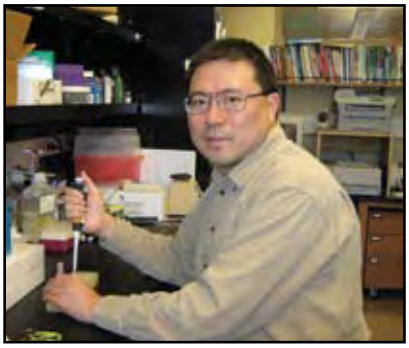
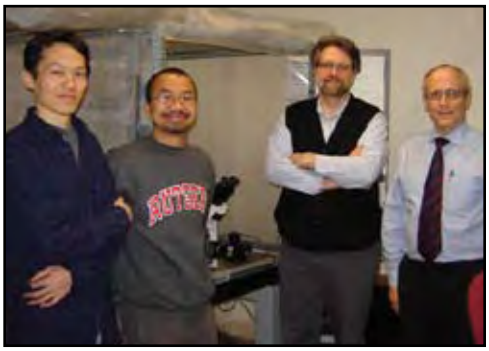
UPDATE
A-T CHILDREN'S PROJECT®
March 2009
kids. hope. cure.

NEW WAYS TO LOOK AT NEURODEGENERATION IN A-T MAY LEAD TO TREATMENTS



Da-Qing Yang, PhD



From left: Jiali Li, PhD, Ray R. Han, PhD, Mark R. Plummer, PhD and Karl Herrup, PhD

IS THE A-T PROTEIN DOING SOMETHING OUTSIDE OF THE NUCLEUS?

For years, scientists have known that the protein missing in children with A-T, known as ATM, is found in the nucleus of our cells. But researchers have always been curious about whether ATM also plays a role in the cell's cytoplasm, outside of the nucleus, especially in brain cells that are so negatively impacted by A-T. To shed light on this question, the A-T Children's Project has funded two research teams who are looking at possible roles for cytoplasmic ATM.

DOES CYTOPLASMIC ATM PROTECT BRAIN CELLS FROM STRESS?

Da-Qing Yang, PhD, a researcher at the **University of South Dakota**, recently found that ATM protects certain human neuron-like brain cells, called SH-SY5Y cells, from death when they are stressed. His research team stressed cells that have ATM, as well as cells that do not have ATM, by depriving them of serum, a blood component they need to grow in a laboratory dish. They found that in the presence of insulin the cells with ATM survived while the cells lacking ATM died.

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DOES CYTOPLASMIC ATM HELP BRAIN CELLS COMMUNICATE WITH EACH OTHER?

Karl Herrup, PhD and his post-doctoral fellow, **Jiali Li, PhD**, neuroscientists at **Rutgers University**, found that ATM interacts with two proteins normally associated with synaptic vesicles, small compartments in the cytoplasm that play an important role in helping brain cells communicate with each other. The two proteins, called VAMP2 and synapsin-1, help brain cells secrete chemical

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THE SEARCH FOR NOVEL BIOMARKERS FOR A-T

An investigator from Indiana, **Mu Wang, PhD**, from the **Indiana University School of Medicine and Monarch Life Sciences, LLC**, will be examining spinal fluid in up to twenty patients with A-T to identify proteins that can be used as biomarkers to monitor the progression of this disease and assess the effectiveness of drugs in clinical trials. If identified, these biomarkers may also provide new insights into the disease process itself.

Biomarkers are substances that are connected with the status of a disease, and can therefore be extremely valuable for diagnosis as well as monitoring disease progression and treatment. Because of their potential to accelerate disease diagnoses and the clinical trial process by which drugs are tested in humans, biomarkers are being sought for a large number of diseases. And now, with funding from the A-T Children's Project, biomarkers will be sought for ataxia-telangiectasia (A-T).

Families of patients with A-T may already be familiar with one biomarker for this disease: alpha-feto protein (AFP). Although elevated AFP levels are a diagnostic biomarker for A-T, they are not helpful in predicting disease progression. In fact, no biomarkers that measure A-T disease progression, or which can be monitored in clinical trials to determine if drugs are effective for A-T, have been

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Coming Soon... See Pages 6-7

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GRANTS RECENTLY FUNDED BY THE A-TCP

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

The Role of the DNA Damage Response in Cerebellar Degeneration in A-T
Ari Barzilai, PhD - Tel Aviv University

Identification and Characterization of Chemicals that Readthrough PTC Mutations in the ATM Gene
Richard A. Gatti, MD - UCLA School of Medicine

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
Shuji Kishi, MD, PhD - Harvard Medical School

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
Martin F. Lavin, PhD - Queenslands Institute of Medical Research and
Michael M. Weil, PhD - Colorado State University

Regulation of ATM Pathways by Oncogenic Phosphatase PPM1D
Xiongbin Lu, PhD - Baylor College of Medicine

Lung Function in Ataxia-Telangiectasia
Sharon McGrath, MD - Johns Hopkins School of Medicine

Relationship Between DNA Damage Detection and Signaling Revealed in Humanized Mouse Models of A-T and NBS
Andre Nussenzweig, PhD - NIH, NCI

The Function of ATM in Neuronal Differentiation: Identification of Targets for High Throughput Screening
Brendan Price, PhD - Dana-Farber Cancer Institute

Impact of Growth Factor (GF) Supplementation on Growth Retardation and Neurodegeneration in Ataxia-Telangiectasia
Ralf Schubert, PhD - Klinikum der Johann Wolfgang Goethe Universität

Increasing A-T Cell Viability by Pharmacologic Modulation of Intracellular Nicotinamide Adenine Dinucleotide Levels
Rodney Shackelford, DO, PhD - Johns Hopkins University and
Howard Lederman, MD, PhD - Johns Hopkins University

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

Generation of a Panel of Monoclonal Antibodies Against the Human and Mouse ATM Proteins
Yossi Shiloh, PhD - Tel Aviv University

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

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.

Signaling Pathways Involved in Oxidative Stress-mediated Neurodegeneration in ATM Gene Deficiency
Paul Wong, PhD - MD Anderson Cancer Center

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

ATM, a Novel Activator of Akt that Regulates Neuronal Survival in Response to Insulin and IGF-1
Da-Qing Yang, PhD - The University of South Dakota

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

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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A Very Special Evening

Audiences were treated to stellar performances yet again at *A Very Special Evening* held at Lincoln Center in New York City. Event Chair **Eric Weinberger** organized tremendous talent including event hosts **Olympia Dukakis** and **Priscilla Lopez**. Ms. Lopez is currently starring in the 2008 Tony Award winning musical *In the Heights*. Ms. Dukakis will be starring in *The Singing Forest* by Craig Lucas at the Public Theater in New York from April 7 to May 17.

Stars of "In the Heights," Christopher Jackson and Mandy Gonzalez

Photos: Courtesy of Ginger Propper

Hosts Priscilla Lopez and Olympia Dukakis

Matt Stamm and friends performed a very touching song he wrote in memory of his brother, Josh, who had A-T. Other performers included **Todd Londagin**, **David Birnbaum**, **Leo Ash Evens**, **Mark Fisher & Devin Ilaw**, **Ari Mayzick** of ***Ron de Jesús Dance***, OBIE Award winner **Mandy Gonzalez** and her special guest **Chris Jackson**. The event was a great success, raising over $50,000.

SOUTH FLORIDA HUNTERS & JUMPERS ASSOCIATION'S LIVE AUCTION BENEFITS THE A-TCP

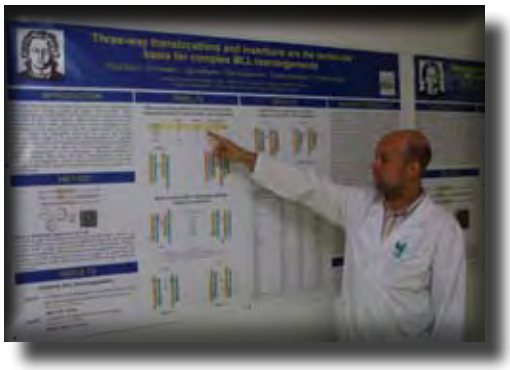
From left: Dave Burton, Jr., Dave Burton, Sr., Brad Margus, Quinn Margus and Karen Senft

The A-T Children's Project was the fortunate beneficiary of the **South Florida Hunters & Jumpers Association**'s charity horse show and auction. Auction organizers **Karen Reaves**, **Karen Senft**, and **Lori Bruno** put together a winning event. Thank you to the SFHJA Board of Directors for continuing to help us find a cure for A-T!

COULD GROWTH FACTORS HELP TREAT A-T?

To determine if growth factors (GFs) could be a potential life-improving therapy for patients with ataxia-telangiectasia (A-T), **Ralf Schubert, PhD** from the **Klinikum der Johann Wolfgang Goethe Universitaet** in Frankfurt Germany will explore the benefits and risks associated with GF treatment in A-T mice.

In addition to progressive cerebellar degeneration, immunodeficiency and a predisposition to cancer development, various endocrine abnormalities, such as poor growth, arrested reproductive organ development and insulin resistant diabetes, are observed in patients with A-T. Such endocrine abnormalities led Dr. Schubert and his colleagues to perform a clinical study in 2005 to determine if patients with A-T are deficient for certain GFs. They found that the levels of one particular GF, named IGF-1, and its interacting protein IGFBP-3 were significantly decreased in blood samples obtained from 19 patients with A-T. This discovery, together with evidence primarily from the study of A-T patients' cells grown in the laboratory, suggests that IGF-1 signaling is disrupted in the absence of the A-T protein. And it has caused scientists to think that patients with A-T might benefit from treatment with a GF.



Ralf Schubert, PhD

Certain GFs, like growth hormone (GH) and IGF-1 regulate sugar and fat metabolism which play an important role in the growth of children and adolescents. However, they are also important for proper brain growth and development. IGF-1 in particular has also been shown to protect the brain in various animal models of central nervous system damage and poor muscle control. Therefore, Dr. Schubert suspects that GH and IGF-1 might be effective in treating the brain deterioration associated with A-T.

Although GH and IGF-1 have appeared to be generally safe in clinical trials of other diseases to date, some research has shown that these growth promoting factors may be associated with the development of certain cancers. This is a concern because patients with A-T already possess a 1000 fold greater risk of developing cancer. Therefore, Dr. Schubert will use the mouse model of A-T to examine both the benefits and risks associated with GF treatment. Not only will this approach determine if treatment with GH or IGF-1 has a beneficial effect on growth and coordination, but it will also allow Dr. Schubert to observe if the GFs promote cancer development in the A-T mice.

Funded by the A-T Children's Project, Dr. Schubert's studies will be critical for determining if GF therapy is a realistic treatment option for patients with A-T to help slow their neurodegeneration without causing unwanted side-effects.

To commemorate his amazing 7th place finish in Beijing in August 2008, three-time Olympian, triathlete **Hunter Kemper,** sold commemorative t-shirts benefiting the A-T Children's Project and raising thousands of dollars for research.

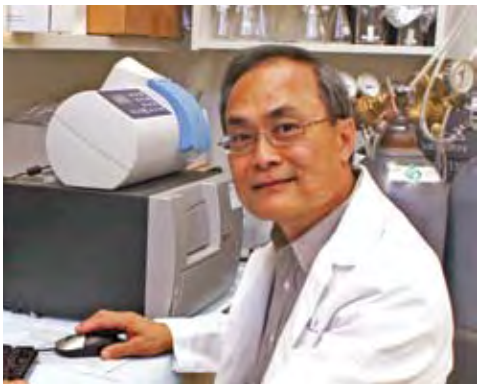
Kemper has also hosted charity benefits with triathlete groups across the country and is actively recruiting people to join him and the A-T CureTeam at the Walt Disney World® Marathon Weekend on January 2010.

Hunter has other surprises up his sleeve, so please check our website, atcp.org for updates.

Our most sincere thanks to Hunter and his wife Val for all of their efforts to help us find a cure!

ASTROCYTES: ANOTHER TYPE OF BRAIN CELL INVOLVED IN A-T?

Research into how the loss of the A-T protein (called ATM) affects a special type of brain cell known as the astrocyte may help explain the brain deterioration seen in A-T and may point to therapeutic options for this disease. To explore this possibility, the A-T Children's Project is funding **Paul Wong, PhD** from **The University of Texas MD Anderson Cancer Center.**



Paul Wong, PhD

Our brains contain two major types of cells: neurons and glial cells. When we think of the brain, we commonly think of neurons, those cells whose communication with each other controls our movements, thoughts, memories and emotions. However, neurons are actually out numbered in the brain (roughly ten to one!) by glial cells. Astrocytes, a particular type of glial cell, support, signal to and influence the metabolism and activities of neurons. For this reason, Dr. Wong suspects that astrocytes lacking the A-T protein may contribute to the degeneration of neurons seen in A-T.

Dr. Wong's laboratory has already shown that astrocytes from the cerebellum of A-T mice show signs of oxidative stress and abnormal positioning relative to their neuronal neighbors the Purkinje cells. This finding makes sense given that the primary brain region affected by A-T is the cerebellum. And a large body of evidence suggests that oxidative stress plays a role in the A-T disease process. With their A-TCP funding, Dr. Wong's research team will explore the effect that dysfunctional astrocytes from A-T mice (so called *Atm* null astrocytes) have on normal neurons and on neurons lacking the A-T protein. They will also determine whether or not treatment with various antioxidants can improve *Atm* null astrocyte function and enhance neuronal survival in these cell culture experiments.

Next, Dr. Wong's lab will move beyond cells grown in lab dishes and will treat A-T mice with the same antioxidants to determine if they can improve coordination in these animals. This A-TCP funded research may uncover a new role for the A-T protein in brain cells and could reinforce the idea that antioxidant therapy may slow or prevent the relentless neuronal degeneration that affects all patients with A-T.

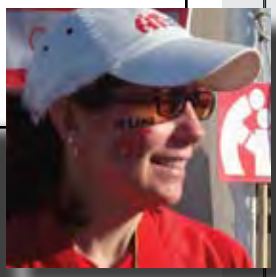
NEW IN 2009!

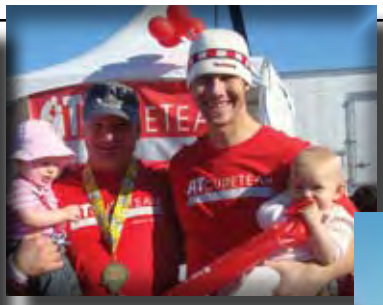
The Kauai Inaugural Marathon and Half Marathon

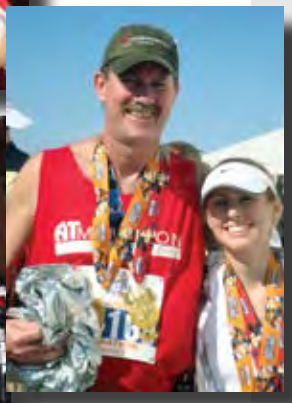
Run in paradise!
Sunday, September 6, 2009 Labor Day Weekend
Poipu Beach, Kauai, Hawaii
Poipu has one of the best climates in Hawaii.
Minimum Fundraising Commitment for Hawaii: $3900
Registration Deadline: May 31, 2009

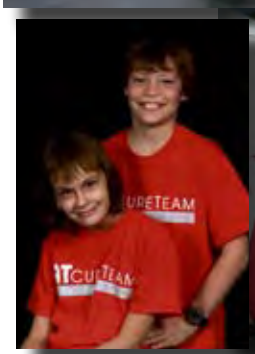
Fundraising Deadline: August 21, 2009
Fundraising commitment includes:

- *Race Registration - value up to $225*
- *Coach airfare from US or Canada*
- *3 nights Grand Hyatt - 2 CureTeam members/room*
- *Pre-race carbo load luau*
- *Personal fundraising web page*
- *Training tools*
- *Fundraising tools & help with fundraising events*
- *Kauai commemorative race shirt, inaugural medallion, complimentary massage, & awards party*
- *A-T race shirt & goody bag*
- *A-TCP medal*









RUN FOR KIDS WHO CAN'T!
MAKE A DIFFERENCE IN OUR RACE FOR A CURE!

HAVE FUN & GET IN SHAPE!
$600 MINIMUM FOR THE FOLLOWING RACES:

Disneyland 1/2 MARATHON WEEKEND
September 4 - 6
Anaheim, CA

Bank of America Chicago Marathon
October 11
Chicago, IL

Rock 'n' Roll San Antonio Marathon & 1/2 Marathon
November 15
San Antonio, TX

Walt Disney World Marathon Weekend
January 7 - 9
Orlando, FL

coming soon

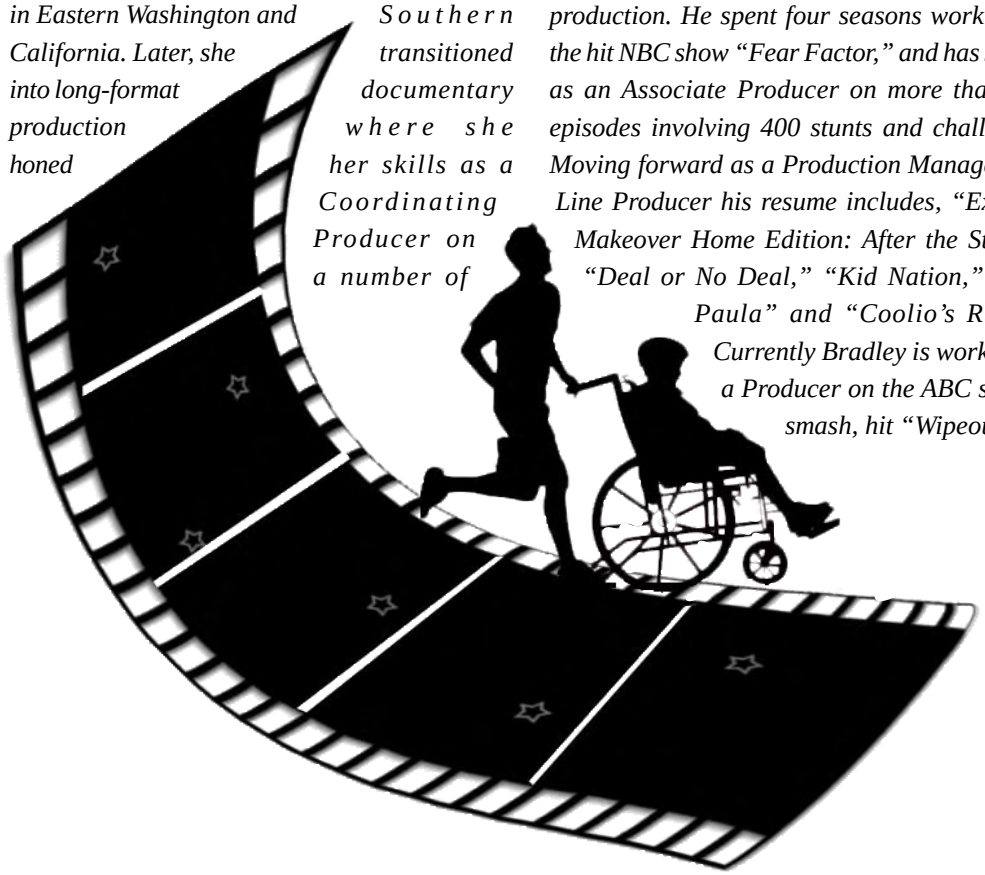
Thank you to Deb and Brad Carr for making FEAT, the documentary about the A-T CureTour, available to the A-T community for fundraising screenings. To volunteer to host a screening in your city, or to find a screening near you, go to atcp.org and click on the FEAT poster, or call 800.5.HELP.A-T.

THE FILMMAKERS

DEBORAH CARR
DIRECTOR / PRODUCER

BRADLEY D. CARR
CINEMATOGRAPHER / PRODUCER

Feat Productions, Inc. is the Los Angeles, California based Production Company headed by husband and wife team, Deborah and Bradley Carr. Both seasoned in television and documentary production, the two met in college where they collaborated to produce the first A-T Children's Project Telethon at the University of Wisconsin Oshkosh in 2000. Professionally, Deborah's television career started in local broadcast news where she was an Anchor and Reporter serving communities in Eastern Washington and Southern California. Later, she transitioned into long-format documentary production where she honed her skills as a Coordinating Producer on a number of documentary specials for The History Channel with Bill Brummel Productions. The 2004 documentary, "Rwanda Do Scars Ever Fade?" was recognized with the prestigious Peabody Award. Her work on human rights focused documentaries continued with "First to Fight: The Black Tankers of WWII" and "Standing Tall At Auschwitz." Deborah has also worked in various production roles on content for ABC, Discovery, Court TV, and the US Army. Bradley has extensive experience in reality television production. He spent four seasons working on the hit NBC show "Fear Factor," and has served as an Associate Producer on more than 130 episodes involving 400 stunts and challenges. Moving forward as a Production Manager and Line Producer his resume includes, "Extreme Makeover Home Edition: After the Storm," "Deal or No Deal," "Kid Nation," "Hey Paula" and "Coolio's Rules." Currently Bradley is working as a Producer on the ABC splash, smash, hit "Wipeout."



Deb and Brad Carr film Tim Borland during the A-T CureTour

FEAT

From the Documentary's Press Packet

Tim Borland, a 31-year-old father of two discovers his talent for endurance running is no longer fulfilled in the competitive realm. He meets 15-year-old Cathryn Achilles who is diagnosed with the rare terminal disease ataxia-telangiectasia (A-T). Despite the progressive loss of her ability to walk, talk, eat and sing, Cathryn's unwavering spirit inspires Borland to draw attention to the little known disease. He embarks on the A-T CureTour.

In the fall of 2007, Borland runs 63 consecutive marathons (26.2 miles) spanning more than 14-thousand miles, 29 States, 1 Canadian Province and 63 communities where children with A-T live.

Every step of the journey, Borland pushes a mobility-jogging stroller that either carries a child with A-T or a banner bearing the name of a child who has died. Battling excessive heat, drastic elevation changes, drenching downpours and hurricane strength winds, one man connects families and children whose hope for a cure and life prolonging treatment is further complicated because so few are impacted.

The harsh reality of what kids with A-T face everyday fuels Borland to complete each day's marathon course. When he crosses the finish line in New York City, he'll get a break. But, the race to find a cure continues. FEAT exemplifies the limitless potential of the human body and spirit when focused on a goal greater than oneself.

DUN & BRADSTREET BECOMES NATIONAL SPONSOR

Tim Borland accepts $5,000 for the A-TCP from D&B

Ultra marathoner Tim Borland spoke at the Dun & Bradstreet Global Senior Leader meeting in Atlanta, GA about his experiences running 63 marathons in 63 days to raise money and awareness for A-T during the A-T CureTour. His presentation had a profound impact on the 140 senior leaders who attended, earning him a rousing standing ovation. Tim will continue speaking about the A-T CureTour to business groups throughout 2009.

Biomarkers - Continued from page 1

identified. Therefore, the A-T Children's Project is funding Dr. Wang to identify new biomarkers from the cerebrospinal fluid (CSF) of patients with A-T.

Obtaining CSF samples requires donors to undergo a lumbar puncture (LP or spinal tap) which can be uncomfortable. However, CSF was chosen because it holds the greatest potential for identifying biomarkers indicative of the brain deterioration associated with A-T. Dr. Wang and his research team will use proteomics techniques to identify proteins that are expressed differently in the CSF of patients with A-T versus CSF from age and gender matched controls. Control and A-T patient CSF samples will be obtained and provided by the A-T Clinical Center and Lumbar Puncture Center at Johns Hopkins Hospital, under the direction of Dr. Howard Lederman, director of the A-T Clinical Center.

DAVID COX, MD, PHD, REJOINS A-TCP SCIENTIFIC ADVISORY BOARD

The A-T Children's Project is pleased to welcome **David Cox, MD, PhD** back to the Scientific Advisory Board. Dr. Cox is Senior V.P. and Chief Scientific Officer of Biotherapeutics and Innovation Center at **Pfizer, Inc.** He is internationally recognized for his research on the molecular basis of human genetic disease.

After receiving his B.A. and M.S. degrees from Brown University in Rhode Island, Dr. Cox obtained his MD and PhD degrees from the University of Washington, Seattle. He then completed his Pediatric Residency at the Yale-New Haven Hospital in New Haven, Connecticut and was a Fellow in both genetics and pediatrics at the University of California San Francisco.

From 1980 to 1993, Dr. Cox held faculty positions in the Departments of Pediatrics, Biochemistry and Psychiatry at the University of California San Francisco. In 1993, he accepted a position as a Professor of Genetics and Pediatrics at the Stanford University School of Medicine as well as the Co-director of the Stanford Genome Center.

From 2000 to 2008, Dr. Cox was the Chief Scientific Officer of Perlegen Sciences, Inc. In August of 2008, Dr. Cox left Perlegen to join Pfizer's newly established Biotherapeutics and Bioinnovation Center. Dr. Cox is certified by both the American Board of Pediatrics and the American Board of Medical Genetics. He has served on several international and national councils and commissions including the Council of the Human Genome Organization (HUGO) and the National Bioethics Advisory Commission (NBAC). He presently serves as a member of the Health Sciences Policy Board of the Institute of Medicine.

David R. Cox, MD, PhD

Dr. Cox's honors include election to the Institute of Medicine of the National Academy of Sciences.

MORE ABOUT THE CSF BIOMARKER STUDY FOR A-T AND THE DONATION PROCESS

Location: A-T Clinical Center, Johns Hopkins Hospital (CSF draw); Indiana University and Monarch Life Sciences (sample analysis)

Investigators: Howard M. Lederman, MD, PhD; Mu Wang, PhD

Purpose: To identify markers within patient CSF which represent signs of disease or disease progression and which can be monitored to determine drug effectiveness in a clinical trial.

Eligibility Requirements: 18 years of age or older (younger individuals may be able to participate if they are going to the A-T Clinical Center for a separate surgical procedure); previously evaluated at A-T Clinical Center at Johns Hopkins or must provide medical records that confirm the diagnosis of A-T; a medical history detailing any prescription, over the counter or dietary supplements will be required for those who donate samples.

Exclusion Criteria: Anyone with a medical illness in addition to A-T (such as diabetes, cancer or thyroid disease requiring medicine) would not be eligible. Anyone who has a history of brain tumor, increased intracranial pressure, severe headache following a previous lumbar puncture or history of spinal fusion would not be eligible.

Other Requirements: Brain MRI and blood tests one day prior to LP

Status: Currently Recruiting

Benefits: MRI; Travel and hotel for patient + 1 to Baltimore

Contact: Karen Rosquist, RN, Nurse Coordinator, e-mail: krosquis1@jhmi.edu

Phone: 800.610.5691

LUNG AND SWALLOWING STUDIES IN CHICAGO AND ORLANDO

Thanks to the people with A-T who participated in recent lung function studies, doctors may understand why some have more lung problems than others.

Clinicians from the A-T Clinical Center at Johns Hopkins Hospital measured patient's lung function by standard clinical testing. Patients were fitted with sterile snug-fitting mouthpieces (similar to a snorkel used for swimming) and soft clips were placed on their noses to prevent air leaks. Then, they were asked to breathe normally through the mouthpiece for 2-3 minutes while the doctors recorded measurements of air flow. This was repeated several times with rest periods. Sometimes, patients were asked to breathe as hard and fast as possible, and other times, to breathe normally.

And, clinicians measured the coordination of swallowing and respiration to look for problems patients may be having with eating or drinking. As a part of this process, they used a special machine (Respirodeglutometer, RDG) to measure the coordination between breathing and swallowing. A small tube was placed just under their noses, two small

A-T patient participates in swallowing study.

sticky pads were placed under the chin, and a third pad was placed either behind the ear or on the forehead. A surface microphone was placed on the neck. They were then asked to take a deep breath and say the "ah" sound for as long as possible on one breath. This task was repeated three times. Next, patients were asked to complete 5 swallows of water, and 5 swallows of pudding.

Thanks to **Sharon McGrath-Morrow, MD**, **Maureen Lefton-Greif, PhD,CCC/SLP, Amber Kelly, CPFT** and **Karen Rosquist, RN** for their dedication to making the study a success.

Yang - Continued from page 1

With additional experiments, Dr. Yang's group confirmed that the brain cells required cytoplasmic ATM to respond to this stress.

With his newly funded A-T Children's Project grant, Dr. Yang will try to identify proteins that are being made by these brain cells when ATM is activated in response to growth factors like insulin. If he succeeds, he and his colleagues will explore the function of these proteins in hopes of finding ones that could be activated in children with A-T to prevent their brain cells from dying.

Herrup - Continued from page 1

messages that are received by other brain cells. Working together with **Mark Plummer, PhD**, an electrophysiologist at Rutgers, Drs. Herrup and Li were able to confirm that brain cells lacking ATM have problems communicating.

With their new funding from the A-T Children's Project, Drs. Herrup and Li will expand their research efforts on the interactions between ATM and the two cytoplasmic proteins. They will also determine how the absence of ATM affects the structure and shape of brain cells. Insights gained from this research could generate new therapeutic strategies to help patients with A-T.

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)

PARTICIPATE IN UPCOMING 2009 EVENTS

Stay updated at atcp.org

March 28 - ***Millsap Mini Marathon***
Cypress, Texas

April 22 - ***Swinging for Emily***
Cypress, Texas

May 1 - ***Kidz Talent Show***
Jenison, Michigan

June 13 - ***A-T Walk for a Cure***
Fort Macleod, ALBERTA, Canada

June TBA - ***Fishing for a Cure Tournament***
Whitewater, Wisconsin

June 29 - ***A-T Walk for a Cure***
St. Benedict, Pennsylvania

July 10 - ***A-T Golf Tournament***
Coaldale, ALBERTA, Canada

July 24 - ***Aaron's A-T Golf Challenge***
Grand Haven, Michigan

July TBA - ***Ham's and Hog's Charity Ride***
Greenville, North Carolina

August TBA - ***Golf for a Cure***
Hudsonville, Michigan

September - October - ***Rémi Aubrun's Solo Transatlantic Yacht Race*** in the Transat 6.50

Sept. 4-6 - ***Disneyland Half Marathon Weekend****, Anaheim, California*

Sept. 5-6 ***Kauai Marathon/Half Marathon***
Kauai, Hawaii

Sept. TBA - ***A-T Masters Golf Scramble***
Hamilton, Michigan

Sept. 27 - ***Hope with Every Step 5K, Kids 1K, & Family Fun Walk*** *- Littleton, Colorado*

Sept. TBA - ***Strike Against A-T Bowling Party,*** *Whitewater, Wisconsin*

Oct. TBA - ***Road Rally***
Hudsonville, Michigan

Oct. 11 - ***Bank of America Chicago Marathon****, Chicago, Illinois*

Oct. TBA - ***Aaron's A-T Walk for a Cure***
Fruitport, Michigan

Oct. TBA - ***Boo Dash Bash 5K and 10K Races****, Greensboro, North Carolina*

Nov. 15 - ***San Antonio Rock 'n Roll Marathon*** *& Half Marathon, San Antonio, TX*

Nov. TBA - ***Samuel Clemens High School Key Club Softball Tournament*** *- Shertz, TX*

Nov. TBA - ***A-T Telethon*** *U. of Wisconsin/ Oshkosh 3pm-12am live at www.attelethon.com*

ATW 2008 HELD AT LAKE BIWA, JAPAN

Group of researchers gathered in Japan to discuss the latest advances in A-T research

The International Ataxia-Telangiectasia Workshop 2008 (ATW2008) was held at the Otsu Prince Hotel, in Shiga, Japan from April 22 to April 26, 2008. The meeting organizers were Drs Kenshi Komatsu and Junya Kobayashi from Kyoto University and Dr. Shuki Mizutani from the Tokyo Medical and Dental University.

Surrounded by beautiful Lake Biwa, scientists heard novel and cutting edge talks on the following topics: Clinical and Translational Research for A-T; ATM/ATR and DNA Repair in the Nervous System; Tumorigenesis, Immunodeficiency and DNA Repair; Activation of ATM and the MRN Complex; The DNA Damage Signaling and Chromatin Response and Other DNA Damage Response Proteins and Syndromes. The meeting also featured a keynote lecture by **Dr. Yosef Shiloh**, a presentation from **Dr. Danilo Tagle**, Program Director at NINDS/NIH, on NINDS resources for translational research and a series of very good short talks from young investigators.

Several A-T Children's Project funded investigators also presented their current research at ATW2008:

Dr. Sharon McGrath-Morrow, a pediatric pulmonologist at the A-T Clinical Center at Johns Hopkins University, presented her work on the measurement of lung function in adolescent patients with A-T.

Dr. Jessamyn Bagley from Brigham and Women's Hospital in Boston told the audience about her novel finding that under certain circumstances the A-T protein is required for the survival of important immune system cells.

Dr. Ari Barzilai from Tel Aviv University shared his research on the DNA damage response in the brain.

Dr. Karl Herrup, a neuroscientist from Rutgers University, presented his laboratory's findings on a novel role for the A-T protein in neurons (for more details see article on page 1).

Dr. Aasef Shaikh, also from the A-T Clinical Center at Johns Hopkins, presented his results from a small clinical trial that examined the effects of a drug called 4-aminopyridine on motor control in patients with A-T.

Researchers from Johns Hopkins Hospital - from Left: Sharon McGrath-Morrow, Tom Crawford, Maureen Lefton-Greif and Aasef Shaikh with Cynthia Rothblum-Oviatt, Science Coordinator of the A-TCP

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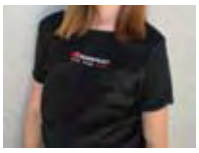

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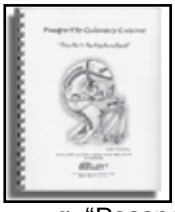

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The A-T Children's Project is a public 501(c)(3) non-profit organization that raises funds to support and coordinate biomedical research projects, scientific conferences and a clinical center aimed at finding a cure for ataxia-telangiectasia, a fatal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

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