) and develop a global neurological rating scale for this disease, the National Institutes of Health, specifically the National Institute for Neurological Disorders and Stroke and the Office of Rare Diseases, and the A-T Children's Project organized **Comparison and Development of Quantitative Neurological Endpoints**, a workshop that focused on this need. Held in Chicago, Illinois, the meeting was the first of its kind for A-T, bringing together patients with a multidisciplinary team of scientists and clinicians. Accurate, reproducible clinical

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UP-TO-THE-MINUTE INFORMATION AND ANAYLYSIS TOOLS

A new web-based, interactive database of information about the complex network of pathways surrounding the ATM protein, which is missing or dysfunctional in people who have A-T, has now been made freely available to A-T researchers around the world. Funded by the A-T Children's Project, the **SPIKE** (Signaling Pathway Integrated Knowledge Engine) software includes analytical and graphic tools that will enable researchers to access up-to-the-minute, comprehensive information about the biological signaling pathways related to the ATM protein. Recently announced to the scientific community by publication in a

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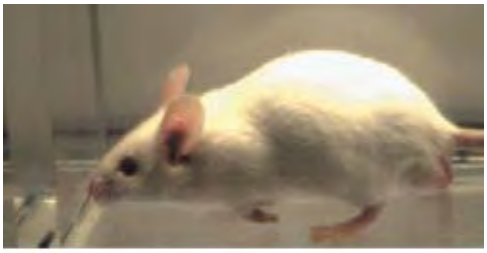
MEASURING THE GAIT OF A-T MICE

Measuring the neurological problems in mice with ataxia-telangiectasia (A-T) is a critical step in analyzing drugs that could be used to treat this disease in humans. Unfortunately, this has been an enormous challenge for scientists because the neurological defects are so subtle in A-T mice. To address this challenge, the A-T Children's Project will fund a Boston based company, **Mouse Specifics, Inc.**, to assess the gait of ataxia-telangiectasia mice as they walk using a sophisticated gait imaging and analysis system developed by the company.

If Mouse Specifics is able to observe significant differences in gait between A-T and normal mice then their automated DigiGait instrumentation



DigiGait

will be of great value to the field of A-T research, allowing investigators to reliably determine if various drugs or cell and gene therapies can correct the neurobehavioral deficits associated with these mice. This in turn would provide scientists with important proof-of-efficacy data before experimental therapies are tried in patients with A-T.

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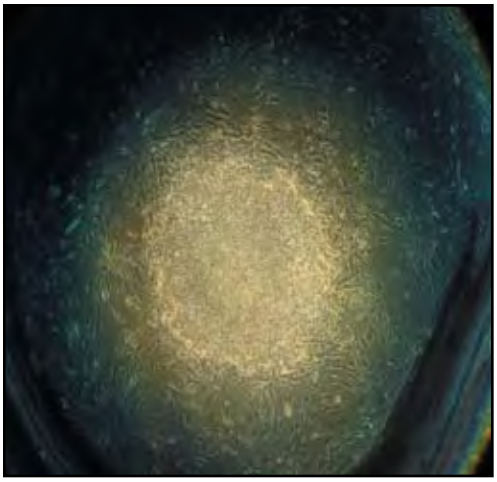
CELLS MAY HELP RESEARCHERS TO IDENTIFY TREATMENTS

By altering existing human embryonic stem cells, the laboratory of **Yang Xu, PhD**, at the **University of California, San Diego**, will try to make new stem cells in which the A-T protein (ATM) can be turned off, thus creating a valuable new resource for A-T research without having to destroy human embryos. Stem cells are valuable research tools because they can be stimulated to turn into the various cell types of the body, including brain cells which cannot be obtained for research purposes from living patients. A-T specific human embryonic stem cells (hESCs), and the unlimited supply of brain cells which can be derived from them, will allow scientists to study why brain cells die in patients with A-T and to identify treatments that prevent this cell loss.



hESC Colony

While the mouse model of A-T has been very valuable for studying many facets of the disease, it does not show the brain cell loss and lack of muscle control commonly seen in patients with A-T. In addition, drugs found to work in mice have not always been effective in people. Therefore, researchers, including A-T investigators, have been eager to study human cells as models for disease. In his own words Dr. Xu explains the significance of his proposed research:

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SCIENTIFIC ADVISORY BOARD

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ATM in Immune Responses
Jessamin Bagley, PhD - Brigham & Women's Hospital

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Maria Luisa Cortes, PhD - Massachusetts General Hospital

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Richard A. Gatti, MD - UCLA School of Medicine

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Steven A. Goldman, PhD - Cornell University

The Role of Pro-apoptotic BID as an ATM Effector in the DNA-Damage Response
Atan Gross, PhD - Weizmann Institute of Science

* Non Traditional Role of ATM in Neurons
Karl Herrup, PhD - Rutgers, the State University of New Jersey

The Zebrafish as a Novel Model System of Ataxia-Telangiectasia and Other Related Diseases
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Correction of the Neurological Defect in Atm Gene-Disrupted Mice by the Insoindolin Nitroxide, 5 Carbocy-1,1,3,3-Tetramethylisoindoline-2-yloxyl (CTMIO)
Martin F. Lavin, PhD - Queenslands Institute of Medical Research

Generation of a Rat Model for Ataxia-Telangiectasia
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Michael M. Weil, PhD - Colorado State University

Regulation of ATM Pathways by Oncogenic Phosphatase PPM1D
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Lung Function in Ataxia-Telangiectasia
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Relationship Between DNA Damage Detection and Signaling Revealed in Humanized Mouse Models of AT and NBS
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The Function of ATM in Neuronal Differentiation: Identification of Targets for High Throughput Screening
Brendan Price, PhD - Dana-Farber Cancer Institute

Iron Chelators as a Pharmacological Treatment to Reduce Spontaneous dsDNA Breaks in Ataxia-Telangiectasia Cells
Rodney Shackelford, DO, PhD - Louisiana State University at Shreveport

Aberrant Regulation of Mitochondrial DNA in Ataxia-Telangiectasia
Gerald S. Shadel, PhD - Yale University School of Medicine

Understanding ATM: Investigation of the ATM-Mediated DNA Damage Response in Neurons
Yossi Shiloh, PhD – Tel Aviv University

Multimodal Stem Cell Action in Inherited CNS Disease
Evan Snyder, MD, PhD - The Burnham Institute

Functional Dissection of an ATM-CREB Signaling Pathway in the Nervous System
Randal Tibbetts, PhD - University of Wisconsin School of Medicine

* Quantitative Proteomic Analysis of Cerebrospinal Fluid (CSF) from Ataxia-Telangiectasia Patients Using LC/MS-based Label-free Protein Quantification Method
Mu Wang, PhD - Indiana University School of Medicine

Gait Analysis in A-T Mice
Michael Weil, PhD - Colorado State University and Mouse Specifics, Inc.

Cell Cycle and Cell Death in atm-Deficient Neuron
Yan Yang, MD, PhD - Case Western Reserve University School of Medicine

Genome (Chromosome) Instability in the Brain and Neuronal Death in Ataxia-Telangiectasia
Yuri B. Yurov, MD, PhD - Russian Academy of Medical Sciences

* Generation of Disease Specific Human Embryonic Stem Cells to Study the Mechanism of Pathogenesis in Ataxia-Telangiectasia
Yang Xu, PhD - University of California, San Diego

* Most recent grants funded

For more information about research grants, contact:
Cynthia Rothblum-Oviatt, PhD, Science Coordinator at cynthia@atcp.org

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INTRODUCING… THE A-T ARTIST BOOK

The A-T Artist Book is a compilation of artwork and biographies of children and young adults afflicted with A-T. In September 2007 faculty, staff and volunteers, from the **McCord Gallery & Cultural Center** in Palos Park, Illinois organized an art workshop in conjunction with an A-TCP research event. Art projects were designed with the interests, talents and abilities of these young artists in mind. The goal was to create several pieces of artwork to visually describe each individual.

The artwork was on display at a McCord special event, from which the A-T Children's Project received a $10,000 check. Thank you to Sara Arnas, Teri Wood, and everyone else who helped with this project.

The books are available for $30 each on-line at the A-TCP Marketplace.

Photography by: Jeremy Smith

GO GREEN AND HELP SINK A-T!

Todd Barber, "*Defender of the Planet*" CNN Hero, of the **Reef Ball Foundation,** and **Larry Beggs** of **Reef Innovations** have donated an Ultra Reef Ball in honor of all kids with A-T. Our challenge is to sink the 3,123 pound Reef Ball for A-T research by getting a donation for each pound. Donations can carry a message from the donor that will be hidden inside the Reef Ball. To help sink the Reef Ball, donate at atcp.org.

Reef Balls are artificial reef modules placed in the ocean to form reef habitats, designed to rehabilitate the world's ocean reef ecosystems and protect natural reef systems. The Reef Ball Foundation has placed over 500,000 Reef Balls in over 59 countries since 1993. Our Reef Ball will be deployed in Sarasota, Florida and added to the Silvertooth Reef, an ongoing reef restoration project destined to become a popular diving destination. It will have a plaque honoring all kids with A-T. The **Help Sink A-T** fundraising campaign is not only a way for us to provide funds for critical A-T research, but also provide an educational opportunity for schools and clubs to learn how to save our coral reefs.

For more information email: fundraising@atcp.org.

Measuring A-T - Continued from page 1

rating scales are critical for monitoring how a patient's disease is progressing as well as determining whether or not a drug given during a clinical trial is effective. Ideally, such scales can be used uniformly by clinical investigators world wide, making multisite clinical trials possible and the results of those trials more consistent.

Attendees included twelve neurologists (several new to A-T), two occupational therapists, one pediatrician and two immunologists. During the workshop, this team of clinicians performed evaluations on 19 patients with A-T ranging from one to 27 years of age. The quantitative neurological assessment scale for A-T previously developed by **Tom Crawford**, a pediatric neurologist at the **A-T Clinical Center at Johns Hopkins Hospital**, was used as the basis for the patient evaluations. Following the evaluations, which lasted a day and a half, the group of clinicians came up with several recommendations for improved scale development for this complex disease.

In addition to the primary neurological examination scale for A-T, the attendees strongly recommended that a functional scale be developed. This scale would be used to cross-check and validate the primary neurological scale. The functional scale for A-T would include elements like school performance, eating and activities of daily living. Importantly, a good functional scale can be helpful as a tool to select patients for clinical trials.

To aid the scale development process, three committees were created at the conclusion of the workshop to: 1) oversee the entire process; 2) develop an examination scale and 3) develop a functional scale. A fourth committee of consultants that includes a neuro-ophthalmologist, a specialist in upper body extremity research, and a speech and swallowing specialist was also formed. Once approved by the committees, the new neurological examination and functional scales will need to be refined and validated during future meetings that again bring together patients and clinicians.

Although scale development requires much time and effort, these evaluation tools are desperately needed by A-T clinician/scientists worldwide, not only to help improve patient care but to enable clinical trials of new drug therapies.

INCREASED RESOURCES FOR FAMILIES AVAILABLE SOON AT ATCP.ORG

Do you ever wonder where you can find specific information about A-T? More resources for families of children with A-T will be available soon on the A-T Children's Project's website at atcp.org including:

- Discussion board
- Resource information and links
- Equipment swap

We welcome your questions, comments or suggestions. Please email your family support inquiries to rosa@atcp.org.

JUST ME FOR A-T
A NEW, SIMPLE WAY TO RAISE MONEY FOR A-T RESEARCH

For those who are not participating in one of our marathon weekends or hosting an event, a **new online fundraising webpage** offers an easy way to raise funds for any special occasion.

Your *Just me for A-T* page can be personalized in minutes with your message highlighting your fundraiser. You can send emails to your friends and family directly from your fundraising page making it easy to solicit donations for A-T research.

Start now! Go to atcp.org and click on the *Just Me for A-T* logo on the home page and follow the instructions.

Your donors will receive automatic receipts immediately via email, and you will be able to send them "thank you" emails from your page. Every time you receive an online donation, you will receive an email notification and you will be able to check on the donations any time you want.

For more information, email fundraising@atcp.org or call 800.5.HELP.A-T.

SMALL CLINICAL STUDY IN ZURICH SENDS PATIENTS SPINNING AND SHOWS POSITIVE RESULTS

A small clinical study performed in Zurich, Switzerland by **Aasef Shaikh, MD, PhD and Dominik Straumann, MD** demonstrated that a drug called 4-aminopyridine (4-AP) reduced or eliminated some of the eye movement abnormalities and tremor associated with ataxia-telangiectasia (A-T).

Patients with A-T often suffer from eye movement abnormalities and tremor, which are primarily a result of cerebellar degeneration. Loss of brain cells in the cerebellum or cerebellar atrophy leads to a reduction in the amount of an important brain chemical called GABA. GABA helps neurons (brain cells) in the cerebellum effectively communicate with other neurons. Without a sufficient amount of GABA produced, impaired motor control results. Therefore, Drs. Shaikh and Straumann hypothesized that if they treat patients with a drug that can increase GABA production, they may be able to improve some of the eye movement abnormalities and tremor associated with A-T.

To test their hypothesis, Drs. Shaikh and Straumann placed four patients in a special machine designed to spin or rotate the entire body in three different planes (please see accompanying photo and caption). Each patient had two sessions on the machine, one before and one after treatment with 4-AP.

In this small patient cohort, Drs. Shaikh and Straumann were in fact able to show that 4-AP treatment improved a special type of nystagmus (rapid and repetitive eye movements) as well as postural tremor.

These results demonstrate that drugs that compensate for GABA deficiency may be able to produce meaningful improvements in function for patients with A-T. To further test this idea a larger clinical trial at the A-T Clinical Center at Johns Hopkins Hospital is currently ongoing.

Thank you to **Maureen Poupard** of the **A-T Society** in England who identified trial participants and organized their travel.

A-T Patient Robert Soper

"Contact lenses would pick up the electrical impulses from my eyes as I was turned around and around. I was seated normally, and the turntable moved through a number of positions. I was lying on my sides, then on my back, swung around upside down, and on each side…… What an experience! We were off, round and round, up and over, back round the other way upside down!"

63 Marathons in 63 Days

Tim Borland ran 63 marathons in 63 days in 63 different communities across the United States and Canada in an effort to raise awareness and funds for the A-T Children's Project.

A-T and the **A-T CureTour 2007** saw unprecedented media exposure with over 70 million impressions, including USA Today, Good Morning America, ABC World News, ESPN, Los Angeles Times, New York Times, Washington Post, and Runner's World.

Thank you to our title sponsor **Octapharma**, who not only gave a huge donation, but also supported the event on the ground! Their staff members volunteered hours of their time helping at events and securing donated items.

Coming soon... FEAT

Filmmakers and longtime friends of the A-T Children's Project, **Brad and Deborah Carr,** followed Tim every step of the way, producing an independent feature film entitled **FEAT,** expected later this year.

FINISH

The A-T CureTour 2007 saw ultra-runner Tim Borland run 63 marathons in 63 consecutive days in 63 cities across the United States and Canada in an effort to raise awareness and find a cure for kids who have ataxia-telangiectasia.

The feature film documenting this effort, FEAT, will be released in 2008.

The spirit of the A-T CureTour continues in 2008 with the A-T Children's Project participating as a charity group in official marathons and with local grassroots athletic events that are planned by families and friends across the country.

WALT DISNEY WORLD MARATHON WEEKEND 2009

Walt Disney World® Resort
January 9 – 11

Hunter Kemper

2 Time Olympian
6 Time US Elite National Champion
2005 United Stated Olympic Committee's Sportsman of the Year
2005 World Ranked #1
2005 Pan American Games Gold Medalist

Hunter Kemper is an Olympic Triathlete and the Honorary Coach of the A-T Children's Project's Danskin® Women's Triathlon Team! Hunter ran the WALT DISNEY WORLD® Half Marathon in January 2008 wearing the A-T racing tank, placing fourth! When he met the family of two young girls battling A-T, he decided to help us in our mission.

ROCK 'N' ROLL 1/2 MARATHON
PRESENTED BY SUNTRUST

Virginia Beach
August 31

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MAY 2-4, 2008
Lady Foot Locker

Walt Disney World® Resort
May 3 – 4

DANSKIN
2008 WOMEN'S TRIATHLON

Walt Disney World® Resort
May 11

START

AT CURETOUR
Marathons & Races
2008

Disneyland 1/2 MARATHON WEEKEND

Anaheim, CA
August 30 – 31

November 16

Marine Corps Marathon
October 26
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Walt Disney World®Resort
September 27
Pairs compete in a 5K, obstacle course, and scavenger hunt

The Twilight Zone
Tower of Terror™ 13K
Walt Disney World®Resort
October 25
The Twilight Zone® is a registered trademark of CBS, Inc. and is used pursuant to a license with CBS, Inc.

5K, 10K, 1K Kids races
Littleton, CO
September 28

Greensboro, NC
5K and 10K
October 25

October 12

Yang Xu - Continued from Page 1

"While ATM-deficient mice [also termed Atm knockout mice] generated by others and us have been used extensively to study many aspects of the pathogenesis in A-T, these mice fail to spontaneously develop ataxia and undergo extensive loss of cerebellar neurons as seen in A-T patients. In addition, many intrinsic differences between mouse and human have lead to the common phenomenon that certain therapeutic interventions work well in mouse models but poorly in humans. Disease-specific hESCs, which can undergo unlimited reproduction of themselves (self-renewal) and also retain the ability to differentiate into [become] all cell types in the body, hold the promise to become the most relevant genetic tools to study the mechanism of pathogenesis in human diseases."

If Dr. Xu's laboratory is able to make hESCs in which the ATM protein can be turned off, they will have created a resource that can be shared with scientists around the world, accelerating the overall pace of A-T research.

With funding from the A-T Children's Project, Dr. Xu's team will apply sophisticated molecular biology and genetic manipulation techniques to hESC lines previously established at Harvard University to make "conditional" ATM knockout stem cells. These stem cells will lack the ATM protein only when exposed to a special enzyme called FLP. A distinct advantage to these conditional hESCs is that the presence of ATM will ensure they function normally when more cells need to be grown. Then, their ATM protein can be disrupted only when the investigator is ready to perform his/her experiment.

When desired, Dr. Xu, and other scientists, will be able to use the FLP enzyme to inactivate the ATM protein in any cell type derived from the new stem cell lines and study the effects of its loss. These special stem cells should prove to be critical biological tools for understanding the brain cell demise associated with A-T and for discovering drugs that can prevent it.

WISCONSIN SCIENTIST EXAMINES A NEW A-T PROTEIN SIGNALING PATHWAY IN MICE

Understanding A-T protein (ATM) signaling pathways (i.e. the way ATM communicates with other proteins in a cell) holds the promise of uncovering specific proteins that could be 'targeted' by drugs to treat ataxia-telangiectasia. **Randal Tibbetts, PhD**, a researcher at the **University of Wisconsin-Madison School of Medicine and Public Health**, will investigate a novel ATM signaling pathway in mice to test whether disruption of this pathway contributes to the neurological problems faced by patients with A-T.

Randal Tibbetts, PhD

Previous work from the Tibbetts laboratory, published in the scientific journal Proceedings of the National Academy of Sciences (PNAS) in 2004 and The Journal of Biological Chemistry in 2007, demonstrated that ATM directly modifies the CREB (Ca2+/cAMP response element binding) protein in response to DNA damaging agents. CREB is a special protein that binds to certain sequences in a variety of genes, thereby promoting the expression of those genes. Genes regulated by CREB play important roles in cell survival. And, notes Dr. Tibbetts, "CREB is a bona fide neuron [brain cell] survival factor." Specifically, the Tibbetts lab discovered that when ATM modifies CREB, by a process called phosphorylation, it effectively inhibits CREB's gene regulatory activity.

Because CREB is a neuron survival factor, Dr. Tibbetts speculates that the ATM-CREB pathway may regulate neuronal homeostasis (maintenance of a stable internal physiological state) or neuronal programmed cell death (termed apoptosis). Interestingly, research performed by others has implicated ATM in regulating programmed cell death during embryonic development. This research demonstrated that in the absence of ATM, developing brain cells which incurred damaged to their DNA, and should have been eliminated, did not die but rather continued to survive. These genetically damaged neurons may be destined to degenerate or die later in the organism's life. This is one reason researchers suspect that brain cells die in patients with A-T.

With his current funding from the A-T Children's Project, Dr. Tibbetts will continue to explore the function of the ATM-CREB pathway in neurons, specifically neurons of the cerebellum, as this area of the brain seems most affected by loss of the A-T protein. Dr. Tibbetts' laboratory will attempt to identify gene targets for the ATM-CREB pathway. In addition, they are in the process of generating gene-targeted "knock-in" mouse strains that produce an altered CREB protein which cannot be modified by ATM. They will examine whether or not neurons from these mice possess defects similar to those from ATM knockout mice (e.g. developing neurons from A-T mice are resistant to irradiation induced programmed cell death and cerebellar Purkinje cells from A-T mice fail to thrive in culture). The CREB knock-in model should also illuminate potential involvement of the ATM-CREB pathway in cancer suppression.

"Our combined studies," states Tibbetts, "promise to elucidate the mechanism of CREB regulation by ATM and will establish whether dysregulation of CREB-dependent gene expression contributes to neurodegeneration in A-T." Should this prove to be the case, new avenues may open for the development of drugs for A-T.

GIRLS SELL CRAFTS FOR A-T

Ten-year-old Kate Veldink, who has A-T, joins her friends Ana, Maddy and Mikaela to sell magnets, pens, candy rolls, Spirit Snapz, bracelets, and painted rocks at a crafts fair in Michigan to raise money for A-T research.

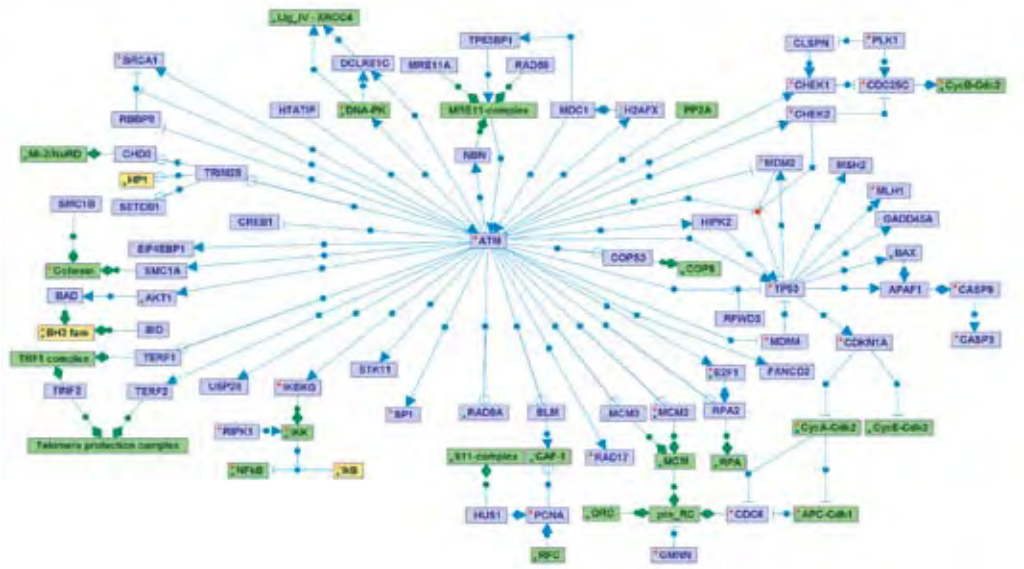
SPIKE - Continued from Page 1

scientific journal, SPIKE is certain to gain the immediate attention of researchers and help them make faster progress toward a treatment for A-T.

Cellular life is governed by many physiological processes that are carried out by numerous proteins that interact and convey signals to each other. Chains of such interaction events are called "signaling pathways." These pathways are the backbone of cellular metabolism. In addition to their own complexity, pathways communicate with each other, creating complex networks, and together these networks form an enormous communication web. These networks ensure that cells properly adjust to changing conditions and to various challenges. Defects in proteins that participate in these signaling pathways result in various human diseases. The ATM protein, is the major regulator of the very complex "DNA damage response" signaling network, which is responsible for the response of the cell to a particular type of highly dangerous challenge - breaks in the genomic DNA. Such breaks are caused by ionizing radiation, by certain chemicals and by various metabolic by-products. Thus, a properly functioning ATM is needed throughout the life of a cell.

The cellular signaling web is extremely complex and novel players are discovered frequently. The ATM-mediated network is no exception. New data on proteins that participate in this network are now accumulating at an unprecedented pace.

For example, to date, ATM is known to directly regulate several hundreds of proteins, each of which regulates several others. To cope with the ever increasing complexity of signaling webs, scientists at Tel Aviv University developed SPIKE (Signaling Pathway Integrated Knowledge Engine) to help researchers analyze and understand complex signaling networks. Large amounts of data are fed into SPIKE and the information is used to create signaling maps that are graphically presented (please see accompanying figure). These maps are dynamic, allowing the user to get deeper and deeper into the complexity of the displayed networks, find novel pathways linking specific players, and gain novel biological insights.



Detailed complexity of the ATM protein cellular signaling web

The description of the first version of SPIKE has just been published (R. Elkon et al., BMC Bioinformatics, 9:110, 2008). In connection with this publication, SPIKE's creators are contacting key labs working on A-T and the DNA damage response with an invitation to join in a collaborative effort to store data in SPIKE, to keep the database up-to-date, and to share new data with the entire community. Its graphical and analytical capabilities make it a very powerful tool for the analysis of signaling networks. It is expected that, with the assistance of the research community, SPIKE will become a valuable asset to experimental work in cell biology labs. SPIKE is available to researchers at http://www.cs.tau.ac.il/~spike/.

From: Yosef Shiloh[1], Ran Elkon[1] and Ron Shamir[2]
[1]Department of Human Molecular Genetics and Biochemistry, Sackler School of Medicine and [2]School of Computer Sciences, Tel Aviv University, Tel Aviv 69978, Israel

CLINICAL & TRANSLATIONAL RESEARCH MONTHLY GIVING PROGRAM

A-T scientists and physicians are making remarkable progress, shifting their focus from basic research projects to studies aimed at specific treatments. These studies, including drug-screening technologies, drug toxicity studies, and clinical trials in children, are more costly, requiring higher levels of funding.

Having a reliable source of funding over the coming months and years will enable the A-T Children's Project to plan and implement these studies. Therefore, funds that come in through this Monthly Giving Program will be earmarked for clinical and translational research.

Now ...

more than ever ...
we need all the help
we can get.

To sign up please use
the enclosed envelope,
visit atcp.org,
or call: 800.5.HELP.A-T
(800.543.5728)

A-T Children's Project is ready to help YOU raise money for A-T research! To learn more please email fundraising@atcp.org

Mouse Gait - Continued from page 1

In 1996, shortly after the discovery of the gene responsible for A-T, reports of the first mouse models for this disease were published. Over the years, these mice have proven to be important tools for A-T research. Mice deficient in the A-T protein (called Atm) share many of the characteristics seen in patients, including radiation sensitivity, immune system defects, infertility, slowed growth and cancer predisposition. By studying these mice, scientists have been able to learn a great deal about how the ATM protein functions. However, like many animal models of human disease, Atm deficient mice do not mirror the human condition exactly. Most striking perhaps is the fact that A-T mice do not possess the hallmark cerebellar degeneration and gross ataxia observed in humans with this disease.

However, neurobehavioral deficits have been observed in A-T mice under certain conditions. For example, when placed on an accelerating rotarod (a spinning rod capable of increasing in speed), A-T mice cannot stay on the rod as long as their normal littermates. Recently, a group of scientists from Australia observed the neurobehavioral defects in A-T mice by using a type of balance beam test wherein the mice were challenged to walk on an edge only 5 mm wide. Some investigators have also observed stride length abnormalities in Atm deficient mice using hind paw print analysis (where the hind paws are dipped in ink and the mouse walks through a tunnel – the length between strides is then measured). Unfortunately, in A-T mice these behaviors can be difficult to observe and/or reproduce from one research lab to another. Therefore, they are not considered very robust observable characteristics of these mice.

Mouse Specifics, Inc offers a novel, automated DigiGait Imaging System capable of early detection of even subtle gait abnormalities in mice and other rodents. With this system, the mouse is placed on a patented transparent treadmill and allowed to walk or run at a range of speeds. The DigiGait system incorporates digital imaging and video recording to analyze approximately 30 metrics (parameters) of posture and locomotion for each limb of the mouse. "These gait metrics," states Dr. Tom Hampton, CEO of Mouse Specifics, "include stride length, step sequence pattern, braking duration, paw placement angles, and step-to-step variability. DigiGait provides early physiomarkers of motor dysfunction, reports drug-induced ataxia, and demonstrates the efficacy of drugs to restore coordinated gait." Dr. Hampton further notes that "recent applications of the patented DigiGait Imaging System have provided new insights into animal models of Parkinson's disease, spinal cord injury and amyotrophic lateral sclerosis (ALS)."

Preliminary experiments performed by Mouse Specifics using A-T and normal mice demonstrated that significant gait disturbances existed in the Atm deficient mice. With funding from the A-T Children's Project, Mouse Specifics will expand these initial studies. A-T and control mice on three different genetic backgrounds will be analyzed with the DigiGait System weekly for three months, and monthly thereafter out to one year. The genetically diverse Atm deficient mice to be used in these studies were generated by Dr. Mike Weil (Colorado State University) as a research grant funded by the A-TCP. Dr. Weil currently maintains colonies of these mice and will breed and ship them to Mouse Specifics for gait analysis.

If Mouse Specifics' automated gait analysis system proves to be a robust and reliable way to monitor the neurobehavioral abnormalities in A-T mice, then scientists will have a readily available test for the preclinical analysis of potential drug therapies for A-T.

More Information for Scientific Investigators

Mouse Specifics

For more information on the DigiGait Imaging System and other services provided by **Mouse Specifics, Inc.** please visit their web site at: www.mousespecifics.com.

Atm +/- Congenic Mouse Strains

Any investigators interested in mice carrying the Atm knockout allele on one of three different background strains – C57BL/6J, A/J or BALB/cByJ – should contact **Mike Weil** by email at: mweil@colostate.edu.

AT MARKETPLACE

kids. hope. cure.

Short sleeve tech shirt
red with marathon logo.
Also in white with A-TCP
logo Sizes: S, M, L, XL,
XXL $25 ea.

Long sleeve tech shirt with
"kids. hope. cure" down
left sleeve and A-TCP
logo on front. Specify
black or white.
Sizes: L, XL, XXL $30 ea.

Black Hoody
Sweatshirt
Sizes: S, L, XL
$30 ea.

Black Sweatpants
Sizes: S, M, L, XL,
XXL $25 ea.

Gray Sweatshirt
Adult Sizes: S, M, L, XL,
XXL $30 ea.
Youth Sizes: YS (6-8),
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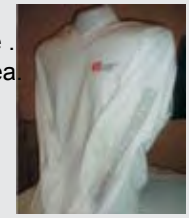

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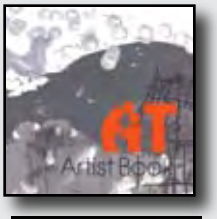

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The A-T Children's Project is a public 501(c)(3) non-profit organization that raises funds to support and coordinate biomedical research projects, scientific conferences and a clinical center aimed at finding a cure for ataxia-telangiectasia, a fatal genetic disease that attacks children causing progressive loss of muscle control, cancer and immune system problems.

A-T CHILDREN'S® PROJECT
668 South Military Trail
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