

NETHERTON SYNDROME: Skin Inflammation and Allergy from Dysregulated Protease Activity

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**This is the continuation from
the Fall 2009 issue.**

**In the last issue you
read about:**

- *A severe ichthyosis with constant allergy*
- *NS is caused by defective expression of a protease inhibitor*
- *Immunohistochemical and molecular diagnosis of NS*
- *Genetic counseling and prenatal diagnosis*
- *What do we know about this protease inhibitor?*

This article concludes with:

- *KLK5 at the center of the disease mechanism in NS*
- *To what extent are these findings relevant to NS patients?*
- *What have we learned about the disease mechanism?*
- *Do these results lead to new treatments for NS?*

KLK5 at the center of the disease mechanism in NS

To further understand LEKTI function *in vivo*, we and others have generated a mouse model in which the murine *SPINK5* gene is invalidated. Lack of lekti expression in mice recapitulates NS features and causes a major skin barrier defect (8). Newborn mice show severe peeling of the skin resulting from premature detachment of the stratum corneum. They display a drastic skin barrier defect which leads to death of the pups by dehydration within 10 hours. Biochemical analysis of skin extracts of these animals identified KLK5 and KLK7 as two major proteases which are overactive in this mouse model. KLK5 hyperactivity leads to the degradation of components of the adhesion complexes ([corneo] desmosomes) which attach the last living layer of the epidermis to the stratum corneum, resulting in cleavage of these structures and premature detachment of the stratum corneum. Terminal differentiation markers and lipids of the stratum corneum are also abnormal, showing that protease dysregulation also affects these important processes of skin homeostasis.

The *SPINK5* knock-out mouse model disclosed a major mechanism of the disease, i.e. hyperactive KLK5 degrades (corneo)desmosomal components leading to premature stratum corneum detachment and a severe skin barrier defect. This was initially thought to underlie the development of allergy in NS through increased penetration of allergens and microbes. However, the fact that other ichthyoses with skin barrier defects do not develop allergies, prompts us to search for a specific cause for the allergic manifestations seen in NS patients.

We recently demonstrated that another mechanism, also driven by KLK5 hyperactivity, was underlying inflammation and allergy in NS (9). This pathway involves the activation of specific receptors (Protease activated receptor-2, or PAR-2) which are present at the cell surface of

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Deadline: February 1, 2010

COMING SOON!
**Online Conference
Registration**

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Correspondence Corner

Dear F.I.R.S.T.,

I love F.I.R.S.T. and continue to sing its praises to my children's pediatric doctor and staff.

My three boys have X-Linked Ichthyosis (XLI), and we have had a challenge at the schools, which is surprising. I am frustrated, and not sure what to do. I feel like it is a constant up hill battle. My son's pediatrician is an absolute God-send, but sometimes even that is not enough.

Last year, my youngest son, Collin, 7 years old, had a playground incident during school. Actually, there have been several incidents over the last few years. In kindergarten, regardless of the doctor and my placing restrictions on recess with the heat advisories, the teachers would continue to send Collin outside and even discipline him by forcing him to WALK in circles continuously in the heat. Twice we had to bring him to the doctor for heat sensitivity, which makes him miserable and risks his health. Last year during the first week of school, they sent the first graders onto the playground without checking the temperature of the play equipment. He went onto the horizontal ladder and badly burned both hands (second degree burns) and fell when he let go, breaking his wrist. To make matters worse, the teacher forced him to "hold" the note in his burned hands and walk himself to the nurse's office. He had huge blisters, red marks everywhere, and his wrist was green. The school says that his ichthyosis caused the burns, but my pediatrician assured us that she had seen other children without ichthyosis that same day from other schools with second degree burns as well. To make matters worse, he had to wear a sterile dressing and bandages because we did not want his skin to become infected. He missed 14 days of school because he could not use his hands to eat, go to the bathroom, or anything, and the pain was difficult for him. Having his hand and arm casted was a new XLI experience as well; we were not sure what his arm would look like and the itching was intense for Collin. Needless to say, between that incident and the over-heating, he is being retained for missing so much school, something that I never had to worry about with my oldest boys who are now in middle school and high school.

It has been frustrating trying to get the school to follow a written OHI, which stands for Other Health Impaired, and a doctor's statement. My older boys are able and aware when they need to cool down or are becoming over-heated; their school has been completely wonderful. I have been busy with the Virginia Department of Education, Parks and Recreation (which oversees our playgrounds at school and elsewhere), and the School Board, Board of Supervisors, Playground Safety Committee, and a local TV station. They now have a wonderful playground report which shares with the schools and community the current temperatures and future temperatures of the playground equipment. Also, the teachers were given additional "retraining" about playground safety and surfaces. It's a small start, but its a start.

I still receive phone calls occasionally from parents of a child with XLI, or a concerned person carrying a pregnancy with XLI who have found my contact information online.

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Correspondence Corner
continued from Page 2

I would really like to become more active with F.I.R.S.T. and attend the regional meetings that I have been hearing about.

It has been an amazingly busy year.

Darcie Kuzik

Chesterfield, VA

Hi All,

I hope everyone is doing well. Wyatt and I have been enjoying keeping up with everyone and all of the pictures from the Regional meetings on the web page.

I am writing to ask for help. I am interested in making my own lotion for Wyatt and am not sure how to go about getting started. I am wondering if there is anyone who has made his/her own lotion before and might have any ideas on how to get started.

We have tried so many different types of lotions, as I am sure so many others have. There is a woman at a local farmer's market making lotion and selling it there for about \$8 for 6 ozs. Since Wyatt is the youngest of 5, I need to find something that costs less than that.

If anyone has any advice or information that can help, please contact me directly at daring65@msn.com or 610-754-1007.

Thanks so much,

Jeri & Wyatt Daring

Schwenksville, PA

Dear F.I.R.S.T. Staff,

I have recently found a soap that works very well for me. It is TONE soap. I find that it is better than Dove as it has a lot of cocoa butter in it.

I would also be interested if any one can recommend any new shampoos that do not cause flaking.

Thank you,

Easton Smith

Hamden, CT

Editors Note: If you have any information for Mr. Smith, please contact the F.I.R.S.T. office.

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Spotlight On

Randy Saunders...comfortable in his own skin.

*By Cathleen F. Crowley, Staff writer, Times Union, Albany, NY
First published in print: Sunday, November 15, 2009
Used with permission.*



Randy with his parents Polly and Rick

Randy Saunders thought the new third-graders were acting a little nervous around him.

So the 11-year-old wrote a note to the principal asking to speak to the younger kids, who had just moved into the building that houses Greenwich Elementary School's upper classes.

The principal, Benjamin Pisani, arranged an assembly for the 70 third-graders and gave Randy the microphone.

"I told them all about my skin," Randy said in his high-pitched, raspy voice.

Randy suffers from a rare genetic disease that makes him look as if his body is covered with third-degree burns. The condition is a severe form of ichthyosis, a disorder that causes his skin to grow and fall off rapidly. Scientists have not found the gene that causes the condition, and there is no cure.

Blotches of Randy's new skin appear red and tender, while other patches are brown and scaly before they slough off. The tops of his ears have grown into his head, and the skin on his scalp mats down his hair. Randy's palm feels like that of a carpenter, not a fifth-grader, when his hand is shaken.

At the assembly, Randy told the younger kids that he was born with the condition, and it's "not catchy." It's OK to touch him, he said, but try not to bump into him too hard because it hurts. Randy explained that he soaks in a tub two times a day to relieve the dryness and itch, and that when he gets out of the bath he covers his body with grease to trap the moisture that his skin can't hold on its own. It makes his skin and clothes look greasy and dirty, even though he's clean.

Can he do everything they can? No -- he can't be out in the sun and heat for long, but he can play low-contact sports; he loves playing video games, four-wheeling, and ice fishing with his dad.

By the end of Randy's speech, the third-graders were more interested in what rides he likes at the Washington County fair. The nerves were gone.

That's how it is in this town of 5,000, just east of Saratoga Springs in the hills of Washington County, New York. Greenwich embraced Randy, a happy and social kid who is comfortable in his own skin.

"Nobody looks at him funny," said his mother, Polly Saunders.

His schoolmates watch out for him and play kickball with him, and they aren't afraid to pat him on the back when he does a good job.

"They are incredibly compassionate," said Pisani, the principal, who dotes on Randy.

Outside Greenwich, it can be different.

Going out in public "is tough for us," said Randy's dad, Rick Saunders Jr. "It doesn't bother him one bit, but it drives me nuts. There are literally people tripping over each other trying to look at the kid."

Beside the stares, some people yell at Randy's parents, accusing them of letting Randy bake in the sun. Another woman screamed at Randy's mother for allowing him outside without a winter jacket. Polly tried to explain that Randy's sweat glands don't work and he was feeling overheated. The stranger didn't believe her.

Randy is one of only eight people in the United States who have ichthyosis en confetti, which earned its name from the white spots that appear on the flesh of people with this form of the disease. Of those eight people, only three suffer from bone and muscle stiffness like Randy.

He walks hunched over and hobbles like an old man. Some mornings, his mother carries him to the bathtub because the stiffness is so bad.

Dr. Keith Choate, a professor of dermatology at Yale School of Medicine who works with Randy, said it usually takes about a month for new skin to grow and shed from the body. Randy's skin renews every 10 to 14 days.

The energy consumed by the rapid skin growth steals calories from Randy, leaving him underweight.

The effect is apparent when he stands next to his twin brother, Ricky, who weighs twice as much and is a foot taller.

Ask Randy how much he weighs and he says, "60 pounds."

"That must have been the chicken sandwich you just ate," said his incredulous dad.

"Getting smart over there," Randy replies, and softly tackles his mother, saying, "C'mon, I'm a big man."

Polly says her son actually weighs 55 pounds.

She sweeps the floors and washes Randy's bedding daily to clear dead skin that collects around the house. She's given up on the grease stains. Her clothes are greasy from Randy's hugs, but she doesn't care. Randy's clothes get so saturated that Polly tosses them after less than a dozen wearings. Washing them is no help.

Polly quit her job as a home health aide in September because she drives Randy to physical therapy in the evenings. But the family fell behind on bills, so she went back to work last week. She works part-time at Kmart and cooks at the Cambridge Guest Home. Randy's dad commutes to Latham every day to work at the Pepsi Bottling Co. They have three other children, including one in college.

Randy feels at home in Greenwich. As for the strangers who stare, he wishes he could tell them about himself and his skin.

"So maybe someday," he said, "they'll want to come over and play."

Editors Note: As a result of this article, the local ABC affiliate in Albany, NY aired a story about Randy. To view this video, go to the F.I.R.S.T. website and click on the link in Randy's story.



Randy talks to his classmates about his condition

Correction ...

In the last issue, further reading material information was mistakenly omitted from the article on Netherton Syndrome written by Drs. Peter Elias and Mary Williams. If you are interested in learning more about the topic, a complete list of reading material is available at our website under Research, then click on the story "Relationship of Netherton Syndrome to Atopic Dermatitis."

Valentine's Day is quickly approaching



A wonderful way to let someone know that you are thinking of them on Valentine's Day is to send flowers. When you send your Valentine flowers, please use flowerpetal.com. They donate 12% of your purchase price directly to F.I.R.S.T. You can simply go to F.I.R.S.T.'s website and click on the flowerpetal.com link on the left under "Giving". There is a link that will take you directly to our flowerpetal.com page. The price listed with the arrangement is the total price. There are no additional charges.

Please spread the word to your family and friends who may be ordering flowers this Valentine's Day.

keratinocytes, and are activated upon cleavage by KLK5. Since *SPINK5* knock-out mice die shortly after birth, we used a graft model of *SPINK5* deficient skin onto immunodeficient mice. We showed that in grafted lekti deficient skin, KLK5 hyperactivity leads to enhanced PAR-2 activity, resulting in the production of several pro-inflammatory cytokines, including TSLP (Thymus Stromal Lymphopoietin), a major molecule which is strongly expressed in atopic dermatitis. TSLP is known to activate Langerhans cells, which are antigen presenting cells present in the epidermis. Langerhans cells activated by TSLP migrate into lymph nodes where they induce the differentiation of T cells into pro-allergic T cells (called Th2 cells). In addition to TSLP, other important cytokines are produced by Lektin deficient epidermis, such as TARC (Thymus and activation-regulated chemokine), MDC (Macrophage-derived cytokine), TNF-alpha and interleukin-8 (IL-8), which contribute to the recruitment and activation of inflammatory cells such as eosinophils and mast cells. These cells also produce major pro-inflammatory cytokines which contribute to a pro-inflammatory environment which favors the development of allergic reactions. This adds to the release of IL-1beta by keratinocytes after mechanical stress induced by stratum corneum detachment.

A remarkable feature is that this signalling pathway is initiated in the absence of any challenge by allergens or microbes, since it is detectable during embryonic life of *SPINK5* knock-out mice as soon as 19.5 days. In addition, this biological cascade is maintained in lekti deficient keratinocytes (epidermal cells) in culture, which demonstrates that it is an intrinsic property of these cells (9).

To what extent are these findings relevant to NS patients?

We subsequently tested patient skin samples to see whether these observations were relevant to patients with NS. Detailed histological, ultra-structural, and immunohistological analyses showed that this was indeed the case. In patient skin, all features of these two pathways were present: one involved stratum corneum detachment associated with increased KLK5 activity, degradation of (corneo)desmosomal components and (corneo)desmosomal cleavage (10); the other involved PAR-2 activation, NF-KB signaling (a major activation pathway in keratinocytes), production of TSLP, TNF-alpha, IL-8 and IL-1beta. All these abnormalities were maintained in patient keratinocytes in culture, demonstrating that they are intrinsic properties of NS human epidermis (9).

What have we learned about the disease mechanism?

From these results, we have learned that LEKTI inhibits major epidermal proteases involved in the desquamation and the inflammation processes of the skin. They have pointed to two major biological cascades involved in NS, both initiated by KLK5 hyperactivity. On one side, KLK5 hyperactivity leads to (corneo)desmosomal cleavage and stratum corneum detachment. In parallel, and even prior to stratum corneum detachment, KLK5 hyperactivity triggers the secretion of major pro-inflammatory and pro-allergic molecules, the first of which is TSLP, a key molecule in atopic dermatitis and in asthma.

For these reasons, although NS is a rare monogenic disease, it serves as a disease model to study the links between skin barrier defects and allergy and, to a further extent, for the study of atopic dermatitis in which the implication of several genes makes the genetic investigation more difficult.

Our results are in agreement with the current notion that epithelia play a major role in the initiation of skin allergy, as shown by the role of filaggrin stop mutations in atopic dermatitis and in

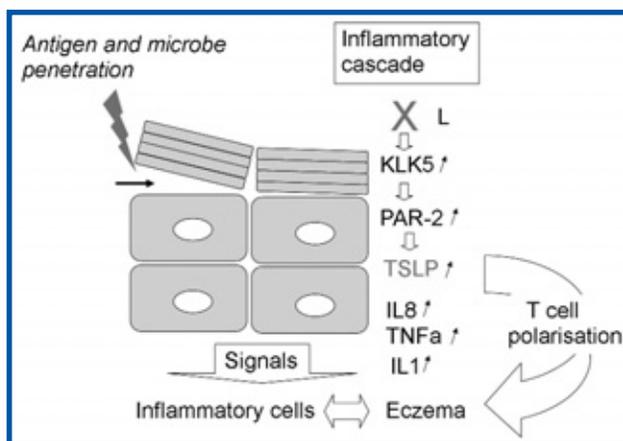


Figure Legend:

Overview of Netherton syndrome dual disease mechanism. Lack of KLK5 inhibition by LEKTI leads to stratum corneum detachment leading to increased antigen and microbe penetration. It also leads to enhanced secretion of pro-inflammatory cytokines (IL1beta, and TNFalpha) by mechanically stressed keratinocytes. In parallel and independently from any environmental stimuli, KLK5 hyperactivity initiates a specific proinflammatory and proallergic cascade through PAR-2 activation. This leads to the production of the major pro-allergic TSLP cytokine, as well as other pro-inflammatory molecules which attract and activate inflammatory cells. TSLP plays a major role in the development of allergy by inducing pro-allergic T lymphocytes (cells of the immunity), as described in eczema.

ichthyosis vulgaris. These data describe a new pathway, which directly links LEKTI deficiency to allergy, and may provide a link with asthma and food allergies.

Further work will focus on the search for immunological abnormalities of T cells from NS patients, the study of the role of LEKTI in the thymus, and the development of new treatments based on these new breakthroughs.

Do these results lead to new treatments for NS?

There is currently no specific treatment for NS. During the neonatal period, prevention and treatment of dehydration and infection, and supplementation of food intake are essential and may require a hospitalization in a neonatal care unit. Subsequently, the use of topical steroids and calcineurin inhibitors (Protopic) is restricted to limited skin areas because of their secondary effects. Emollients and moisturizing to minimize the skin barrier defect, as well as antiseptic treatment to prevent skin infection, are key elements, but a specific treatment is still missing.

Our work has identified several potent target molecules for therapeutic intervention. These include KLK5, a direct LEKTI target which initiates the biological cascades causing skin barrier defect, inflammation, and allergy. Although KLK5 appears as the first target, due to its role in initiating both stratum corneum detachment and PAR-2 activation, more downstream actors include PAR-2, TSLP, TNF-alpha, and IL-8, all actors whose inhibition has the potential to diminish the inflammatory and allergic cascade. Some therapeutic agents, such as antibodies which specifically block each of these molecules, already exist and are commercialized, but the benefit/risk ratio should be considered and their use in NS requires pre-clinical studies in animal models. Other therapeutic strategies involve pharmacological approaches (identification of new KLK5 inhibitors through intensive high throughput screening efforts), gene therapy approaches aimed at degrading specific mRNAs, or replacement therapy using the most potent LEKTI fragments whose size is compatible with skin penetration. While these different approaches are being currently developed, the prevention of the consequences of the skin barrier defect by the regular use of moisturizing agents and emollients, and the prevention of infections are important elements of the treatment to pursue.

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Executive Director's Report

Dear Members and Friends of F.I.R.S.T.,

On behalf of everyone at the F.I.R.S.T. office, I want to extend a Happy New Year to you and best wishes for a great 2010!

This past November, 18 board members met in Philadelphia for our biennial board retreat. With a full agenda, the board worked very hard for two days discussing and reviewing the progress of our four-year strategic plan. We also brainstormed new ideas for the future and renewed three-year board terms for Jon Dyer, MD, Angela Godby, Mark Klafter, and Janet McCoy.



Of particular note, Dr. Philip Fleckman was recognized for completing three 3-year terms on our board, which is the maximum allowed in accordance with our bylaws. Dr. Fleckman's dedication and commitment to F.I.R.S.T. has been truly inspiring. His most notable accomplishment is the creation and maintenance of the Ichthyosis Registry housed at the University of Washington. He also served in many leadership roles at F.I.R.S.T., including Vice-President for six years.

Although Dr. Fleckman will be rotating off the Board of Directors, he was unanimously elected as a Board Member Emeritus, joining Dr. Leonard Milstone, the late Dr. Peyton Weary, and Dr. Mary Williams in this distinguished role.



Looking toward the future....

F.I.R.S.T. will be continuing its Research Program for the fifth straight year. Grant applications are being accepted for Epidermolytic Hyperkeratosis (EHK) grants only this year. F.I.R.S.T. will also be supporting this year's prestigious Gordon Conference, which will focus on the role of the transglutaminases in disease.

See page 12 for important details about the 2010 Family Conference, "*F.I.R.S.T. Rocks the House with Mickey Mouse!*" The conference is scheduled for June 25, 26, & 27. Online registration will be available in January on our website, www.scalyskin.org. Discount tickets are also available for all the Disney theme parks for conference attendees. Please call the office if you have any questions.

Two days prior to the family conference, F.I.R.S.T. will be hosting a scientific meeting entitled "*Frontiers in Ichthyosis Research.*" The meeting agenda is designed to combine reports of recent progress in a few cutting-edge areas of ichthyosis research, and frank discussion about how to efficiently and effectively move research forward. The goal of the meeting will be to identify new ways in which the investigators, patients, and patient support groups can achieve ongoing synergistic interactions for better patient care.

In March, F.I.R.S.T. will once again be participating in the annual American Academy of Dermatology convention and meeting with our Medical & Scientific Advisory Board for our yearly meeting in Miami, FL. We will also be hosting our fifth annual Testimonial Dinner, featuring this year's honorees—Dr. Phillip Frost and Dr. Gerald Weinstein.

It promises to be an exciting year! Thank you for your continued commitment and financial support of F.I.R.S.T. It is greatly appreciated.



Sincerely,

Jean R. Pickford
Executive Director

Texans show support at Region 6 meeting

The Region 6 one day meeting, the second regional meeting hosted by F.I.R.S.T. this year, was held in Austin, Texas on September 19. The families and individuals attending the Region 6 meeting were thrilled to meet fellow region members and fellow Texans. There were 11 families in attendance, all from the state of Texas! The meeting was facilitated by Dr. Moise Levy, Chief of Pediatric Dermatology at Dell Children's Medical Center, Clinical Professor of Dermatology and Pediatrics at Baylor College of Medicine, and also a member of F.I.R.S.T.'s Board of Directors and Medical & Scientific Advisory Board. Dr. John Browning, who is an Assistant Professor of Pediatrics and Dermatology, and Chief of Pediatric Dermatology at the University of Texas Health Science Center at San Antonio, attended the meeting as well. Dr. Browning is co-medical director of Camp Dermadillo, a camp near Brenham, Texas for children with severe skin disease. He shared his experiences at camp and the experiences of the children, ages 9-16, who attend the week long program.



Participants at the Region 6 meeting



Drs. Moise Levy and John Browning sharing information about AAD Camp Dermadillo

The meeting touched on many topics ranging from sunscreen usage, natural remedies, and shampoos. Discussions were held on how to best and effectively communicate with your dermatologist and what to expect from your medical team. Attendees shared product information with one another and learned new skin care tips. The meeting concluded with a preview of The F.I.R.S.T. Story, a DVD from the 2008 Family Conference in Chicago.

If you would like to keep updated with Region events through email, please email Moureen Wenik or contact the National Office with your current email address.

Region 8 meeting in Las Vegas a terrific success!

Las Vegas proved to be a great setting for the Region 8 meeting. The October 3rd event hosted 21 families in attendance. Dr. Mary Williams, a pediatric dermatologist, who is semi-retired from the University of California San Francisco, opened up the meeting with a discussion called, "What is Ichthyosis," which was followed by a question and answer session. The families were asking great questions, such as "Why does skin heal so fast?" and "How is the best way to handle wound



The Region 8 Meeting participants

care?" The afternoon brought a new twist to guest speaking. With the use of Skype, Dr. Sherri Bale, from GeneDx in Maryland, presented an audio power point discussion on the "Genetics of Ichthyosis," which was also followed by a question and answer session. The children enjoyed spending the day in the childcare room, staffed by a professional childcare company, where they made crafts and played games. There was an opportunity for three breakout groups; parents and caregivers, adults, and teens. The meeting brought families together who had never met before, as well as a family that had communicated on the phone through the Support Network and finally had the chance to meet face-to-face for the very first time!

Grassroots Fundraising

Open House also Opens Hearts

Every year for the past 5 years, The Monogram Shop in Houston, Texas has an Open House at its store.

This year the owners decided to donate 10% of sales from the event to F.I.R.S.T.! The Foundation is close to the hearts of the owners because they are friendly with F.I.R.S.T. member Hollie Hugenberg Pfeiffer. Hollie's daughter Kate, affected with Lamellar/CIE, is a pre-schooler at St. Michael's School, where Hollie teaches. Hollie was thrilled to participate in this event as it also helped raise awareness in the community about Kate and ichthyosis. The event was a tremendous success, with goodie bags being given out and raffles. One attendee purchased 50 raffle tickets for the hot item, a piece of pink Brighton luggage. The participant put Hollie's name on all of the tickets and Hollie wound up winning the pink luggage for Kate! There was a great crowd and the day raised more than \$1,600 for F.I.R.S.T. Many thanks to The Monogram Shop and the residents of the area who participated to make this such a wonderful event.



Four-year-old has a Fundraising Facebook Page for F.I.R.S.T.

Ethan Edwards, a 4-year-old affected with non-bullous CIE, started taking an interest in incubating eggs and hatching chicks. With the help of parents Chip and Erin, Ethan turned that interest into an opportunity to raise awareness and funds for F.I.R.S.T. The Edwards family raise chickens and have created a Facebook page offering their chicks and eggs for sale, with a portion of the proceeds going to the Foundation. Ethan was very proud to send in a donation of \$15 to F.I.R.S.T. and is very excited about the opportunity to spread the word about ichthyosis and F.I.R.S.T.

Nancy O...hard at work for F.I.R.S.T.

Foundation member Nancy Osentoski, a long-time grassroots fundraiser, once again put her jars to work. Nancy placed jars in local Michigan businesses, Charlie Brown's and Pamida's, and collected donations for F.I.R.S.T. She raised more than \$175 through her efforts.

If you would like information on holding a grassroots fundraiser, please contact Greg Wilson, Development Director, at (215) 619-0670 or e-mail him at gwilson@scalyskin.org.

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 F.I.R.S.T, but also to raise awareness about ichthyosis in your community.

Monster Dash/Fun Run

Dedicated Foundation Member Dawn Johnson hosted her 9th Annual Monster Dash/Fun Run fundraiser on October 17, 2009 at Friendswood High School in Friendswood, Texas. This phenomenal event was once again a huge success. Friends, neighbors, family members, and Friendswood residents participated in either the one-and-a-half mile course or the five-kilometer course. Children participated in a half-mile run or walk. Every participant received a t-shirt. Many local businesses donated a variety of raffle items. The proceeds from this year's event totaled more than \$8,600!! Dawn and her family dedicate many months to plan for this event each year. F.I.R.S.T. is very grateful for her tireless dedication.



Children take your mark.



The children's race gets underway.

Accenture Holds 2nd Denim Drive

During last summer, Accenture Supply Chain Management in Reston, Virginia held a denim drive in their offices, with proceeds benefiting F.I.R.S.T. At that time, Scott Zailer, who is the uncle of Portia Cina, affected with CIE, made a presentation about F.I.R.S.T. to the staff members asking for their support. Again, in October, Scott went to the Accenture staff, set up a table with information about F.I.R.S.T., and asked for their support. The employees responded yet again! Scott raised more than \$150 in donations for F.I.R.S.T.



Wine Tasting held in New Jersey

Sean and Jolie Cina, parents of 2 year old Portia who is affected with CIE, hosted a wine tasting at their home in Roseland, New Jersey. They sent out beautiful invitations asking their family and friends to attend. The cost was \$25 per person and each person enjoyed appetizers and sampling a variety of wines. If any of the 20 participants had a favorite wine, they had the opportunity to purchase a bottle. The wine was provided by Wine Legend of Livingston, New Jersey who also donated a portion of their proceeds to F.I.R.S.T. This first-time event raised approximately \$700.00 for the Foundation. Many thanks to the Cina family for their dedication.

Pumpkins and Softball: A winning combination



The lott family held their 3rd Annual Pumpkin Paint and Bake Sale on October 3 at the Flandreau Aquatic Center, in Flandreau, South Dakota. Pumpkins were donated by lott's Greenhouse, whose owners are grandparents of Rylee lott, affected with CIE. Approximately 70 pumpkins were painted and about 100 people attended. Friends and family donated baked goods for sale. The event raised more than \$1,000 for F.I.R.S.T. and much fun was had by all.

In addition to their annual Pumpkin Paint, the lotts also hosted their 1st Annual Co-ed Softball tournament, held at the Flandreau City Park. Seven teams entered at a cost of \$100.00 per team entry fee. Approximately 80 ball players participated. After the tournament, close friends of the family grilled pork ribs, chicken, bratwurst, and potluck. A free will donation bucket was placed at the serving line and raised another \$300 for the Foundation.

Many thanks for the lott family for their continued efforts on behalf of F.I.R.S.T.

F.I.R.S.T. Rocks the House with Mickey Mouse!



2010 National Family Conference
Friday, June 25 – Sunday, June 27
Regal Sun Resort in
Walt Disney World Resort



See Page 13 for details about discounted Disney tickets!

Join us at F.I.R.S.T.'s signature event. You will benefit from stimulating discussions about causes, treatments, and research updates. Share your personal connections with others who understand. Meet new and old friends to exchange ideas, support, and advice. Gain knowledge about your disease and helpful products and resources. Help expert physicians and investigators advance our understanding of the different types of ichthyosis and related disorders. Come be educated, inspired, and connected!

Workshops & Events at a glance....

Friday, June 25

10:00 – 12:00 pm	Registration
11:00—12:00 pm	Session for 1st Time Attendees
11:00—12:00 pm	RSN Volunteer Training
12:00—1:00 pm	Lunch
1:00—5:00 pm	Kids' & Teens' Camp (ages 17 -under)
1:00—1:45 pm	General Session
1:00—8:00 pm	Clinical Screening Appts.
2:00—4:00 pm	Workshops I
4:00 pm	On your own

Saturday, June 26

7:00—8:45 am	Breakfast
9:00—5:00 pm	Kids' & Teens' Camp (Field Trip)
9:00—10:00 am	General Session
10:00—12:00 pm	Ask the Experts
12:00—1:00 pm	Lunch
1:00—3:00 pm	Workshops II
3:00—5:00 pm	Workshops III
6:00—10:00 pm	Dinner & Family Social

Sunday, June 27

7:00—8:45 am	Breakfast
9:00—12:30 pm	Kids' & Teens' Camp (ages 17 -under)
9:00—11:00 am	Workshops IV
11:15—12:30 pm	General Session & Closing
12:30—2:00 pm	Farewell Lunch

Teen Field Trip

Teens and tweens, ages 11-17, will participate in an offsite field trip to Disney Quest in Downtown Disney.

Kids' Camp



Special educational and social programs for the affected children and their siblings are an integral part of the conference. Each day, children in the kids' and teens' camp will enjoy activities, entertainment, educational programs and refreshments. Special thanks to the Vaseline Skin Fund for their very generous sponsorship.

Clinical Screening Appointments

All affected individuals and their families have the opportunity to meet with leading expert physicians for a free, private 15-minute consultation on Friday, June 25. Participation is voluntary. Sign-up is required prior to the conference by completing the Clinical Screening section on the Conference Registration Form.



F.I.R.S.T. Rocks the House with Mickey Mouse!



Registration: Online registration will be available beginning in January on our website, www.scalyskin.org. The Conference Registration Form and payment must be submitted to the national office by June 4th. Registrations without a completed form and payment will not be considered complete. *Please note:* Registration does not include your hotel room. Accommodations at the Regal Sun Resort must be made separately.

Cancellations & Refunds: Cancellations received prior to June 6th will be refunded, less a \$25 per person administrative fee. No refunds issued after June 4th.

Dress Code: Conference attire is casual, including Saturday evening's dinner & family social.

Meals: The conference registration fee includes lunch on Friday, June 25; breakfast, lunch and dinner on Saturday, June 26; and breakfast and lunch on Sunday, June 27. All registrants are on their own for dinner on Friday evening.

F.I.R.S.T. Idols Talent Revue: Back for its second year...this revue, which is open to children ages 5 to 18, is guaranteed to be a popular and heartwarming event for children to showcase their talents to our audience. The Talent Revue will take place on Saturday evening, June 26, after dinner. If you wish to participate, complete the F.I.R.S.T. Idols Talent Revue section on the registration form.

Director of Fun: The Regal Sun Resort provides a FUN Director whose only job is to make sure kids are having a good time! The FUN Director organizes daily activities and games within the hotel property for kids to enjoy. There is also a "Kids Corner," located in the main lobby along with a daily activity schedule. Check hotel for availability and hours.

Discounted Disney Tickets: As attendees of the Ichthyosis Family Conference, you can purchase discounted tickets for all Disney Theme Parks plus other bonuses. Half day tickets are available for those who want to visit the parks after the day's meetings have ended. You can also purchase discounted full day tickets and multi-day tickets, which include one free visit to DisneyQuest, Typhoon Lagoon, Blizzard Beach, Wide World of Sports, or the Oak Trail Golf Course. To order tickets, visit www.disneyconventionear.com/IFC or call 407.566.5600 and mention the Ichthyosis Family Conference. Orders must be placed by June 20, 2010. You may also visit our website and click on 2010 Orlando Family Conference and search for Discount Disney Ticket Program for more details.

Visit by Disney Characters: At Saturday night's dance party, you will have an opportunity to hang out and take photos with two surprise Disney characters!

Free Hotel Shuttle: The Regal Sun Resort provides a free shuttle to all the Disney parks and attractions. The shuttle departs every 1/2 hour from the hotel.

Hotel Accommodations: The discounted room rate negotiated with the hotel is \$85 for a Standard Double, \$89 for a Lakeview Double, and \$95 for a Tower Standard Double. This rate also includes the resort fee of \$15 per night per room. This rate is available from June 21 through June 30. All attendees must make their own reservations at the Regal Sun Resort by calling toll-free at 800.624.4109 or visit www.regalsunresort.com. To receive the discounted room rate, you must identify our group name as "Ichthyosis Family Conference." Internet users must enter ICFC0610 as the group code or visit the following link to be connected directly to F.I.R.S.T.'s online reservation site:

https://reservations.ihotelier.com/crs/g_reservation.cfm?groupID=312876&hotelID=14929. *Reservations must be received on or before 5 pm on June 3, 2008.* All reservations must be accompanied by a first night room deposit guaranteed with a major credit card. Other hotel rules and restrictions may apply. For questions, contact the hotel directly.

Driving Directions to Hotel: Contact the Regal Sun Resort at 407.828.4444 or visit their website at www.regalsunresort.com. Their address is 1850 Hotel Plaza Boulevard, Lake Buena Vista, FL 32830. There is no fee for self-parking.

Air & Hotel Transportation: Orlando International Airport (MCO) is the major airport for Disney hotels. It will be approximately a 45-minute ride from the airport to the hotel. At baggage claim, you will see the ground transportation options available for your travel to the Regal Sun Resort. F.I.R.S.T. has made arrangements with Mears Transportation to pre-purchase your tickets at a discounted rate. Visit our website, www.scalyskin.org and click on 2010 Orlando Family Conference and search for Mears Discount Coupon.

Air Charity Network: You may be eligible for free transportation using the Air Charity Network, formerly the Angel Flight America Program. If you live within 1000 miles of Orlando, Florida, Air Charity Network will fly a family in a 4-seater or 6-seater plane to and from the conference at no cost. Contact the National Patient Travel Center at 800.296.1217 and refer to the 2010 Foundation for Ichthyosis Family Conference Special Lift Program.

Concerned about the heat? Contact "Guest Services" at the theme park of your choice to explain ichthyosis and your heat intolerance issues. Be sure to bring a doctor's note along with FIRST's overheating fact sheet (available online). The theme park can issue a special guest pass to make accommodations for standing in lines in the heat. This is completely at the discretion of each theme park's management. Other suggestions include planning your trip to the parks in early morning or late afternoons, when the heat is less severe. You may also want to map out your visits within the park to take advantage of air-conditioned or covered attractions during the heat of the day.

NIH Supported Ichthyosis Research

by Leonard Milstone, MD

The National Institutes of Health (NIH) has recently awarded a 2.7 million dollar grant to a group of investigators led by Roger Kaspar, Leonard Milstone, and Christopher Contag. The grant, which has important implications for treatment of rare genetic skin diseases, is designed to develop consistent, relevant models for testing nucleic acid delivery to human epidermis. Nucleic acids are the building blocks of genes, and easily can be custom made to target disease-causing mutant genes and RNA. Small nucleic acids with therapeutic potential include siRNA, antisense RNA, triplex-forming DNA, and decoy oligonucleotides. Numerous laboratory experiments have shown that small nucleic acids administered to cells and tissues can correct the effects of mutant genes. Yet the promise of nucleic acids as therapeutic agents in people has not been realized. For diseases of epidermis, such as the ichthyoses, one of the major obstacles to therapeutic use of small nucleic acids is delivery: how can adequate amounts of the therapy be delivered to the target tissue without wasting valuable drug on non-target tissues or exposing non-target tissues to needless risk. The principal investigators of this grant realized that scientists around the world were using a wide variety of test systems to predict effective delivery to human skin. The goal of the grant is to reliably test and compare various delivery methods, and this will be accomplished by producing and validating two living skin models that can become generally available.

The participants in this effort represent nine universities and six biotech companies. The work will be conducted mainly at Transderm, Inc in Santa Cruz, California, Yale University in New Haven, Connecticut, and Stanford University in Palo Alto, California. This award had its genesis in a discussion among members of the Medical and Scientific Advisory Board of F.I.R.S.T. concerning how to stimulate translational research in rare skin disease. As a result of that discussion, Ervin Epstein, Barbara Gilcrest, and Leonard Milstone organized a conference, entitled Obstacles to Translation, held in San Francisco in 2006. F.I.R.S.T., along with the NIH and several other patient support groups and pharmaceutical companies, co-sponsored that meeting. One obstacle identified and discussed at that meeting was delivery of nucleic acids to skin. Many of the participants in the newly awarded grant initially met each other at a symposium on new delivery methods, sponsored by the Society for Investigative Dermatology in 2007. The idea for the grant application was hatched at a follow-up symposium organized by the patient support group, Pachyonychia Congenita Project, last May in Montreal. Funds for the award are provided as a one-time Grand Opportunity (GO) Grant through the American Reinvestment and Recovery Act (ARRA), also known as the 2009 Congressional stimulus package. F.I.R.S.T. was a strong supporter of the application, as it has been through the entire process that led to the award.

By William Rizzo, MD

F.I.R.S.T. has been instrumental in helping scientists gain much needed funding for ichthyosis research from the federal government this year. The National Institute of Child Health and Human Development and the Office of Rare Diseases at the NIH have recently awarded a Rare Diseases Clinical Research Consortium (RDCRC) grant to Dr. Robert Steiner at the Oregon Health & Science University to study genetic diseases of sterol and isoprenoid metabolism. The grant will fund collaborative research at 6 medical centers around the country and will focus on understanding the natural history of rare diseases, develop biomarkers to monitor therapy, and train new young scientists to dedicate their careers toward rare disease research. One of the diseases to be studied, Sjögren-Larsson syndrome, falls under the umbrella of F.I.R.S.T. Sjögren-Larsson syndrome is a form of ichthyosis that is associated with neurologic symptoms and developmental delay. The disease is caused by genetic deficiency of an enzyme involved in lipid (fat) metabolism, including a type of isoprenoid lipid called farnesol. With support of the RDCRC grant, Dr. William Rizzo at the University of Nebraska Medical Center will develop a method to measure farnesol in patients with Sjögren-Larsson syndrome and hopefully gain insight into new therapies for this disease. The support of F.I.R.S.T. and similar patient support organizations was a key factor in convincing the NIH to fund this research.



Foundation for Ichthyosis & Related Skin Types, Inc.™
2010 Family Conference - Orlando, FL
Scholarship Application



Application Deadline: February 1, 2010

Name: _____

Address: _____

City: _____ State: _____ Postal Code: _____

Province: _____ Country: _____

Home Phone: _____ Work Phone: _____

Cell Phone: _____ Email: _____

How many people will be attending the conference? _____

Name: _____ Age: _____ Type of Ichthyosis: _____

Have you attended a F.I.R.S.T. Family Conference before? Yes No If so, when? _____

How many persons are you applying for a scholarship for? ____ Adults (14+) ____ Children (13 & under)

For what are you applying? _____ Registration Fees _____ Hotel Reimbursement

Annual Family Income:	_____ Under \$20,000	_____ \$51,000 - \$60,000
(please include a copy of	_____ \$21,000 - \$35,000	_____ \$61,000 - \$75,000
Your most recent W-2)	_____ \$36,000 - \$50,000	_____ Over \$75,000

Why do you want to attend the F.I.R.S.T. Family Conference? (Use additional paper if necessary)

Please return this form to the F.I.R.S.T. office by February 1, 2010.

Applications received after February 1 will not be considered.

F.I.R.S.T. and its officials reserve the right to disqualify any application that is incomplete.

Cut here



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Camp Discovery 2010

In 1993, the American Academy of Dermatology (Academy) started Camp Discovery with a single camp location in Minnesota serving about 50 kids. Little did they know that Camp would be so successful! More than 3,000 kids have benefited over the past 16 years.

This year the Academy is proud to offer four camping sessions for young people with chronic skin conditions who are between the ages of 8 and 16. Under the expert care of dermatologists and nurses, Camp Discovery gives campers the opportunity to spend a week with other young people with skin conditions, while participating in everything from swimming and fishing to horseback riding to lots of camp games and just plain fun!

There is no fee to attend this very special camp. Full scholarships, including transportation, are provided by the Academy through generous donations from its members, outside organizations and individuals. All campers must be referred by their dermatologist.

2010 Dates:

- June 27 – July 2, Junior Camp in Crosslake, Minnesota (ages 10 – 14)
- July 11 – 16, Teen Camp in Crosslake, Minnesota (ages 14 – 16)
- August 8 – 13, Camp Dermadillo, Burton, Texas (ages 9 – 15)
- August 14 – 21, Camp Horizon, Millville, Pennsylvania (ages 8 – 13)

For more information about attending or volunteering, please visit their Web site at campdiscovery.org or contact Janine Mueller at 847-240-1737 or jmueller@aad.org.

