

April 2010

DOCTORS SEEK TO IMPROVE LUNG HEALTH IN PEOPLE WITH A-T



From left: Maureen Lefton-Greif, PhD, CCC/SLP, Howard Lederman, MD, PhD, Thomas Crawford, MD, Cynthia Rothblum-Oviatt, PhD and Sharon McGrath-Morrow, MD.

The A-T Children's Project held a workshop entitled "Pulmonary Disease in Ataxia-Telangiectasia." This workshop, which focused on the lung problems faced by people with ataxia-telangiectasia (A-T), had two goals: 1) to discuss "best practices" for managing lung disease associated with A-T and 2) to better understand the changes in patients' lungs that may ultimately lead to lethal consequences so that strategies can be developed for preventing such lung disease.

A world-class group of pulmonologists and immunologists, many of whom were from outside of the A-T world, gathered in Baltimore, Maryland to lend their expertise to the workshop. These clinicians, who normally focus on patients with Cystic Fibrosis, Muscular Dystrophy or Parkinson's Disease, discussed a variety of lung issues, and the A-T Children's Project's Science Coordinator, Cynthia Rothblum-Oviatt PhD, provided the attendees who were new to A-T with background information on the molecular basis of this disease.

The workshop will have important implications for patients with A-T of all ages, and the clinician/scientists involved are currently co-authoring a state-of-the-art publication for the journal *Pediatric Pulmonology* that will help people with A-T worldwide to live as healthfully as possible.

MEETING TOPICS

- Neurology
- Lung Disease: Aspiration, Sleep and Experiences in Managing and Maintaining Lung Health
- Interstitial Lung Disease
- Infections and Immunology
- Long Term Follow-Up, Interventions and Preventative Strategies
- Finalizing Best Practices and Future Directions for Research

NEW RESEARCH CHALLENGES OLD BELIEFS

Every so often research comes along that challenges old beliefs and forces us to look at things in a different light. A neuroscientist at Rutgers University with funding from the A-T Children's Project is performing just this type of groundbreaking research on the A-T protein.

Although scientists have known for some time that the A-T protein functions to coordinate the cell's response to damaged DNA, Karl Herrup, PhD and his collaborator, Mark R. Plummer, PhD have found evidence that the A-T protein plays an entirely different, but perhaps equally critical, role in the brain. While the DNA damage response takes place almost exclusively in the cell nucleus, the Herrup and Plummer teams are exploring new and distinct roles for ATM in the cytoplasm of nerve cells. This finding may open doors to new therapeutic strategies for A-T, and provide a common link between A-T and other neurodegenerative diseases like Alzheimer's.

In addition, Dr. Herrup has found preliminary evidence that one of the most popular A-T mouse models actually possesses A-T protein in the brain (though this protein is absent in other tissues like the thymus, immune system, skin and reproductive organs). If verified, this unexpected finding may explain why this particular mouse model of A-T lacks any brain abnormalities, and it may have implications for the neurological variability seen in the human disease.



Karl Herrup, PhD



Mark R. Plummer, PhD

FEAT Awards and More

2

G-TUBES IN A-T One family's story

3

PROGRESS REPORT Novel Biomarker for A-T

4

MARATHONS AND RACES

6



In addition to several private screenings benefiting the A-T Children's Project, the documentary FEAT has been featured at several film festivals where it has won several prestigious awards, including:

- Audience Award, Best Documentary – Big Bear Lake International Film Festival 2009
- Professional Best of Show – Interrobang Film Festival 2009
- Helping Hand Humanitarian Award – Rhode Island International Film Festival 2009

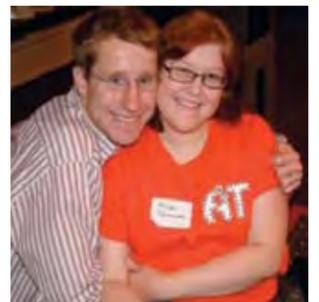
FEAT chronicles Tim Borland's coast-to-coast quest to run 63 marathons in 63 days during the A-T CureTour in 2007.

Visit atcp.org to find out where FEAT will be playing next.



A sold-out crowd gathered at the FEAT screening in Des Moines, Iowa. The screening and auction held at the Meredith Corporation raised over \$27,000. Olympic triathlete Hunter Kemper and wife Val worked tirelessly to make this screening happen.

FEAT producers, Deb and Brad Carr are working to secure distribution for the documentary. Please visit their website at featmovie.com to learn more.



Hunter Kemper with Paige ▲ and Alex Champion ▼



PROGRESS REPORT: COULD GROWTH FACTORS HELP TREAT A-T?

To determine if growth factors (GFs) represent a potential life-improving therapy for patients with ataxia-telangiectasia (A-T), Ralf Schubert, PhD and Prof. Stefan Zielen, MD from the Klinikum der Johann Wolfgang Goethe Universitaet in Frankfurt Germany have been examining the benefits and risks associated with GF treatment in A-T mice.

Results from Dr. Schubert's A-T Children's Project funded research have recently been published in the journal *Growth Factors*. His key findings from this publication include the following: no change in weight gain or food intake in growth hormone (GH)-treated A-T mice; an increase in longevity or life span of A-T mice treated with GH; improvement in immune cell abnormalities in treated mice and a trend towards decreased neurobehavioral deficits in A-T mice treated with GH. The vast majority of A-T mice die from an aggressive form of cancer called thymic lymphoma. Given that growth factors may be associated with the development of certain cancers, and 10-30% of patients with

A-T develop cancer in their lifetime, this was an important risk factor for Dr. Schubert to examine in the mice. Dr. Schubert's observations suggest that GH does not contribute to the development of thymic lymphoma in A-T mice.

Since treatment with GH had positive effects on the general condition of A-T mice, Dr. Schubert

and his team are encouraged to continue their mouse studies. They now plan to treat A-T mice with the growth factor IGF-1 alone and in combination with GH to investigate whether or not they can improve upon the effects they have already seen. These studies will help determine if GFs can be used as a therapeutic option for A-T without causing unwanted side-effects.

In addition, a two year clinical trail has begun in Frankfurt Germany which will investigate whether or not patients with A-T are able to generate GH or IGF-1 appropriately. Prof. Zielen and Dr. Schubert will also examine growth failure and body weight in the study participants. Along with the results from the mouse studies, positive results from this human study could lay the foundation for a trial examining the ability of GH or IGF-I to provide some level of neuroprotection in children with A-T.

For more details on the current GH/IGF-1 trial, please visit <http://clinicaltrials.gov/> and search for Schubert and Zielen.



Prof. Stefan Zielen (3rd from L), Ralf Schubert (2nd from L) and members of the Zielen Laboratory along with Mr. Hermann Stimm (L) and his daughter Dagmar (center)

“OLD KATE” IS BACK! by Mary Veldink

“Kate, you have to eat something!” I yelled.

“I’m not hungry!” screamed Kate. And so it went. Meal after meal. Day after day.

“Drink your Ensure!”

“I can’t believe you are making me drink this gross stuff! I won’t do it!”

A year and a half ago, if you would have come to our house during meal time, it would not have been pretty. You would have seen tears and heard screaming. Mealtime was stressful for everyone.

Today, we would love to have you and your family over for dinner. (Okay, I’m not the best cook, so maybe we’d order in!) There is no screaming, no yelling, and no tears. Why the difference? We finally got Kate a feeding tube.

The doctor told us we should get one for her. Dave, Kate, and I resisted. We thought we could get her to gain the weight she so desperately needed. We tried everything...bribery, McDonald’s shakes, and Vitamin D chocolate milk. Nothing worked. In the meantime, Kate was getting thin...too thin. Her stomach was shrinking. She was full after eating just a few bites of macaroni and cheese. Finally, our doctor convinced us to meet with a surgeon. We met with him, and he answered all of our questions about putting this tube into our daughter. We decided to give it a try.

The surgery was nothing like we thought it would be. It took much less time and the hospitalization stay was shorter than we imagined. Our surgery, hospital stay, and getting accustomed to tube feedings was so simple. Almost immediately we noticed a change in Kate. She was happier, had more energy and she began to grow! She hadn’t changed sizes in forever, and now it seemed as if I needed to get her a new pair of jeans every couple of weeks. We felt like we had the “old Kate” back.

Today, Kate is twenty five pounds heavier than she was a year and a half ago. She isn’t tired when she comes home from school and meal time isn’t stressful anymore. We don’t care whether or not she eats the food that is put in front of her. We know she will get all the nutrients she needs during her nightly feeding.

I was worried that Kate’s tube would show through her clothing. I went out and bought swing tops and loose fitting shirts. I shouldn’t have. Kate is able to wear tee shirts and even a tankini bathing suit without noticing the button. She also still enjoys eating regular food at times. She is actually eating more now than ever because her stomach has expanded. You should see her eat at Panera Bread!

When Dave and I are out, Abby, our fourteen-year-old daughter, is in charge of Kate’s feedings. It is no problem for her to “hook her up” and start the process. Last weekend, Kate went to a youth group outing. While the kids were goofing around, Kate’s tube came undone. Her friend lifted her shirt, plugged the tube back in, and the kids were back to goofing around! It really is very easy.

The results are amazing. Getting a [G-] tube has truly changed Kate’s life! It has also made our family life much more enjoyable.



The Veldinks: Abby, Mary, Dave, Olivia, Kate and Buttons

GASTROSTOMY TUBES IN ATAXIA-TELANGIECTASIA

By Maureen Lefton-Greif, PhD, CCC/SLP

We swallow approximately 600 - 900 times daily. Swallowing is critical for survival and its jobs are to: (1) direct food, liquid, and saliva from the mouth to the stomach while keeping the airway protected; and (2) deliver enough of the right types of liquids and foods for adults to stay healthy and children to grow and develop. Dysphagia [dis-fā`ja] is the term used to describe swallowing problems. Over time, dysphagia can cause respiratory or nutrition problems, or both. Dysphagia can cause breathing problems when liquids or foods enter or are aspirated into the airway. Dysphagia can also cause nutrition problems if it prevents someone from getting enough to eat or drink. In turn, respiratory and nutrition problems may cause other significant health problems and adversely affect a person’s quality of life.

Some people may have problems getting enough to eat or drink even when they do not have swallowing problems. These people may be extremely picky eaters or have very poor appetites. Poor feeding that results in growth and nutrition problems can also have a negative impact on a person’s health and well-being.

Dysphagia is common in A-T and typically presents during the teenage years. Poor feeding can occur for many reasons and at any age. Minor swallowing or feeding problems may be treated with changes in feeding routines and dietary intake. Adjustments in the manner of feeding may not be enough to prevent breathing or nutrition problems when even minor swallowing or feeding problems are present for a long time, or when they become more severe. When swallowing or feeding problems threaten to cause breathing or nutrition problems, a gastrostomy tube (G-tube) may be recommended. G-tubes are feeding tubes that are surgically placed directly into the stomach and can provide a means for getting safe nutrition. In our experiences at the A-T Clinical Center at the Johns Hopkins Hospital, G-tubes work well when they are placed before dysphagia causes significant breathing or nutrition problems.

Persons with A-T, their caregivers, physicians, and other health care providers should discuss the risks and benefits associated with placing a G-tube as soon as swallowing, nutrition, or breathing problems arise. After G-tubes are placed, many people continue to eat foods and drink liquids that are the easiest for them to swallow and can still enjoy mealtimes with their family members.

The *Eric H. Weinberger Fund for Research* was established on January 18, 2010 at Lincoln Center in New York City during the 15th annual *A Very Special Evening*. John Feeley, A-T Children’s Project board member, made the announcement honoring Eric for his ongoing support producing and directing this annual event which has



Renate Klein, Eric Weinberger and Tori Bement-Schramm

raised almost \$600,000 over the years. Emcees Priscilla Lopez and Louis Zorich introduced some of New York’s finest performers who dazzled the audience with their talent. This year’s event was another great success raising over \$45,000 for research.

NEW PUBLICATION ON INFLAMMATION AND A-T

Sharon McGrath-Morrow, MD, a pediatric pulmonologist with the A-T Clinical Center at Johns Hopkins Hospital, has found that levels of a pro-inflammatory molecule in the body called IL-8 are often elevated in patients with ataxia-telangiectasia (A-T).

IL-8 is associated with premature cell aging, cancer progression and chronic inflammatory disorders. In her

study, Dr. McGrath-Morrow found that IL-8 levels in patients with A-T were higher than that of patients with cystic fibrosis, non-A-T immunodeficiency, and healthy controls. These results, which have recently been accepted for publication in the *Journal of Pediatrics*, suggest that systemic inflammation may play a role in A-T. With further study, these findings may represent an avenue for potential therapy.

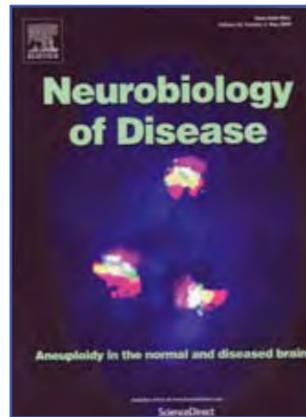
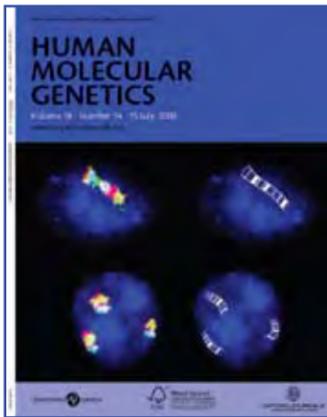
PROGRESS REPORT: GENOMIC INSTABILITY IN THE A-T BRAIN

Over the years researchers have proposed various reasons as to why brain cells die in people suffering from ataxia-telangiectasia (A-T). With funding from the A-T Children's Project, Prof. Yuri Yurov, MD, PhD and his collaborators from the Russian Academy of Medical Sciences explored the possibility that chromosome or genomic instability contributes to brain cell death in A-T.

Dr. Yurov's A-TCP funded studies resulted in several publications, including articles in the prominent scientific journals **Neurobiology of Disease (Aneuploidy in the normal, Alzheimer's disease and ataxia-telangiectasia brain:**

differential expression and pathological meaning. Iourov IY et al., *Neurobiol Dis.* 2009 34:212-20) and **Human Molecular Genetics (Increased chromosome instability dramatically disrupts neural genome integrity and mediates cerebellar**

degeneration in the ataxia-telangiectasia brain. Iourov IY, et al. *Hum Mol Genet.* 2009 18:2656-69). Dr. Yurov's impressive molecular cytogenetics research also made the cover illustrations of these issues of the journals. These important studies provide the first evidence that genomic instability dramatically alters the integrity of the brain genome and disrupts specific genes which are crucial for vitality of cerebellar brain cells in A-T. In addition, Dr. Yurov's results have revealed a new genetic mechanism of neurodegeneration connecting it to cancer-like processes in the diseased brain. It is hoped that Dr. Yurov's research will lead to novel therapeutic approaches for A-T.



PROGRESS REPORT: THE SEARCH FOR NOVEL BIOMARKERS FOR A-T

Biomarkers, or substances connected with disease state, can be used to monitor disease progression and/or assess drug effectiveness in clinical trials. Biomarkers can also provide new insights into the disease process itself.

With a grant from the A-T Children's Project (A-TCP), an investigator from the Indiana University School of Medicine and Monarch Life Sciences, LLC has been attempting to identify new biomarkers for ataxia-telangiectasia (A-T) from the cerebrospinal fluid (CSF) of donors suffering from this debilitating disease. Using sophisticated, state-of-the-art proteomics techniques Mu Wang, PhD has been able

to identify changes in the levels of certain proteins in the CSF of patients with A-T versus normal controls. These preliminary results are very promising, but will require extensive confirmatory studies. If the additional studies produce similar results, Dr. Wang will have successfully identified biomarkers for A-T that can potentially be used to follow disease progression and monitor future treatments.

Special thanks to the A-T Clinical Center at Johns Hopkins Hospital for their aid in the donor recruitment process and coordination of the lumbar punctures. It is possible that recruitment for this study may reopen again in the future, in which case families will be notified.

KIDS HELPING KIDS



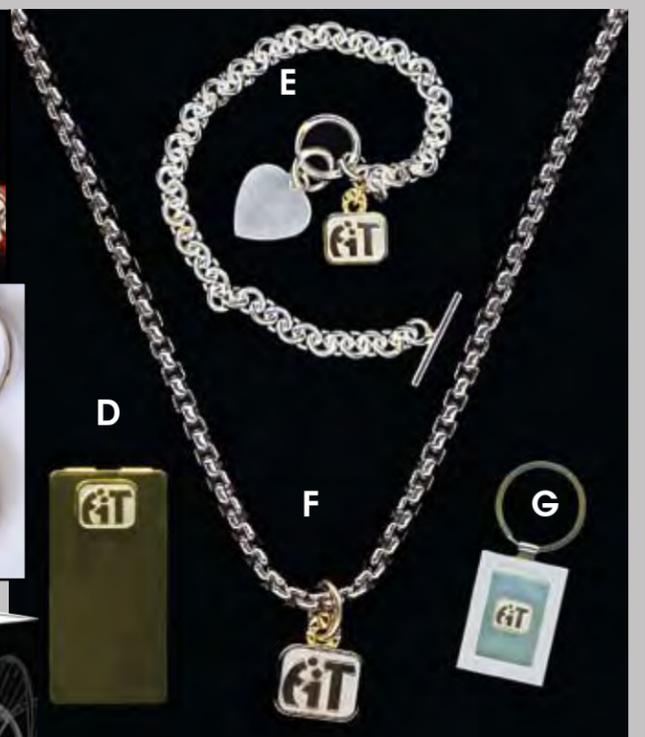
Kids from all over the country are helping their friends and relatives who have A-T by raising money at birthday parties, school events, and neighborhood get togethers.



NEW DONATED LOGO MERCHANDISE AVAILABLE ON A-TCP MARKETPLACE

New jewelry items and a window decal (Items A through G) have been generously donated to the A-T Children's Project. Order online at atcp.org or call 800.5.HELPA-T so that 100% of the funds can be used for our mission.

- A - A-T Silicone Bracelet \$7
- B - A-TCP Auto Decals 5" x 2.5" 2/\$5
- C - Silver Key Ring - \$12 (Engraving \$15 - max. 8 characters)
- D - Gold Plated Money Clip \$25
- E - Sterling Silver A-T Toggle Bracelet \$72
- F - Sterling Silver Necklace \$90 or Two Tone Silver/Gold Necklace \$173
- G - Sterling Silver and Gold Plated A-T Key Ring - \$25
- H - 3" cube with message: "Kids with ataxia-telangiectasia deserve first-rate research" - \$15 each or 2 for \$25



YACHT CALLED THE A-T CHILDREN'S PROJECT RACES ACROSS THE ATLANTIC

When Corentin Corre and Nancy Charves, whose daughter Caroline has A-T, decided to do a fundraiser to benefit the A-T Children's Project, they never dreamed that it would involve an international yacht race and two events that would shatter all expectations.

A dear friend of Corentin's, Rémi Aubrun, sailmaker, innovator, and skipper, chose to name his racing yacht the A-T Children's Project and entered it in the Transat 6.50, a grueling, transatlantic solo race of 4200 nautical miles. Leaving from Charente-Maritime, France to Funchal (Madeira Island, Portugal) and finishing in Salvador de Bahia, Brazil, the Transat is one of the most challenging ocean races for amateurs and professionals alike. Competitors usually hand steer for about twenty hours a day, only leaving the helm to eat, rest and navigate.

The Squantum Association, a private club in Rhode Island where Corentin is the General Manager, became a sponsor by raising \$5,000 to emblazon Rémi's main sail with their logo during the "Squantum Sails for Caroline" Kick Off Cocktail Party in May of 2009. This fundraiser was followed up by a casual Caribbean Casino Night in August where nearly 100 club members and their friends and families enjoyed camaraderie, great food, cocktails, auctions, and dancing. With the help of Jerry Masa, Deb Moretti, Nancy and Camille Corre, and the rest of the committee, these events raised over \$35,000 for A-T research.

Countless supporters followed Rémi's Transat voyage online and sent messages of encouragement every step of the way. After 39 days, coming in 13th overall out of 85 yachts, Rémi landed in Brazil. It was an incredible finish and a dream come true for Rémi, especially since he was able to help in finding a cure for Caroline.



▲ Rémi Aubrun at the helm of the "A-T Children's Project"



◀ Caroline and Camille Corre "gamble away"



▲ Cheryl Lamontagne, Lisa Sullivan, Larry Brillon, Jennifer Brillon and Lori LeMay

CLINICIAN RESPONDS TO H1N1 CRISIS

In a quick response to the growing H1N1 fears in the fall of 2009, Dr. Howard Lederman at the A-T Clinical Center at Johns Hopkins provided up-to-the-minute recommendations regarding flu vaccines and treatment for people with ataxia-telangiectasia, synopsis as follows:

- At this point, there is no experience or information available about whether people with A-T are at greater risk of getting H1N1 than people in the general population.
- Prevention - Everyone receiving the seasonal influenza vaccine should also receive the H1N1-A vaccine.
- Flu Shot – This killed virus vaccine is the type that people with A-T should receive.

- FluMist® - This live vaccine may have a risk for people with immune deficiencies, so it is a general recommendation that patients not be given this form of vaccine.
- Everyone in the family should be immunized to create a protective "cocoon" around the person with A-T.
- If there is a known direct contact with someone who has the flu by someone who has A-T, that person should take Tamiflu once a day for 10 days.
- If the person with A-T develops symptoms of the flu, he/she should take Tamiflu twice a day for 10 days.

This synopsis is just meant to provide a brief overview. For the complete recommendations, please visit our website at atcp.org.

GENES & JEANS ... A NATURAL FIT



The A-T Children's Project is partnering with The Global Genes Project (GGP) on several "Denim and Diamonds" events, keeping with their theme of "Hope. It's in our Genes." While we are using materials developed by the GGP, 100% of all proceeds of these events will benefit the activities of the A-T Children's Project.

The Global Genes Project, a grassroots effort with a simple goal: to increase awareness for the prevalence of rare diseases and help those affected by them. There are currently just over 7,000 rare diseases identified, affecting 30 million people in the US alone. Although these numbers are staggering, what is of even greater concern is that approximately 75% of those affected are children, making this disease category one of the most deadly and debilitating for our country's children.

"Denim and Diamonds" parties are happening near Chicago, Las Vegas, and Arlington, VA, ranging from a house party, to a dinner/dance, to an auction. To plan a "Denim and Diamonds" party near you, please email fundraising@atcp.org or call 800.543.5728.



TO JOIN OUR ONLINE COMMUNITIES GO TO WWW.ATCP.ORG AND CLICK ON THE LOGOS



Join the A-T CureTeam at one of these upcoming races and experience the most inspiring weekend filled with hope.

REGISTER TODAY AT ATCP.ORG

- Low fundraising minimums
- Race shirts
- Medals
- Parties
- Fundraising web pages

Hy-Vee Triathlon

West Des Moines, Iowa
 June 12-13, 2010

Join Team Kemper at the Hy-Vee Triathlon

- No fundraising minimum
- Pasta dinner with Hunter Kemper

Disneyland Half Marathon Weekend

Anaheim, California
 September 3-5, 2010

Create family memories in the Happiest Race on Earth!

- Disney's special 5th anniversary castle
- Family 5K available

Kauai Marathon and Half Marathon

Poipu Beach, Hawaii
 September 5, 2010

Join us in paradise for the run of your life

- Carbo-load luau included
- \$600 fundraising minimum **or** \$3,900 (includes coach airfare and luxury hotel)

Bank of America Chicago Marathon

Chicago, Illinois
 October 10, 2010

Coveted spots available for this marathon -- the pinnacle of achievement for elite athletes and everyday runners from all 50 states and more than 100 countries

Hope with Every Step

Livermore Falls, Maine
 October 2010

Naples, Florida
 December 2010

Walt Disney World® Marathon Weekend

Lake Buena Vista, Florida
 January 7-9, 2011

Have a magical weekend with Mickey and Minnie and over 30 A-T families and friends at the marathon where every mile is filled with Disney Fun and the memories are magical. One of the most inspiring and awesome weekends of the year!



Front row from left: Connor Dzembo, Katie Smith, Jennifer Powell, Emily Hughes, Kate Veldink, Olivia Veldink, Aaron Biros and Alyssa Wood Second row: Tyler Smith, Joe Kindregan, Jake Benarath, Savanna Hamrick, Andrew Martin and Keaton Sakowich Back from left: Jarrett Margus, Quinn Margus, Douglas Fickel, Rob Smarz (standing) and John Matejko

A-T CureTeam Friends and Families Making a Difference



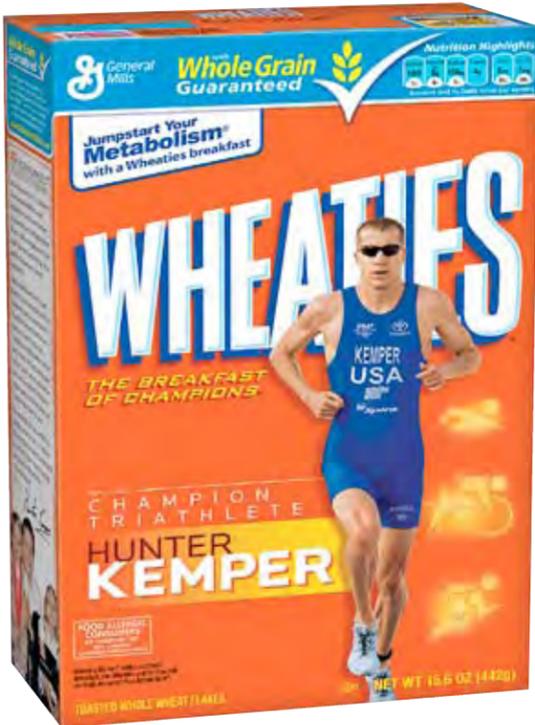
Girls with A-T gathered during the marathon weekend to talk about what it's like to have A-T. Even though they live miles apart, this is a graphic reminder that they are not alone.

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
 5300 W. Hillsboro Blvd., Suite 105
 Coconut Creek, Florida 33073 U.S.A.
 atcp.org • 800-5-HELP-A-T

NON-PROFIT ORG.
 U.S. POSTAGE
 PAID
 BOCA RATON, FL
 PERMIT NO. 770

When **Hunter Kemper** graced a WHEATIES® box this past summer, he made sure that an entire side panel was dedicated to the A-T Children's Project.

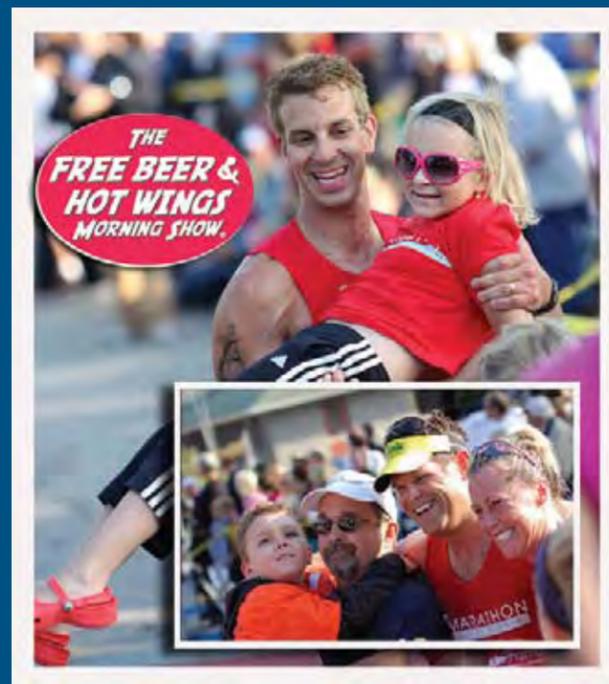


Join US Olympic Triathlete Hunter Kemper's **A-T CureTeam** for a 1.5k swim, 40k bike and 10k run in an Olympic-distance race at the Hy-Vee Triathlon in Des Moines, Iowa on June 12 & 13, 2010

- Do you plan on racing the Hy-Vee Triathlon this year?
- Are you looking for a great race to participate in?
- Would you like to watch the top 50 men and women in the world compete for the largest prize purse in the world?
- Would you like to hang out with Hunter for a weekend?
- Would you like to experience the joy of making a difference in the lives of kids that struggle with a deadly genetic disease?



If you've answered "yes" to any of these questions, you **MUST** sign up for "Team Kemper" at the Hy-Vee Triathlon this June! It will be a weekend you won't want to miss! Register with the Hy-Vee Triathlon and then go to www.atcp.org to sign up for Kemper's A-T CureTeam.



RADIO DEEJAY AND FRIENDS RACE IN TRIATHLON WITH A-T KIDS

On September 12, 2009, radio talk show host Eric Zane of the nationally syndicated morning show Free Beer and Hot Wings raced in the Reeds Lake Triathlon in Michigan. Joined by Kevin Diekevers and Pam Otto, the three racers pushed and pulled three children with A-T during the run, bike and swim.

In the weeks prior to the race, Zane raised tens of thousands of dollars from his listeners. The donations poured in with words of encouragement and hope.