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First-hand reviews are a great way for FIRST to know how we fulfill serving our mission, and also to show the impact of FIRST's work to the general population.

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The National Registry for Ichthyosis & Related Disorders will cease operation after 2012.

Enrollment in the registry stopped in 2004 and the Registry continued only on a maintenance basis. FIRST funded maintenance of the Registry over recent years and has now determined that research is now being conducted effectively in other ways. Investigators who wish to utilize the Registry until it ceases operations should contact the principal investigator via the Registry website, www.skinregistry.org.

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Study Estimates Number of Ichthyosis Patients in US

There are widely accepted incidence figures for the common forms of ichthyosis, ichthyosis vulgaris, and X-linked ichthyosis. Until now, however, figures for the incidence of rarer, generally more severe forms of ichthyosis have been approximations. Accurate figures for incidence of moderate to severe ichthyosis are important when advocating on behalf of those affected and when requesting funds from governmental or private, non-governmental agencies.

A new study published in the September 2012 issue of Archives of Dermatology by Dr. Leonard Milstone, of Yale University and Chair of our Medical and Scientific Advisory Board, shows that every year, in the United States alone, at least 200 babies are born with a moderate to severe form of ichthyosis. Dr. Milstone, along with Kay Miller, Merle Haberman, and Jayna Dickens of Thomson-Reuters, found that the incidence of moderate to severe ichthyosis is 5-10 per 100,000 people in the United States. This means that for every 100,000 babies born in the United States, 5-10 will have moderate to severe ichthyosis. If 4 million babies are born each year, this translates to 200-400 new cases of moderate to severe ichthyosis each year.

The group used three independent databases, two insurance databases and one hospital discharge database for their study. Every disease is assigned a number called an ICD-9-CM code. Some diseases can be given multiple codes and some codes cover many diagnoses. The ICD-9-CM code for ichthyosis is 757.1, and Milstone and



Dr. Leonard Milstone

colleagues reasoned that moderate to severe ichthyosis would be diagnosed at birth and would not easily be confused with other, milder forms of ichthyosis or related skin conditions. The analysis captured the number of babies less than 1 year old who were discharged from the hospital or who appeared on an insurance claim and were given the 757.1 code. They found that the calculated incidence of ichthyosis was rather consistent each year over the period 2001 to 2010.

The actual incidence of ichthyosis may be even higher, however. The newly published rates do not reflect the much larger number of newborn babies affected with milder forms of ichthyosis such as ichthyosis vulgaris and x-linked ichthyosis.

FIRST's ability to provide current information when advocating on behalf of those affected with ichthyosis requires accurate, up-to-date statistics. Kudos to Dr. Milstone and his colleagues for this great work!

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Correspondence Corner



Dear FIRST,

Eighty-one years ago my mother gave birth to a healthy baby boy (me), who exhibited ichthyosis. Three and a half years later my kid brother was born, with similar skin problems.



With current medical advances, the dubious status of being the oldest living soul in the Foundation for Ichthyosis and Related Skin Types (FIRST) database becomes more elusive for me, and yet more feasible as I am very healthy for having lived eighty-one years since birth. I take no statins, blood thinners or cortisone and the like; only vitamins, glucosamine and various lotions to alleviate dry skin. Perhaps I will elude the appointment with the funeral director long enough to reach my goal.

Until a FIRST seminar during October 2011 in Chicago, I thought ichthyosis affected males only. Several of the attendees were female. My illness is mild compared to some attendees.

I did not realize that excessive ear wax is a side effect of ichthyosis; participants use safety pins to remove it. Another participant purchased a side loading clothes washer hoping to save the planet. His service man said that next time the washer needs de-greasing, it would cost \$250. The participant promptly purchased a top loader.

Perhaps I will patiently amass years to achieve "oldest ichthyosis sufferer" (if there be such a classification) in the FIRST data base; perhaps not. In any case, I enjoy life and will continue to as long as my health keeps up.

David Allen
Hobart, Indiana

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Sequestration – What Is That And What Does It Mean To Me?

Sequestration. It's an odd word that will dominate the agenda in Washington, DC this fall. Sequestration is the term used to describe the automatic spending cuts that will go into effect on January 2, 2013 unless Congress acts to stop them.

Facing unprecedented budget deficits and possible default on our federal debt, Congress passed the Budget Control Act of 2011. That legislation set up a framework to force all parties to the table to deal with the budget crisis in America. The bill tasked a small group of legislators to come up with a plan to cut the deficit by \$1.2 trillion over 10 years. Unfortunately, that plan did not materialize, thus so-called sequestration will take place in just a few short months.

What programs does sequestration affect? It will cut everything except mandatory spending programs such as Medicare, Medicaid, Social Security and veterans benefits. Sequestration will take away over \$2.5 billion from the National Institutes of Health (NIH) budget with a "b" from the National Institutes of Health that means that vital biomedical research will be cut in its tracks. The progress that was made in the NIH budget will be virtually eliminated.

So, will this really happen?? That is the \$6 million question, say "trillion", question. After the election, Congress will return to deal with sequestration and the lame duck Congress. This Congress will

be unique in that there will be at least 75 members of Congress not returning to the new Congress due to retirements, running for other office, etc. That is not even counting members who will possibly be defeated in the general election and a possible change in the



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Correspondence

Dear FIRST,

I have lamellar ichthyosis and recently of us with ichthyosis worse than the average would help, so I decided to give it a try.

I mixed 1 teaspoon of sugar with 1 teaspoon of lemon juice together. Then I added a spoonful of olive oil to the mixture. I applied it to the areas of my skin that had the shingles rash and I was very surprised that it really soothed the rash.

I would love to know if anyone else has ever tried this and if it has worked for them.

Sincerely,

Margaret Jones

Greenville, South Carolina

To let Margaret know if this has worked for you, please contact the FIRST office at 215.997.9400 or email Lisa at lbreuning@firstskinfoundation.org.

Editor's Note: Neither the Foundation for Ichthyosis, its Board of Directors, Medical & Scientific Advisory Board, or staff endorses any treatment regimen. Please consult with your physician before trying any new treatments.

Executive Director's Report



Dear Friends and Members of FIRST,

Hello to everyone. I hope you are all doing well and enjoying the new cooler temperatures with the arrival of the fall and winter months. Despite the cooler temperatures, the lower humidity and dry indoor heat can have a negative impact on our members' skin. If you need a listing of products or advice from others, I encourage you to contact the national office. We have a lot of useful information that can help make these upcoming winter months a little more comfortable.

For the fifth year in a row, FIRST has been extremely fortunate and grateful to receive a grant from the Lennox Foundation. This grant funds many of our strategic priorities, and I'd like to update you on some of the initiatives we are tackling this year. First, we've been really working hard on ramping up our long and short-term communications goals. Technology and access to information is constantly changing, and FIRST is committed to getting the most accurate and timely news to our members, medical professionals, and the public.

A new feature will be added to our communications with physicians and healthcare providers. An electronic one-page newsletter will be emailed on a monthly basis featuring the latest research updates, patient perspectives, and resources from FIRST available to physicians and their patients. It was recently reported at the summer American Academy of Dermatology that the top three reasons dermatologists do not refer patients to patient advocacy groups, like FIRST, was that they are not aware of the group, are not aware of the group's resources, and they do not have the time. Although we can't do much about their time commitments, FIRST is working hard to change their awareness of our organization.

Applications are currently being accepted until November 16 for our second Clinical Scholar Award of \$40,000. The broad goals of the Fellowship Program are to identify and train the next generation of clinicians who will treat patients with ichthyosis and who, through their own clinical and laboratory investigations, advance understanding of this group of diseases.

As you will see on page 9, FIRST funded two research grants this year. The newest grant is awarded to Dr. Amy Paller and her team, and a renewal grant was awarded to

Dr. Anders Vahlquist in Sweden.

I traveled to Washington, DC in September to meet with other leaders from skin disease patient advocacy groups, along with members of the Society for Investigative Dermatology and the American Academy of Dermatology. We collaborated on important issues facing skin disease patients, including the impact of the presidential election on healthcare. Suffice it to say, no one has a clear cut answer as to what will happen, so at this point, we'll just have to wait and see.

As I write this report, I am preparing to head to Indianapolis to conduct a site visit for our 2014 national family conference. I'm excited to select a hotel and announce the official dates. In the meantime, start thinking about attending one of our 2013 Patient Support Forums (new term for what was formerly called Regional Meetings). You don't have to wait for two years to get together with other families and network. FIRST is hosting (5) one-day Patient Support Forums (see page 11) and chances are one of these forums is close to you!

On the fundraising agenda, this past fiscal year (which closed on September 30) recorded the best grassroots fundraising total ever! Let me remind everyone what a "grassroots fundraiser" is. It's an event held/organized/promoted by a FIRST member, family, friend, etc. that involves their community, friends, family, or others to rally around FIRST and raise awareness and/or funds to support our important work. We had a record number of members across the country who were involved in an event this past year. Many different kinds of events add to our grassroots goal—concerts, car washes, bingo nights, accepting donations in lieu of birthday gifts, walks, school drives, girls night outs, are just a few samples of how our members outdid themselves this year. We've also seen an increase of marathon/5K runners collecting donations and running in honor of a FIRST member. It's really catching on! You can read about the most recent grassroots events on page 13.

Continued on page 5

I'd like to end my letter by thanking and recognizing several board members for their kind service to making us a better organization. As you know, FIRST's Board of Directors is a wonderfully dedicated group of volunteers who govern the organization. The Board has a myriad of responsibilities, including policy-making, fiduciary, and overall management. We couldn't do it without their leadership. They care deeply about FIRST.

Dave Scholl has been our dedicated leader as president for the past seven years. He is a true visionary. His leadership of, and love for, FIRST has allowed us to become a more vibrant and well-run organization. His dedication led us to accomplish so many amazing and strategic goals to advance our mission. Dave will be handing over the reigns as president to Mike Briggs on January 1st. He will remain a Board Member for an additional year and a life-long volunteer.



David Scholl

John Schoendorf has been serving as FIRST's Chief Financial Officer for the past seven years. He has seen us through some tough economic times, but through it all, John has fiscally led FIRST in the right direction. Financially, FIRST is on solid ground and continues to grow financially, which is a result of the excellent stewardship of our donor's gifts, led by John and the Finance Committee. John will be stepping down as CFO at the end of this year but will remain a Board Member for another two years.



John Schoendorf

Janet McCoy has been serving on our Board of Directors for nine years and will be rotating off at the end of this year. She has served as our Secretary and a member of FIRST's Executive Committee for the past four years. She has also served on various committees, including our Strategic Planning and Board Development Committees. Janet is so dedicated to FIRST, and she will remain a staunch volunteer for years to come.



Janet McCoy

Mark Klafter will be rotating off our board at the end of this year as well. Mark has served FIRST in many different capacities over his nine year term. He served as CFO and a member of our Website and Finance Committees. He was instrumental in getting our Research Program off the ground six years ago. He and his family have hosted multiple and very successful grassroots fundraisers in his hometown. Although Mark is leaving the board, he will continue to help raise funds by serving as our liaison to the Power Up! Energy Program (see page 16).



Mark Klafter

Sherri Bale, PhD, Angela Godby, and Mark Dunkin will also be leaving our board at the end of the year. Sherri will continue to serve on our Medical & Scientific Advisory Board and will continue to be our "go to" person for genetics questions and concerns. Angela, who will continue to serve as our Advocacy Chair, will remain a committed volunteer and our "eyes and ears" in Washington, DC. Mark has also stepped off our board to pursue other responsibilities at home and work but will remain active as a volunteer and donor.



Sherri Bale, PhD



Angela Godby



Mark Dunkin

It has been a pleasure to work with all these individuals. With these vacancies, the Board Development Committee has been working with several key individuals to join the Board in January. I'm excited to introduce our new board members in the next issue of the Focus, so stayed tuned!!!

Sincerely, 

jpickford@firstskinfoundation.org | @pickjeanie on Twitter

Spotlight On ...

Ashlynnne Biggs

The day Ashlynnne was born was the best, and scariest day of my life all rolled in to one. Four weeks early, she decided she was ready to meet this world. I knew there was a chance of complications, due to her being slightly premature, but after coming out of recovery, and seeing the look on the doctors' faces, I knew there was a larger problem than low birth weight. They started using words with me I had never heard before, and all I really got out of the explanations, was that she was going to be life flighted out of our hometown hospital, to a larger NICU in Topeka, KS. I never got to hold her before she was loaded into that helicopter and taken away. After 5 days, I finally got to hold my little girl, and after 13 days in the NICU, I got to bring her home... with way more care than I ever could have imagined one child would take.

Nine years later, Ashlynnne is healthy, and happy. She has a form of ichthyosis called ichthyosis en confetti. She has a long bath and lotion routine each morning and night, and lotions several times throughout the day. She has physical therapy. We have to watch the heat, and I am in constant fear of a skin infection that I might not catch in time.

It's sometimes hard to explain ichthyosis, because when people hear Ashlynnne has a skin disorder, they picture eczema or psoriasis. They don't really understand how much this affects her. This affects EVERYTHING. It causes stiffness in her joints, due to her skin being tight, which causes her to move stiffly, and slowly. She can't hear as well, because the skin builds up in her ears. She gets overheated easily, because she doesn't sweat. Not to mention, the time that is lost out on playing and just doing kid things because she has to soak for so long in the bath tub at night, in addition to all of the time spent throughout the day applying lotions. She feels self-conscious any time she goes out in public because people stare at her.

Even with all of this, I wouldn't change a thing. Do I wish I could take it away from her sometimes, or take her place? Yes. But Ashlynnne's ichthyosis does not define her. She is an absolutely beautiful child, inside and out. She has the funniest personality, a very mature, dry, sarcastic sense of humor, the most contagious smile, and a very kind heart. She

loves animals and bugs, or anything "creepy" as she says, and scary movies. She just wants to do normal kid things, like swim, have sleepovers with her friends, and go shopping. She wants to be a veterinarian when she grows up, and a rapper. And she wishes she could do all of these things without the stares that so often come when she is in a place where not very many people know her. However, with every stare, and whispered comment, comes a chance to educate, and inspire one more person. And inspire she does. She is the strongest person I know. She has taught me about compassion, and patience, and perseverance. She has taught me more in the past 9 years than I could ever teach her. She has made me a better person, a better mom, and I am thankful for everyday that God trusted me to care for and love her. More than anything, in today's very vain world, she has taught me the meaning of TRUE BEAUTY.

Cora Cossel (Ashlynnne's mom)

Abilene, Kansas



Ashlynnne enjoys meeting Jordan Flake at FIRST's Conference in Denver

ESSENTIAL FATTY ACIDS, LIPOXYGENASES, AND ICHTHYOSIS

By: Alan Brash, PhD, Professor of Pharmacology, Vanderbilt University

*Yuxiang Zheng, PhD, First author of the Journal of Biological Chemistry paper
Post-doctoral fellow, Department of Systems Biology, Harvard University, Boston MA*

*Christopher P. Thomas PhD visiting Marie Curie Scholar
Home institute: Cardiff University*



Dr. Alan Brash

Recently, a Vanderbilt University team headed by Alan Brash, PhD made a connection between a genetic cause of ichthyosis and the dietary requirement for certain lipids known as essential fatty acids (EFA). The work explains why, in healthy skin, the essential fatty acid cannot be replaced by other lipids and why its oxidation is important

in maintaining a normal skin barrier.

The background to this story begins over 80 years ago, when man-and-wife biochemists George and Mildred Burr discovered the dietary requirement for lipids they named “essential fatty acids” (EFA). They carefully adjusted diets to exclude a type of fatty acid called linoleic acid, which they identified as the primary EFA. Importantly, the Burrs noted the symptoms of a dietary deficiency of EFA, and one of the most obvious was a dry scaly skin.

Scaly skin!...might EFA have something to do with the genetic diseases of ichthyosis? Indeed, this is where one of the genetic causes of ichthyosis comes in. Among the genes identified with mutations in ichthyosis patients are two related genes named ALOX12B and ALOXE3. These two genes produce enzymes called lipoxygenases (LOX). LOX enzymes oxidize particular lipids – they oxidize only EFA.

So, you need both EFA and the LOX enzymes for healthy skin, but why are they necessary for skin barrier function? Linoleic acid, the primary EFA in the outer epidermis, is attached to another lipid called ceramide. The Vanderbilt team found that oxidation of this EFA by the LOX enzymes is required to release the ceramide for subsequent chemical bonding to proteins. This is a key event in sealing the epidermal water barrier. “Knockout” mice lacking one of the LOX enzymes were unable to oxidize the EFA, they had almost no protein-bound ceramide in the epidermis, and they showed a severe epidermal barrier defect that would lead to ichthyosis.

Are there implications for the treatment of ichthyosis in these findings? Yes, there are, although dietary supplementation with linoleic acid is not one of them! There is plenty of linoleic acid from many sources in a balanced diet, and

being deficient is almost unheard of in our society. What is more likely is that new synthetic oxidized lipids formed from linoleic acid may have promise for topical treatment of LOX-related ichthyosis, or it may prove beneficial to treat skin with the “released” ceramide. Finding which lipids are linked with a specific genetic cause may make it possible to tailor topical treatments for each individual.

The results of this study, with first author Yuxiang Zheng, and Christopher Thomas, PhD, visiting Marie Curie Scholar were reported in a “Best of the Year” paper in 2011 in the Journal of Biological Chemistry. Researchers who collaborated with the Vanderbilt team were Dr. David Beier of Harvard University and Dr. Peter Elias of the University of California, San Francisco. The work was funded by the Institutes of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) and of Child Health and Human Development (NICHD) of the NIH.



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Tips for Bullying Prevention

by Lisa Breuning



With the new school year in full swing, our focus changes from purchasing new supplies, to ensuring that our children are completing assignments, studying for tests, and developing friendships. Once the nuts and bolts of homework are completed, the opportunity arises for meeting people, making new friends, and playing with old friends.

As many parents know, navigating the social situations that present themselves with children can be tricky even on a good day. If a child is a target of meanness or, worse yet, continued bullying, going to school becomes a horror. Bullying can take several forms. Most adults understand bullying to be physical confrontation. According to stopbullying.gov, bullying is defined as “unwanted, aggressive behavior among school aged children that involves a real or perceived power imbalance. The behavior is repeated, or has the potential to be repeated, over time.”

Today, bullying can become an even more pervasive problem. With the explosion of the internet and social networking, cyber bullying is becoming an epidemic. One aspect of cyber-bullying that makes it worse than the in-school bullying is that it pervades the child’s entire world. There is no escaping it. Where the comfort of home used to be an escape from the bullying for children in the past, now even if the child is in his or her room their space can be invaded with the torment of hurtful comments.

According to the National Crime Prevention Council (NCPC) website, “bullying can be a gateway behavior, teaching the perpetrator that threats and aggression are acceptable even in adulthood.” The NCPC has a page dedicated to bullying with great information and a variety of resources for parents, teachers, and students. Visit their website at <http://www.ncpc.org/topics/bullying>.

The best way for parents to help with this problem is to teach their children how to be kind to everyone they meet. The best approach for this lesson is modeling the behavior for your child. Children watch their parents for cues about how to behave

in certain situations. If you model accepting, kind behavior, your child will follow suit.

Of course, this will not cure the bullying epidemic over night, so how can you help your child if they are confronted by a bully, or witness someone else being bullied? In addition to the National Crime Prevention Council, there are many organizations dedicated to stopping the rise in bullying and cyber-bullying that we currently experience.

The Pacer Center is a parent center for families of children and young adults with disabilities. Along with the National Coalition for Parent Involvement in Education, the NEA, and the National PTA, the PACER Center sponsors bullying prevention month.

StopBullying.gov is designed to help parents identify what is bullying, who is at risk, how to prevent it and respond to it, and also, how to get help. Visit the website at www.stopbullying.gov/ for ideas to help your child deal with this issue. Of particular interest to FIRST members is the link at the bottom of the page with information about ‘Bullying and Youth with Disabilities and Special Health Needs.’ Information is offered for creating a safe environment for children with disabilities and special needs. There is also a wonderful tip sheet on this page with step-by-step information about what you can do to help your child.

As a parent, another way to stay informed about bullying is to attend any informational programs or seminars that are held in your school or school district. Even when you think you have heard all of the tips and know what to do, these seminars can offer a new idea or something that you may not have known. Mr. John Halligan, who lost his son Ryan as a result of bullying, travels the country hosting seminars about bullying, how to recognize it, and most importantly how to learn the signs that your child is being bullied. Visit his website www.ryanpatrickhalligan.org for detailed information about the presentation and also for a schedule of Mr. Halligan’s appearances across the country.

The most important thing you can do to help your child is to be informed on this issue.

If your child is experiencing any type of bullying, please visit one of the websites provided, or talk to the school counselors for guidance on how to work through this problem.

**The End
of Bullying
Begins
with You.**

By Joyce Quigg, 2010 PACER.org Bullying

Research Grant Program

The Foundation's Research Grant Program started in 2006. Since its inception, FIRST has received numerous grant requests and have provided funding for 13 worthy projects totaling just over \$1,400,000.00. The staff and Board of Directors of FIRST are very thankful to the Research Review Committee and all of our medical and scientific advisors who helped review these grant applications. These talented and experienced individuals diligently reviewed the work of their peers in the ichthyosis community. Remaining consistent with our mission and good stewardship of our funds, the successful grants were carefully selected to be sure the funds that so many of you have generously contributed over the past few years are used for the best possible research.

Dr. Amy Paller Awarded FIRST Grant



Dr. Amy Paller

The research of Dr. Paller's project entitled "Topical delivery of keratin 10 mutation-specific siRNA-gold nanoparticles for epidermolytic ichthyosis (EI)" (formerly called epidermolytic hyperkeratosis or EHK) was approved for a \$75,000 grant for the 2012 Research Grant Program. The blistering and thickening of skin seen in EI usually results from a change in a single letter of the DNA code (a

mutation) in one copy of the gene that provides the codes for manufacture of a keratin protein in the upper layers of skin. Small interfering RNAs (siRNAs) are small pieces of genetic material that can identify DNA pieces and bind to them, preventing the gene from being translated into protein. siRNAs are able to distinguish the mutated DNA from the normal DNA, and thus are able to prevent only the abnormal keratin protein from being formed. The problem with siRNA has been getting it through the skin barrier to where it needs to go. Dr. Paller and her team have found a way to get the siRNAs through the skin, through nanotechnology. By putting about 30 copies of the siRNA all around a central gold nanoparticle (leading to what her group calls "spherical nucleic acids"), the siRNAs are able to be rubbed into skin in a simple moisturizer, Aquaphor ointment. In the grant proposal, Dr. Paller's team will deliver an siRNA that specifically recognizes the common mutation of EI, R156H, with the intent to turn down production of the abnormal protein, while maintaining production of the normal protein. Dr. Paller has grown skin cells from several patients with EI and is using these to test if this technique will work for EI using both the cells in culture and a mouse model in which the human cells are grafted to the back of a mouse.

How is this work relevant to the Foundation for Ichthyosis & Related Skin Types?

The results of the project have many potential benefits for individuals with EI, as well as other ichthyotic conditions in which there is a localized mutation that can be targeted and the gene product reduced (another example is the most common form of palmoplantar keratoderma). While the project has very exciting potential, Dr. Paller notes that the proposed studies are just the first step in moving the technology towards human trials. In addition, since the siRNA that is developed in this proposal is precisely geared towards decreasing the manufacture of a very specific, mutation-based keratin protein, additional siRNAs would

have to be developed to match the needs of each person with EI.

Dr. Amy Paller is the Walter J. Hamlin Professor and Chair of Dermatology and Professor of Pediatrics at Northwestern University's Feinberg School of Medicine.

Dr. Heiko Traupe Reports on TGM1 Mouse Model



Dr. Heiko Traupe

Lamellar ichthyosis is a severe skin disease, which belongs to the genetically heterogeneous group of autosomal recessive congenital ichthyosis (ARCI). About 48% of all ARCI cases can be ascribed to transglutaminase 1 deficiency due to mutations of the corresponding gene TGM1. For assessment of therapeutic approaches and further molecular characterization,

a faithful pre-clinical model is needed because naturally we cannot test new drugs directly on patients. An existing animal model for transglutaminase 1 deficiency does not recapitulate (copy) the human disease. Obvious drawbacks of the so-called TGM1 knockout, in which transglutaminase 1 is not functional, are the lack of clinically visible hyperkeratosis and an excessive impairment of the epidermal barrier, which protects the skin against external pathogens and dehydration (transepidermal water loss.) Moreover, these mice die within 4-5 hours after birth due to dramatically increased transepidermal water loss. Therefore, the project supported by FIRST concerned the establishment of a stable skin-humanized mouse model of transglutaminase 1 deficient lamellar ichthyosis.

In a first step, we took biopsies from patients with transglutaminase 1 deficiency and established the isolation of the skin-cells (keratinocytes and fibroblasts.) These cells were used to generate human skin equivalents; fibroblasts were used to mimic the dermal part of the skin and keratinocytes to form the epidermis.

In a second step, these skin equivalents were transplanted onto the backs of nude mice which lack an immune system to prevent rejection of the artificial skin.

Four to six weeks after the transplantation process, the transplanted skin (grafts) show a full recapitulation of the human skin phenotype of transglutaminase 1 deficiency with a very thick and packed stratum corneum and a pronounced scaling of the skin. These grafts are stable for at least 20 weeks and are an excellent tool for testing of new drugs.

Continued on page 10

In addition to clinical examinations and the sequencing of the TGM1 gene, we use two other methods for efficient and rapid diagnosis of transglutaminase 1 deficiency; the monitoring of transglutaminase 1 activity on frozen skin sections, and the investigations of the so-called ultrastructure showing cholesterol clefts as important markers. Investigations of these diagnostic markers showed a complete absence of transglutaminase 1 in the transplants. Ultrastructural investigations revealed cholesterol clefts.

Proteomic analyses, meaning analysis of the whole protein-composition, of normal human skin/normal grafts versus transglutaminase 1 deficient human skin/transglutaminase 1 deficient grafts confirmed the deficiency and gave important and interesting insights into altered epidermal protein composition.

Our skin-humanized mouse model faithfully recapitulates the human disease and is an excellent tool for testing of novel therapeutic approaches.¹ Indeed, right now, we already have tested the first liposomal formulations with encapsulated recombinant (man-made) transglutaminase 1 using this mouse model to develop a specific, curative enzyme replacement therapy for patients suffering from transglutaminase 1 deficiency. The very preliminary results of this project in which we try to replace the missing enzyme, transglutaminase 1, in the skin are quite promising.

1 Data published in Aufenvenne K, Rice RH, Hausser I, Oji V, Hennies HC, Rio MD, Traupe H, Larcher F. Longterm faithful recapitulation of transglutaminase 1-deficient lamellar ichthyosis in a skin-humanized mouse model, and insights from proteomic studies. *J Invest Dermatol.* 2012 Jul;132(7):1918-21.

Vahlquist & Törmä Funded for a Third Year



Dr. Anders Vahlquist



Dr. Hans Törmä

Epidermolytic ichthyosis (EI, formerly called epidermolytic hyperkeratosis) is a rare, inherited disease characterized by blistering in the upper layers of the epidermis due to instability of the cytoskeleton in certain skin cells (keratinocytes). The affected cytoskeletal proteins (keratin 1 and 10) are important for the structural integrity of keratinocytes. The EI patients suffer life-long problems from a stiff, painful, and malodorous skin that is easily infected. No drugs are known to significantly or consistently improve the widespread blistering and scaling in EI.

The model system for EI that we use is cultured keratinocytes obtained from EI patients with different keratin mutations and clinical symptoms. We have found that such cells, when exposed to external heat stress, show a collapse of the cytoskeleton, which also causes the blisters in skin of EI patients. Pre-treatment of the cells with certain compounds that stabilize the cytoskeleton has been shown to prevent this collapse after heat stress. This protective

effect suggests that they are putative drugs for treating EI. However, some of the compounds used in our initial studies are toxic and not suitable for treating EI patients.

In our continued search for improved therapeutic options in EI we are utilizing patients' cells or artificially produced mutant cells and expose them to chemicals from a compound library to screen for other drugs with ability to protect the cytoskeleton.

Methods:

Cells which express mutated keratins are treated with the chemicals and subsequently exposed to a stress-situation. Under such conditions untreated cells show a cytoskeletal collapse. The structure of the keratin network is studied by automated high content screening methodology using fluorescence microscopy, which allows us to rapidly search for compounds that prevent the collapse in vitro.

Importantly, the safety and pharmacokinetics of such new drug candidates need to be tested in pre-clinical trials before controlled clinical trials in patients can be commenced.

Dr. Roop Receives Additional Funding to Continue His Work



Dr. Dennis Roop

One of the goals of our FIRST-funded project is to generate induced pluripotent stem (iPS) cells from epidermolytic ichthyosis (EI) (formerly called epidermolytic hyperkeratosis) patients. iPS cells are patient-specific reprogrammed adult skin cells that have essentially all of the properties of embryonic stem cells. The process of reprogramming, or inducing pluripotency, basically involves taking a committed adult skin cell and introducing factors into these cells that are capable of removing all of the cell's memory and reverting that cell back to an embryonic-like state. To obtain the adult skin cells, a biopsy is taken from the skin of an EI patient, and the skin cells are grown in culture. Reprogramming factors are then introduced into the adult skin cells and over time, colonies or clones of iPS cells appear in the culture dish. The advantage of generating patient-specific iPS cells is that these cells can be grown indefinitely in culture and they can be frozen and stored indefinitely for future use. Having an unlimited supply of patient-specific iPS cells provides us with the opportunity to genetically correct the defect, in the case of EI, mutations in either the keratin 1 (K1) or keratin 10 (K10) gene. We have recently been successful in correcting the defect in the K1 gene in one patient's iPS cells with a technique that uses zinc finger nucleases. Zinc finger nucleases are like molecular scissors that allow us to open up the K1 gene near the site of the mutation and replace the defective region with a normal region of DNA. We are currently performing tests on the corrected iPS cells to make sure that they are genetically stable. Once this has been confirmed, we will differentiate the corrected iPS cells into keratinocyte stem cells and determine if these cells can form a normal epidermis when grafted onto mice.

Regional Support Network

by Moureen Wenik

Have You Connected with Another Member?

The Regional Support Network has been busy connecting families and individuals together. So far in 2012, FIRST has connected 98 individuals. Many of these individuals are connected by region and are also connected outside of their region by disease type. Many people simply want to know they are not alone, or are looking for some advice, or just someone to listen to them. If you would like to be a part of the Regional Support Network and volunteer to be connected with others, email Moureen Wenik at mwenik@firstskinfoundation.org.

Small Gatherings Make Big Impact

Face to face interaction is so important for families and individuals affected by ichthyosis. Ellen Clemmer hosted an afternoon lunch in her North Carolina home in June, 2012 and had a great turnout. Many members from FIRST attended this successful afternoon. FIRST is asking our members to consider hosting a gathering or small event in your town or region. These gatherings could be a few hours in your home, or other locations such as a church hall or community room. Or perhaps you would like to organize an outing for families in your region to the local attraction or park. FIRST can email invitations to the members in your region, and help advertise the event. Contact Moureen Wenik at mwenik@firstskinfoundation.org for more information.

Patient Support Forums for 2013 (Formerly Regional Meetings)

FIRST is currently planning Patient Support Forums in the surrounding areas of New York, NY; Columbus, OH; Kansas City, MO; Dallas, TX; and San Jose, CA. These one day meetings are an opportunity for individuals to come together in a small setting and meet one another. A medical expert will be available for a question and answer session and topical sessions will be planned for each meeting. Dates and exact locations will be announced on our website and Facebook page.



JANE & HENRY BUKATY SKIN CARE FUND

Thanks to the generosity of Jane and Henry Bukaty, FIRST has established the Jane & Henry Bukaty Skin Care Fund to help alleviate some of the financial burden that may be facing our members. Here's your opportunity to apply for some financial assistance for ichthyosis treatment. Since the fund is limited, the following criteria must be met by the applicant in order to be eligible for a grant.

The applicant must be registered in our database and is required to submit an application indicating his/her need for funding. The application can be downloaded from FIRST's website. The requests the specific product/treatment for which funds are needed, and a demonstration of the financial need for this product/treatment.

Awards will not exceed \$200.00. Applications will be awarded two times per year as determined by the Review Committee. Applicants will be eligible to receive one award every two years.

Requests can be downloaded from FIRST's website and, emailed to the national office at jpickford@firstskinfoundation.org, faxed to 215.997.9403, or mailed to the attention of:

Foundation for Ichthyosis & Related Skin Types, Inc.®
Jane & Henry Bukaty Skin Care Fund
2616 N. Broad Street • Colmar, PA 18915

The next cycle of funds awarded will take place in December 2012. **The deadline for application is December 31, 2012.** You will be contacted by the office if you have been awarded aid from this fund.

WORKING WITH THE MEDIA TO GET YOUR MESSAGE OUT

Recently we had the enlightening experience to see how quickly a story about ichthyosis can be featured in the media and then taken to even higher levels!



Tyler Hartmann, Leilani Brooks, and Wyatt Daring

Wyatt Daring, a 5-year old with an unknown type of ichthyosis who lives near the national office, had his cooling vest stolen from his family's car. A generous business, Waltz Golf Farm, agreed to host a fundraiser to help the family raise money to replace the vest. Their local newspaper, *Pottstown Mercury*, interviewed Wyatt and his family to promote the fundraiser and the article appeared on a Monday morning edition. That evening, the family was contacted by the *Fox News* affiliate in Philadelphia and they were featured on the Tuesday evening news in the Philly market. The next day, the family received an invitation to appear on the national live *Anderson Cooper Show* in New York City. Wyatt and his mom, Teri, were whisked away in a limo to NYC for that Thursday morning show.

The fundraiser the following week at Waltz Golf Farm was great fun for the Daring family and their friends. FIRST members Kevin and Angeline Hartmann, traveled from Maryland, with their son Tyler, who is affected with epidermolytic ichthyosis (formerly called epidermolytic hyperkeratosis) and his kindergarten classmate, Leilani Brooks, to join the festivities. Several more follow-up stories appeared on the *Philly Fox News* and *Pottstown Mercury*.

What we learned from all this excitement is that even though the media focused on the hurtful act of stealing Wyatt's cooling vest, it created an opportunity for FIRST and ichthyosis to be in the spotlight. We ask all our members who are hosting events or have a unique story to share, contact your local newspaper. You can see how quickly a small, hometown story can go national!

FIRST is always working to promote our message and distribute accurate information about ichthyosis and how it impacts those affected, but we need your help. We encourage you to use our website, www.firstskinfoundation.org as a



Wyatt and Tyler enjoy a snack

resource because it is updated constantly with the most accurate, reliable information. Together, we can inform the public about ichthyosis and how to help our children and affected adults.

Some wonderful outcomes resulted from this media whirlwind. First, the public was able to learn about ichthyosis, which makes life much easier for those affected. Second, thanks to the generosity of others, Wyatt and his family were able to raise the money to replace the vest (plus much, much more for his care). Third, FIRST was mentioned in a follow-up article in our local area and was chosen as one of the charities for a large corporate office's United Way Campaign. And, fourth, Teri has committed to starting a nonprofit cooling vest exchange for families in need of these cooling products.

To see the media coverage about Wyatt and his stolen cooling vest, just type in "Wyatt Daring" in Google.



Jean Pickford speaks with a local reporter about FIRST

Editors Correction

In the Ichthyosis Awareness Month section of the Summer 2012 issue of *Ichthyosis Focus*, we listed DeDe Fasciano's name as DeDe Haggis. Her mom is **Diane Haggis**, **DeDe Fasciano** is, of course, **Evan's** mom, as many of you know. We apologize for the error.

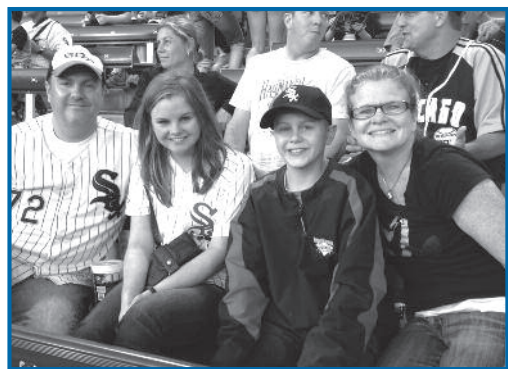
The Foundation is very thankful to all of our wonderful members for their hard work. Grassroots fundraisers are a great way not only to raise money for FIRST, but also to raise awareness about ichthyosis in your community.

FIRST Night at the Chicago White Sox

On Wednesday evening, August 8, the Chicago White Sox hosted the Kansas City Royals in an American League Central division match-up. FIRST member, **Frank Osowski**, led 196 friends, family members, and members of FIRST to the game. Frank, whose son **Ben** is affected with epidermolytic ichthyosis (formerly known as epidermolytic hyperkeratosis), is no stranger to raising money and awareness on behalf of FIRST. Frank hosted the very successful evening at Harry Caray's restaurant on the eve of the 2008 Chicago Family Conference and in the fall of 2010, Frank auctioned a Notre Dame football package with the proceeds going to FIRST.



Frank and Jacky Osowski



The Kouba family

FIRST Night at the White Sox was the 3rd evening at a Major League ballpark this year. In May, similar events took place in Philadelphia and New York.

Frank enlisted help from Chicago-area members to create this successful evening of awareness, fundraising, and fun! **Matt and Kathy Kouba** are the parents of 14-year-old **Alicia** and 11-year-old **Ben**, both of whom are affected with CIE. The Kouba's brought a group of friends and family to cheer on the Sox. **Laura Hogan**, an active member of FIRST who is affected with lamellar ichthyosis, brought friends to the game. **Dr. Amy Paller** of Northwestern University, FIRST Board member emeritus, and Medical & Scientific Advisory Board member, brought a group of friends and colleagues including her

husband **Etahn Cohen** and her son **Ben** to enjoy the evening.

Osowski family members made signs to hold up and attract the attention of the cameras, and FIRST's brochures were available for those curious about our group.

Friends and business associates of Frank's who couldn't attend the game were also generous with donations for the evening.

The grand total raised for the event was more than \$5,000! Many, many thanks to Frank Osowski for all of his hard work on this event and to the FIRST members who encouraged friends and family members to join.



Dr. Amy Paller with Etahn and Ben

A Thoughtful Retirement Gift

Thomas Petelin is the grandfather of **Emma and Austin Knabe**, both of whom are affected with lamellar ichthyosis. Tom was one of the founding teachers at Westlake High School in Westlake Village, California 32 years ago. After 39 years of teaching, Tom decided to retire. Instead of a watch or traditional retirement gift, the faculty of the Social Sciences Department where Tom taught, held a luncheon in his honor and presented him with a donation that they had collected for FIRST. What a wonderful tribute to Tom's years of dedication to his students.



Tom with Emma and Austin

Release the Butterfly Concert in Pennsylvania Benefits FIRST

FIRST members **Tracie Pretak** and her daughter, **Bailey**, who is affected with lamellar ichthyosis, have hosted concert evenings for FIRST frequently over the past 15 years. These concerts have been held at a local church and feature spiritual music performed by church members and friends.

This year, their "Release the Butterfly" concert was held at the Johnsonburg High School Auditorium on a Saturday evening in September. This concert spotlights friends of Bailey's with dancing and/or singing talents performing songs selected because the lyrics share messages about what it is like to live being "different."

The name "Release the Butterfly" was selected from literature that FIRST created during our early years. At that time, a story was shared that some parents were concerned about their child being born with ichthyosis. The doctor told them to think of their child as a butterfly in a cocoon and that they must "release the butterfly." Thanks to love and support from family, friends, and the community, that has happened in Bailey. The hope is to now be able to do that in every child affected with ichthyosis.

Friends of the Pretak's who joined with them showcasing their talents were:



Tracie and Bailey



The concert performers

Dancers: Claire Grazioli, Bry Harvey, Nicole Holland, Kaitlin Yankovich, Madison Yankovich, Jensine Coudriet, Kristin Dippold, Sophie Herzing, Rachel Keller, Ellen McGowan, Maddie O'Leary, Kaitlin Quinn, Kaarina Hemdal, Sarri Swanson, and Kate Undercoffer

Singers: Tara Hart, Sami Ferragine, Nicole Rose, Haley Freeburg, Betty Schogren, Rene Smith, Maddie O'Leary, and Kaitlin Quinn

With 100 people in attendance, the evening was a wonderful success.

In addition to the concert, the faculty at Johnsonburg Elementary School, which Bailey attended as a youngster, organized a jeans day to raise money for FIRST. The combined amount raised through these efforts was more than \$1,700. FIRST is so grateful to Tracie, Bailey and all of their friends for their efforts on our behalf.

An Evening at Souplantation Restaurant in California

Adam and Meghan Knabe from Moorpark, California are the proud parents of four-year-old **Emma and Austin**, two years old, both of whom are affected with lamellar epidermal nevus.

During Ichthyosis Awareness Month in May, Adam and Meghan hosted their 2nd evening at a Souplantation Restaurant, a popular chain in California, to raise funds for FIRST and awareness about ichthyosis.

The Knabe family had attended fundraisers at Souplantation in the past and thought it would be a good way to have an event. The basis for the event is that participants bring a flyer to Souplantation on the night of the event, and a portion of the proceeds generated from those sales will benefit FIRST. They planned their event for May 31. With family and friends spreading the word the attendance was too numerous for the Knabes to count!

The outpouring from their church, friends, and students of Meghan's father, **Thomas Petelin**, who taught at the local high school until his recent retirement, was overwhelming. Adam and Meghan had a wonderful time connecting with those who attended. The **Terranova** family attended with their son, **Nicholas** who is affected with lamellar ichthyosis. Nicholas' mom, **Cristina** was able to chat with Meghan during the evening and both women look forward to connecting again soon. Almost \$500 was raised during this evening for FIRST.



The Knabe family



Meghan and Cristina chat during the event

Grassroots Fundraising

Friends for FIRST in California

Suzanne and Eric Phelps of San Jose, California have long been staunch advocates for FIRST. Many of our members know the story of their precious son *Dane*, who passed away in 2008 when he was just 3 1/2 years old. Dane was affected with an unknown type of ichthyosis and additional medical issues. Dane was a very special little boy and touched so many people in his short time. Over the years, Dane's older siblings, *Chandler and Cade*, have organized lemonade stands and garage sales to benefit FIRST. The entire family also continues to attend FIRST's national family conferences to connect with others and offer their love and support.

Suzanne is a descendant of D.W. Norris, who founded Lennox International. This company led to the development of the **Lennox Foundation** by many of the descendants. This foundation has been very generous with grants to FIRST over the years. These grants have funded many of FIRST's initiatives including FIRST's new website design, purchase of new donor-management software, and funding of FIRST's Regional Meetings.

Eric and Suzanne wanted to do more to further ichthyosis research and create awareness. They held the first annual *Dane's Friends for FIRST Concert* on September 1 at the Campbell Heritage Theater in Campbell, California. Food was provided by California business, MOJO burger, and a local Jamba Juice. Many family members and friends provided entertainment for the evening. There were performances by Dane's brother, Cade; former X-Factor contestants and now professional musicians Ryan Sims and Ethan Newman; singer-songwriter and teacher James Nobriga and his wife Katie Joy; and the phenomenal vocalist, songwriter, and musician Joyce Randolph. Howard Dietz, a high school senior and award-winning saxophonist, joined other musicians for a 5-song set, and Kat Lernihan, a high school freshman and guitarist/vocalist took the stage as well for a three-song set. The evening also featured many performances by the Capitol Dance Company competition team dancers. Leading off the night was Dane's sister, Chandler Phelps, with a lyrical dance solo, "You'll Be in my Heart" dedicated to her brother, Dane, and all her friends at FIRST.

During FIRST's family conference in Denver, Eric, Cade, and Chandler interviewed young people affected with ichthyosis. This video was then played at the event, providing participants with a true picture of how ichthyosis impacts those affected.

The evening also featured a silent auction and raffle. Items offered included a complimentary wine hour with wine donated from many local wineries, including Savannah Channele, Joseph George Winery, and Fernwood Cellars.

There were some great trips, sports memorabilia, and music classes included in the silent auction. Some of the highlights include: a 7 night Puerto Vallarta Trip (with all amenities included), a Lake Tahoe 4-7 night stay, and a San Francisco 2-Night Get Away.

Long-time FIRST member and "West Coast Ambassador" *Les Avakian* made the drive up from his home in Fresno to join the Phelps family. As those of you who are active in the online community know, Les is affected with X-linked ichthyosis and is a wonderful advocate for FIRST and ichthyosis.

The evening was a tremendous success, raising more than \$20,000 for FIRST! Eric and Suzanne received such a fantastic response from their community and the evening was such a success that next year's event is already planned for September 2013!



All three Phelps children, Chandler, Dane, and Cade



Suzanne with "West Coast Ambassador" Les Avakian



Cade on guitar



Suzanne addresses the crowd surrounded by some of the performers of the evening



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