Ichthyosis Focus

F.I.R.S.T.
Foundation for Ichthyosis and Related Skin Types

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Autosomal Recessive Congenital Ichthyosis (ARCI)

by Matthew Herman, M.D.

The term ichthyosis refers to a variety of different scaling disorders, ranging from the relatively common ichthyosis vulgaris (IV) to recessive X-linked ichthyosis (RXLI) and epidermolytic hyperkeratosis (EH). Our lab has been studying yet another kind of ichthyosis: autosomal recessive congenital ichthyosis (ARCI).

ARCI is rare, with an estimated occurrence of 1:200,000-1:300,000 in the US. The term ARCI refers to lamellar ichthyosis (LI), non-bullous congenital ichthyosiform erythroderma (NBCIE), and the extremely rare harlequin ichthyosis (HI). Mutations are changes in the base sequence of genes (the genetic code represented by the letters A, T, C, and G) that cause a change in a part of the body's inner machinery, and ARCI is associated with mutations of genes that reside on autosomal chromosomes. Humans have 22 autosomal chromosomes. Non-autosomal chromosomes, the chromosomes X and Y, are associated with sex determination. Humans posses two copies of all autosomal chromosomes (and therefore two copies of every gene on those chromosomes). ARCI is recessive, which means that, in order for someone to develop ARCI, an individual must have one mutation in each copy of a single gene that could potentially cause ARCI. ARCI is called congenital, since it appears at birth or shortly thereafter. Newborns who will develop ARCI are often born in a tight translucent sheath called a collodion membrane, and these newborns are often referred to as collodion babies.

Five genes that cause ARCI have been identified. A recent study by our lab found that the most often mutated gene in North Americans with ARCI is called the transglutaminase-1 gene (*TGM1* gene). *TGM1* encodes

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Economy Update

by John J. Schoendorf, CFO

Due to the state of our economy, I wanted to share my thoughts on how the Foundation is faring and what has been done to protect your investment in our future. I would also like to solicit your continued support as we move through these troubled times. Later in the year, when our public accountants have completed their audit, you will receive my full annual report.

As our asset base has increased over the past few years, it has been my and the Board of Directors utmost concern to protect and preserve those assets so that the Foundation can continue to not only improve the level of its services, but also increase its level of ability to fund research grants. To that end, and prior to the drastic fluctuations we have seen recently, approximately 80%of our liquid assets were placed in interest bearing cash accounts. As a result, although we have not made a tremendous profit from interest, we have been protected from the market's deterioration. The remaining 20% of our liquid assets are in relatively stable blended fund investments. It looks like we have temporarily experienced a deterioration of approximately 15% on this portion as of September 30th due to the craziness of the market. Fortunately, this is a very small loss compared to what many foundations and other investors have experienced. Putting this loss into perspective, it equates to about 3% of all our liquid assets.

It has become apparent that due to the sheer size of our asset base now, we need to acquire an investment manager. This position will invest our assets with a closer eye, according to guidelines set by the Board of Directors, of course. Management by such a person would be done on a regular basis, be it daily, weekly or monthly, depending on market conditions. I had previously looked into filling this position but no one was really interested since our base was so low. Currently, I am receiving final proposals from several organizations that the Finance Committee, Executive Board and Board of Directors will ultimately pass judgment on in the near future.

In closing, I hope I have provided a measure of confidence in how the Foundation's assets have been managed. We are all concerned about the future and how our legislators will handle the challenges ahead. On behalf of your Board of Directors and myself, please consider the Foundation's fundraising needs as you wrestle with these trying times.

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The Foundation for Ichthyosis
& Related Skin Types
1364 Welsh Road, Suite G2
North Wales, PA 19454

215.619.0670 • 800.545.3286
Fax: 215.619.0780
Email: info@scalyskin.org
Web: www.scalyskin.org

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The editor invites your correspondence. We welcome your comments, observations, and suggestions. Please send your letters to Ichthyosis Focus at the address listed above.

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Correspondence Corner

Dear Jean,
I just wanted to share these with you. My daughter, Chandler, told me two weeks ago that so many people donated money to FIRST for her brother's cause, and that she wanted to have a garage sale to raise money for Dane. So....we put one together....and she raised $405.00 for FIRST. She didn't even ask for a single penny. Cade also contributed his things for his little brother's cause! I'm so proud of them, especially since it was their idea (Chandler's idea)...but from both of their hearts. I know our little Dane was smiling down on them. Just wanted to share this with you!

Love,
Suzanne Phelps

Dear Jean,
We had a really nice time at the DeGarmo golf outing. The DeGarmos were so nice and the boys, Jaydn and Carson, were adorable. Keith participated in part of the golfing but the temperature was over 100 degrees. They had a lot of fun. Keith's speech was so great: I was really proud of him. He told what it was like growing up affected with ichthyosis and it was really touching. Jaydn even got up with the help of his dad and spoke a little. Thanks for asking Keith to give the speech; it was a real confidence booster. Keith and I have been discussing having an event here in El Segundo.

Sincerely,
Beverly Charsha

Dear F.I.R.S.T,
I have become highly allergic to grasses, mold, and dust mites according to the report I received from my allergist. I am in the process of purchasing a new mattress and box spring, and the salespeople tell me of a latex mattress that is non-allergenic, and that dust mites cannot live on these surfaces. I am concerned the latex will be hotter to lay on, and with my dry skin, I need a surface that is breathable. I never realized there were so many variables (cost, comfort, air flow, support, allergy resistant, etc.) to buying a bed. If any of our members have faced the same problem, I would be interested in their experiences.

Sincerely,
Les Avakian
LesThan@aol.com

Dear Jean,
During a recent trip to Seattle, we came across an organic skin care product that seems to be helping our son very well. Not sure if it is something that can be shared through a link on the website. They were prompted to develop the products due to their daughter's condition; in particular, it is the HEALING HEMP SALVE. The website for the product is www.thefayfarm.com.

Sincerely,
Stephen Olsthoorn

Dear F.I.R.S.T.,
I happened to come across some very old family papers which were stored away in my closet. My grandfather, H. B. Hastings, wrote a 4-page letter to my grandmother, Annie, in which he described the diagnosis of their son Sidney (my uncle) who had ichthyosis. The letter, dated April 10, 1909, specifically identified the disease as "Ichthyosis." It is quite legible. The doctor in New York had some quaint remedies, such as "goose grease & alboline in equal parts" with a little oil of rose geranium. Glycerine and rose water were also recommended. They warned my grandparents that no cure was available at the time.

My uncle managed to hoodwink all of his nieces and nephews (including me) and we never learned he had *the disorder* until he was in his mid-eighties. My uncle always covered himself, so it wasn't known by us until his later years. It was described by my uncle as "fish scales." He did tell me about his skin condition, and that he saw a little boy who had the disorder. Apparently he convinced the boy that he could grow up to live a "normal" life. I understand that my uncle's visit with the boy was inspirational to both the boy and his family. I wish that I could have gotten more details from my uncle.

My uncle also confided to me that this disorder plagued the czars of Russia. Whether that's heresay, I don't know. I thought you might be interested about this trivia. Nobody else in our family has been afflicted with this disease.

Sincerely,
Paul Hastings

Dear Jean,
Hope everyone is doing well. I have been using new products on Wyatt and wanted to share the information with you. Both products are from Bath & Body Works. The wash is called For Heaven's Sake', Super Softening Oil-to-Cream Bath and Shower Wash with Sake', and the lotion is called Mystic Silk 24-Hour Ultimate Moisture Body Lotion with Silk Protein & Rice Bran Oil. I went to Bath and Body's web site and sent them an email explaining Wyatt's condition and what I was using their products for. They sent me a code to get 20% off on online orders. I sent a picture of Wyatt for you to see how his skin has improved.

Thanks,
Teri & Wyatt Daring

Dear Jean,
I wanted to drop in a bit of personal information about something I have been doing for my skin that has made an enormous difference. Based on the article in the newsletter about the German dermatologist who recently died, I tried adding several handfuls of sodium bicarbonate (baking soda) to my weekly exfoliating bath. The results are astounding--at least twice as much exfoliation, and areas that have never been clear are clear and soft as baby skin. This, plus the application of ammonium lactate lotion in the morning of the day I bathe (which I was already doing), is all I'm currently doing besides maintaining with Lubriderm and Cetaphil lotion. Thought you'd like to add this to the next newsletter because I think there are a lot of EHK folks who would be interested.

Sincerely,
Terry Melton

Dear F.I.R.S.T.,
I ordered a new product from Avon for my daughter Bailey to try. The product is Moisture Therapy Glycerin Moisture Gel. The ad caught my attention when it said it increases moisture by 224%. Bailey, who has severe lamellar ichthyosis, applied the gel one morning WITHOUT TAKING A SHOWER first, so her skin was very dry. She ran some errands and expected to have to shower when she came home. By lunch time, her skin was amazing! The last time I remember it being that soft and smooth was when she wore a diaper! The real surprise was that by 11 PM that night, her skin was STILL really soft and smooth! In 22 years of trying a variety of creams, lotions, and everything else, I have never seen anything work like this did to soften, smooth, and moisturize her skin! There is no acid in it, so it won't help with reducing the scaling, but I am excited about how this product worked and will definitely keep it on hand to use over her AHA lotion. We found it to be miraculous! Hope it works this well for others!

Thanks!
Tracie Pretak

Grassroots Fundraising

F.I.R.S.T is very thankful to our members who have held grassroots fundraisers over the summer. Their efforts continue our mission to educate, inpire, and connect those touched by ichthyosis and related disorders through emotional support, information, advocacy, and research funding for better treatments and eventual cures.

Chris and Michelle Dugan, aunt and uncle to five-year-old Mattingly Dugan, hosted their 2nd Annual Drive for a Cure Golf Tournament. It was held on Sunday, August 17th at the Brockport Country Club in Brockport, NY. Once again, the event was a huge success and raised over $2400.00 for F.I.R.S.T.! The Foundation is very grateful to the Dugans for their willingness to support our important work of educating, inspiring and connecting those touched by ichthyosis.

Josh and Amie DeGarmo of Napa, CA held another successful golf tournament to benefit the Foundation. Their 3rd Annual Golf Tournament was held at the Silverado Country Club, in Napa on July 9. More than $20,000 was raised for F.I.R.S.T. The Dugans are parents to Jaydn, 6 years old, and Carson, 3 years old; both affected with Lamellar Ichthyosis. Both boys are featured in our Spotlight On section this month.

Dawn Johnson, of Friendswood, Texas, held her 7th Annual Monster Dash. Dawn, whose daughter Jordan is affected with CIE, has been an avid volunteer and supporter of the Foundation over the years. With over $8,400 raised, this year's event was a tremendous success. In the aftermath of Hurricane Ike in Texas, it is a testament to Dawn and the Friendswood community that they were able to produce such a successful event. The Foundation thanks Dawn and all of her wonderful volunteers for their invaluable efforts.

2nd Annual Phantom Tea Another Success!

We are very pleased to announce that our 2nd Annual Phantom Tea has been very successful. We asked 1,700 member families to mail personalized "tea packages" to their family and friends. This invitation asked for a small donation while enjoying a cup of tea and celebrating those affected with ichthyosis. The response was terrific with over $35,000 raised.

Seventy families responded to say they would help. We quickly went to work and assembled over 2,000 tea packages and distributed them to our participating families. Once they received the packages, their job was to address and mail them to their family and friends. The success of this Phantom Tea fundraiser is tremendous! Not only does this national event raise money for the Foundation, it also creates awareness among members' families and friends because each invitation includes a descriptive paragraph about ichthyosis.

If you would like information on holding a grassroots fundraiser, please contact the Foundation office at (215)619-0670 or e-mail us at info@scalyskin.org.

Executive Director's Report

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

In this issue of the Focus, I am proud to announce the three new research grants that have been approved for funding by our Research Review Committee and the Board of Directors. As you will read on page 6, there is promising research that is being funded by F.I.R.S.T. and executed by talented and committed investigators. Ideas and new discoveries are being explored, which provides hope and encouragement for all of our member families.

Since the inception of our research program (in just three short years), we have funded nine grants, some of which are multi-year. Your continued support of our research fund is critical to the success of this program. All our efforts combined will help make advances toward better treatments and, hopefully one day, a cure.

Remember the strategic plan I wrote about in the last issue of the Focus? Plans are well underway and we have already accomplished one key strategic initiative. Over the past several months, F.I.R.S.T. invested in the services of a professional consultant to review, analyze and make recommendations as to how we can improve our fundraising programs to ultimately better serve our members' needs. Through feedback from this review and input from key members and leaders of F.I.R.S.T., the Board of Directors recently approved a new comprehensive development plan to bring the organization's fund raising to a new level. To accomplish this exciting new plan, the office staff will be expanding and re-organizing. F.I.R.S.T. will also be adding a new staff member to our join our talented team in the upcoming year.

Three additional key initiatives will be the focus of our efforts in the next few months. First, the Marketing Committee will be identifying and developing a strategic marketing plan for F.I.R.S.T. Second, an ad hoc committee will be searching for a new database system that can improve the tracking and managing of our members' information, so we can build stronger relationships. And, third, a volunteer committee is being recruited to update and restructure our website. You will be reading more about all these exciting initiatives in future newsletters and on our website, www.scalyskin.org.

As the end of the year approaches, it is time for our Board Development Committee to interview interested members for vacant positions on our Board of Directors. If you know someone who has a vested interest in seeing F.I.R.S.T. grow, has the time to dedicate to this responsibility, and is committed to our mission, please let me know at jpickford@scalyskin.org.

The Vaseline Skin Fund has been extremely generous to F.I.R.S.T. and is making a sample of Vaseline available to our members free of charge; see page 14 for more details.

Finally, in June, I began my tenth year as the director of F.I.R.S.T. Over the past decade, I have seen this organization grow in leaps and bounds. We have accomplished so much together, and I look toward the future with hope and excitement about all the new things we can do. As always, please stay in touch with our office. A simple email to say "hello" or to introduce yourself allows our staff to connect with our members and donors. After all, you are the reason we are here! My very best to you and your family.

Sincerely,

Jean

Jean R. Pickford
Executive Director

F.I.R.S.T. Money at Work

First Results of the Liposome-Formulation Project for Future Enzyme Replacement Therapy of Lamellar Ichthyosis.

By: Heiko Traupe MD, Associate Professor for Dermatology, Muenster

Lamellar Ichthyosis (LI) is a severe type of ichthyosis that is often caused by a deficiency of the enzyme transglutaminase-1. Transglutaminase (TGase)-1 is important for the formation of the stratum corneum (horny layer) which is thickened very much in LI. One of the tasks of TGase-1 is to attach lipids to the so called "cornified envelope," i.e. a protein envelope which surrounds the cells in the stratum corneum. Current thinking is that when the lipids cannot be attached to the cornified envelope the lipid mantle of the stratum corneum becomes disturbed and this will result in considerable problems such as increased water loss and in the end, ichthyosis. It is important to know that within the keratinocytes the TGase-1 is located at the inner side of the cell membrane.

Long term aim

In the long term, we want to develop an enzyme replacement therapy for TGase-1 deficient LI by making use of a cream that contains the enzyme. An essential intermediate step for this aim is a successful packing of TGase-1 in a suitable liposome vehicle.

Short term aims of the current liposome formulation project

The first aims of the liposome formulation project which is funded by F.I.R.S.T. are

a) to produce large quantities of the enzyme TGase-1
b) to develop suitable lipid vesicles (liposomes) into which the enzyme can be packed
c) to actually encapsulate TGase-1 within liposomes
d) to cultivate skin cells (keratinocytes) from patients with established TGase-1 deficiency
e) to show that the liposomes are taken up by the keratinocytes and can pass the cell membrane and release the enzyme at the inner side of the cell membrane.

PhD-student, Mrs. Karin Aufenvenne, pictured left with lab technician Tatjiana Walker, is in the lab of Dr. Dathe in Berlin.

So far we successfully expressed large amounts (more than 10 mg) of TGase-1 in our lab making use of insect cells and the so called baculovirus system. For the second goal we developed together with our partner Dr. Dathe from Berlin a liposome prototype which contains a protein named apolipoprotein E peptide. This peptide was added to the liposome in order to facilitate the uptake of the liposome into the keratinocytes. Moreover, this liposome prototype also has a fluorescent marker in order to 1) visualize the liposome within the cell; 2) demonstrate that it can be taken up by keratinocytes; and 3) show that this vehicle releases the enzyme to the inner side of the cell membrane where TGase-1 should go. To sum up, we have so far achieved in our current project steps a) to c) and are currently working to show that the liposomes are indeed taken up by (normal) keratinocytes and release the enzyme to the inner side of the cell membrane. In initial cell culture studies, we isolated primary keratinocytes from three patients with transglutaminase-1 deficient lamellar ichthyosis. We also observed that keratinocytes from these patients grow very slowly when compared to normal keratinocytes and are difficult to cultivate.

Perspectives and work packages for the second work period

In the second work period we want to

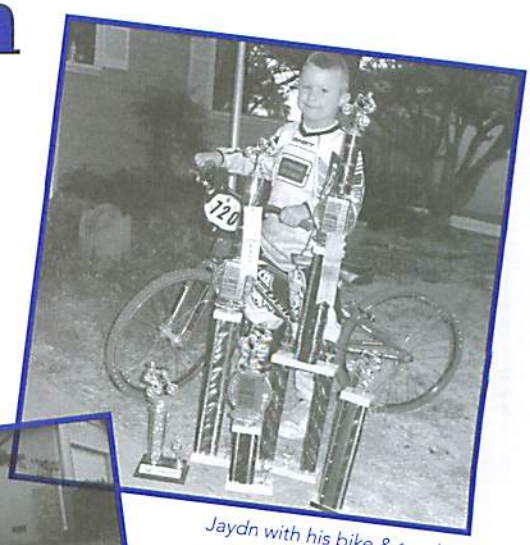
a) continue with expression and purification of TGase-1 protein
b) further investigate the liposome protein complexes and further characterize them with respect to stability and size distribution.
c) further investigate the uptake of the liposome-TGase-1 complex to normal keratinocytes
d) attempt to develop a three-dimensional ichthyosis model in a cell culture called a skin equivalent model and to treat this model with a liposome/TGase-1 complex.

This last aim (d) will start to address a major potential hurtle: getting the liposome/TGase-1 complex through the thick stratum corneum and into the proper skin cells.

Spotlight On

The DeGarmo Boys Take on BMX Racing

by Josh and Amie Jo DeGarmo



Jaydn with his bike & trophies

Carson with his bike & trophies

Jaydn, age 6, has always loved to ride his bike along with his cousins. Through a classmate of his, he got involved in BMX racing. Now Jaydn, Tristan, his 13-year-old cousin, and Teagan, his 6-year-old cousin, are active BMX racers. Jaydn's younger brother, Carson, age 3, does what they call a training wheel race before the bigger kids ride.

The biggest obstacle for us to overcome with BMX racing is the overheating. However, we have been able to keep this in check pretty well due to the races lasting only 1-2 minutes. We use a pop-up canopy for shade and are always keeping his shirt wet. Since we start racing in mid June, the weather has been between 75 and 100. Unlike other traditional sports such as football, soccer, and baseball, the short exposure to direct sun during a race has really allowed us to maintain Jaydn's body temperature so he can participate.

In BMX racing you start out as a novice until you win 8 races. Jaydn just recently won his 8th race. So now he is going to be in the intermediate class. By accomplishing this and meeting so many other children at all the tracks we travel to, he is really feeling good about himself. Last week, he had the chance to meet and get an autograph from Team USA BMX rider Donnie Robinson, who is from Napa. Jaydn now talks about his goal of representing the USA in the Olympics when he gets older! He still is a little reserved with the questions about his flushed red face and the dry skin; however, he simply replies, "I have a rare skin disorder, and if you want to know more ask him" (and points to dad).

We feel that Jaydn's story of BMX riding can inspire others to step outside the box of traditional sports with their children and to keep encouraging their children if playing a sport does not work out. There are many ways to keep your children active and get them to interact with their peers. We personally feel that the BMX community is one of the most caring and understanding. No matter where we race, we can always find people who are like long-lost friends and are willing to share and give friendship at all times.

Jaydn is 6 years old and Carson is 3 years old. Both are affected with mild to moderate lamellar ichthyosis. The DeGarmos have no family history of ichthyosis.

F.I.R.S.T. Research Dollars Fund Grants

The Foundation's Research Grant Program is pleased to announce the funding of three worthy research projects. Maurice van Steensel, MD PhD and Michel van Geel, MD, from University Hospital Maastricht, the Netherlands were awarded $50,000 for the project called "A Mouse Model for Keratitis-Ichthyosis-Deafness Syndrome." Mason Freeman, MD, from Harvard Medical School in Boston, MA, was awarded $75,000 for his project titled "A Null Mouse Model of the Lamellar/Harlequin Ichthyosis ABCA12 Transporter" and Robert Rice, MD, from the University of California, Davis was funded $25,000 for his project "Proteomic Analysis of Ichthyosis: LI/CIE Focus."

Dr. van Geel and Dr. van Steensel at their lab.

Drs. van Steensel and van Geel summarized their project.

Keratitis-ichthyosis-deafness (KID) syndrome is a rare genetic disease characterized by severe ichthyosis, keratitis (inflammation of the cornea) leading to blindness and deafness. People with KID syndrome are also more sensitive to skin infections and can even develop skin cancer. This severe disease is caused by mutations in the protein connexin26, which is part of specialized communication channels between cells called *gap junctions*. After several years of research, we know that mutations in connexin26 can cause a range skin disorders, some similar to KID syndrome but most quite distinct. The reason for this diversity is not understood because we have a very limited view of what gap junctions do in the skin. As a consequence, we have no good treatment for our patients. In addition, it is difficult to study gap junction disorders of the skin because they are so rare. To remedy this situation, we decided to develop a mouse model for KID syndrome. To do this, we transfer a human connexin26 gene with a KID syndrome mutation into mouse embryo cells. Because we are interested in the ichthyosis that patients with KID syndrome develop, we use modern transgene technology to make a mouse that develops skin abnormalities but not the keratitis or the deafness. We also make sure that the disease gene is inducible, which means that it only becomes manifest when the animal is given an antibiotic. This approach reduces animal discomfort. Because we can switch the disease gene on and off at will, we can examine whether the skin disease is reversible. If it is, that means that patients might benefit from cutting-edge treatments that prevent the mutant protein from being made. Finally, we have constructed the transgene in such a way that we can easily exchange the disease gene for another one so that we, or other groups, may study other types of ichthyosis.

We are excited that F.I.R.S.T. is funding the development of our mouse model and we have begun the process of making mutant embryos. If all goes well, we will soon have a versatile model in which to study a severe form of ichthyosis and its treatment.

Dr. Mason Freeman is pleased to share his work with our F.I.R.S.T. members.

In our laboratory at the Massachusetts General Hospital, we have spent most of the past twenty years studying the role of cellular proteins that move lipids into or out of cells. Lipids are fats and are not dissolvable in water, so cells have developed special mechanisms for moving them around inside cells, as well as from inside a cell to outside a cell. One of the mechanisms cells use for this activity is a class of proteins called ABC transporters. ABC stands for ATP Binding Cassette. These transporters are proteins that bind the energy molecule of all cells, called ATP, and use its energy to move lipid molecules wherever the cell wants them to go. Both lamellar ichthyosis and harlequin ichthyosis have been associated with alterations in the gene encoding one of these ABC transporters, ABCA12. We recently generated mice in which the ABCA12 gene was deleted, and these mice share many of the same features that children with harlequin ichthyosis have. The mice have thickened skin and water evaporates through this skin much faster than normal. We used our many years of experience measuring different lipids to identify a defect in the skin of these mice, and we discovered a very unusual and specific lipid to be missing. This result makes us think that the activity of ABCA12 that is missing, in children with the scaly skin problems linked to the ABCA12 transporter, must cause the special

lipid we identified not to get to its appropriate location in the cell. This failure means that it does not get processed to the final, correct form needed to make the skin look and work normally. In the work that F.I.R.S.T. is funding us to perform, we will try to understand if this idea is correct and if there are any ways to correct the defect or re-supply the missing critical lipid. We are very excited about this work and grateful for the support of the Foundation. Most importantly, we want to help find better ways to treat those who have developed these very serious skin disorders.

Dr. Bob Rice explains his project.

A frequent problem in diagnosis and treatment of the ichthyoses is to understand the molecular basis for the severity of the disease. Patients with the same genetic diagnosis, for example, may suffer a range of severities. This project investigates whether variations in the proteins expressed in the epidermis can help explain the variation in severity. To determine which proteins are present, epidermal scale is digested with a protease that produces specific protein fragments that are then analyzed by mass spectrometry. Preliminary results indicate that more than 50 proteins can be identified in this way and that samples from several ichthyosis patients show deficiencies in certain proteins. Building on this information, the present work will examine more samples and look for characteristic deficiencies. It will also seek more quantitative information on variations in levels of targeted proteins known or suspected of contributing to differences in severity. This information may also assist in monitoring or designing therapies.

Using the Internet to Raise Funds for F.I.R.S.T.

GoodSearch and GoodShop for F.I.R.S.T.

Shopping online and donating to F.I.R.S.T. has never been easier. GoodSearch and GoodShop offer non-profits an opportunity to receive donations through searches and shopping. Every time you click over to one of the partner merchants from the GoodShop site, and then make a purchase, F.I.R.S.T. receives a donation. The percentage of the sale is posted for each merchant on GoodShop and F.I.R.S.T. receives 100% of the donation displayed. Simply go to www.goodsearch.com and click on the GoodShop link or go to www.goodshop.com. In the "Who do you GoodShop for" box, type Foundation for Ichthyosis. Next, click through to the partner retailers and start shopping!

Send Flowers for The Holidays

The holidays are fast approaching. Sending flowers is one way to remind your family and friends you are thinking about them at this wonderful time of the year. F.I.R.S.T. is a partner of flowerpetal.com, which offers a wide selection of arrangements to choose from for all occasions. When you order flowers, flowerpetal.com will donate 12% of the total sale price back to F.I.R.S.T. To place your order, follow the instructions below.

- Visit the Foundation website, www.scalyskin.org
- Click on the link and order your flowers from the arrangements shown.
- The price listed with the arrangement is the completed, shipped price.
- There are no additional charges.
- At checkout, there will be an option to make an additional donation, if you choose.

What a terrific way to further help the Foundation. You don't have to spend any additional money and F.I.R.S.T will receive additional donations. Spread the word to your friends and family members who may be ordering flower arrangements.

eScrip Fundraising

eScrip registers merchants and shoppers through its website and returns a portion of your shopping dollars to the Foundation. If you are interested in supporting the Foundation by redirecting your shopping dollars through eScrip, learn how by contacting F.I.R.S.T.'S national office, 1-800-545-3286, or visit eScrip's website, www.escrip.com. Many national merchants, such as Budget Rent-A-Car, Eddie Bauer, Office Max, Payless Shoe Source, and Spiegel, participate in this program. Many regional merchants also are registered with eScrip; the office can provide you with a list. This program does not cost you any money or raise the price of the products you normally buy. The registered merchants have agreed to return a portion of their profits to the Foundation if you shop their stores through eScrip. The Foundation's Group ID number is 2440285.

Camp Is Not Only For Kids

By: Jean Cahill

Are you an adult or child with ichthyosis? Are you a parent and have a son or daughter with ichthyosis? If so, you need to know about this very important treatment. I believe that it is the best thing for any individual who lives with ichthyosis. I was born a collodion baby and lived with lamellar ichthyosis all my life. In almost 40 years of trying new treatments, which can be very costly, nothing compares to this free treatment! I am happy to try my best to share my experience with you. I say "try" because words cannot describe how much I love it! The treatment is one week at what I call "the best place on earth," and that is "Camp Horizon," held on the grounds of Camp Victory in Millville, Pennsylvania.

This past August was my 13th year attending this amazing camp for children ages 8 – 13 who have a skin disorder. Unfortunately, when I was a child, there was no such thing as a camp for kids with skin disorders that I could go to. Therefore, I cannot tell my experience of attending camp as a child, but I can share with you that I wish there was one when I was a child, because each year I see these kids meeting other kids their own age with ichthyosis and also adults with ichthyosis. I can see the excitement in their eyes and smiles on their faces. I have the privilege of seeing them included in so many fun activities such as swimming, arts and crafts, and archery to name a few. I feel honored to see them show off their talents on the evening of the Camper Talent Show.

Since I have been going to camp for many years, I've seen several kids come back year after year knowing that they are not alone and making lifelong friends. I have seen 13-year-old kids graduate and then return to camp when they reach the right age to be staff members, which proves to me that it had an impact on them as campers.

Sometimes, I wonder what my life would have been like if I had had the opportunity to be a camper, but going to Camp Horizon as an adult has still changed my life forever. I can honestly say that I have made not only lifelong friends, but also most of my best friends are camp friends, and some of them are what I also call my "angel" friends.

Have you ever heard that you can learn a lot from kids? Well, let me tell you, that is so very true! I have also found some really cool dermatologists who don't treat you like a guinea pig, but rather are out there to have a great time and be a friend instead of a doctor.

Camp has helped me to grow and has also helped me to deal with my ichthyosis. It helps to know that you

Jean Cahill, right, pictured with F.I.R.S.T. Executive Director, Jean Pickford and Program Director, Moureen Wenik. Also pictured: Maria Tedesco, Hunter Steinitz, Mohamid Mehmood, and Ryan Balog.

are not alone. Living with such a rare disorder can be very trying at times. I will admit that there have been times when I have gotten depressed about having ichthyosis, but now, if that starts to happen, I try to think about camp, and it helps. Camp Horizon is the one and only thing that I really and truly look forward to every year! I could go on and on about camp, but I think I'll stop here or else I'll never stop.

Again, words cannot express what camp means to me. Before I go, I do want to say a couple of quick things. One is that if you are a parent of a child with ichthyosis, please give your child the opportunity that I did not have and send them to Camp Horizon as a camper. Camp is a safe place for them to just be kids and have fun. It is a place where everyone counts as a normal human being, a place where lifelong friends are made, and a place where wonderful memories last forever.

If you are an adult with ichthyosis, remember it is never too late to join the Camp Horizon *family*. Yes, family, that is exactly what it feels like. Trust me, it will change your life in many ways.

Also, I want to thank the Academy of Dermatology who pays all the expenses, including staff and camper flights, etc. Their generosity gives everyone a chance to attend camp for free.

Last but not least, I want to give the biggest "Thank You" to not only one of my best friends, but also one of my "angel" friends who has helped me and many others. His name is Howard Pride. He is the one who started this wicked cool camp! Without him, Camp Horizon would not exist. So hey, "Thanks, Howard."

I have one other thing to say and that is, "Hello to all Camp Horizon campers and staff! I miss you all, and I look forward to seeing you again at Camp Horizon 2009."

Camp Is Not Only For Kids
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News on the Hill

FY09 Appropriations Still Stalled As Congress Considers More Funding For FY08

When Congress adjourned for its annual summer recess, only one of 12 fiscal year 2009 (FY09) appropriations bills had passed the House of Representatives and none of the bills had passed the Senate. The new fiscal year began October 1, 2008. The bill funding the Department of Defense is likely to be the only other appropriations bill passed by Congress this fall. All other federal agencies are expected to be funded under a continuing resolution until next spring. A continuing resolution operates the federal programs at the same level of funding as the previous year.

While the FY09 process is stalled, Congress is considering an additional supplemental spending bill for FY 08 On July 30, Senate Appropriations Committee Chair Robert Byrd (D-WV) released details of a $24.1 billion supplemental spending measure he hopes to take to the Senate floor this fall. Chairman Byrd's proposal is being described as a "stimulus supplemental" that is aimed at providing funding for infrastructure projects, economic recovery measures, and natural disaster relief programs.

The Senate's new supplemental spending plan includes an additional $500 million for the National Institutes of Health (NIH). House Speaker Nancy Pelosi (D-CA) also has expressed interest in enacting companion legislation in the House prior to Congress adjourning this year. President Bush and congressional Republicans have been less receptive to the idea of a second supplemental package for FY08.

Please continue to contact your legislators to express support for increased NIH funding -- an additional $500 million in FY 08 and a 6.6% increase in FY09. You can find more information about how to contact Congress by visiting www.house.gov and www.senate.gov.

News on the Hill keeps members current with the legislation in Washington, DC. This column is written by Angela Godby, Assistant Vice Chancellor for Federal Relations for the University of Texas System." She is affected with Lamellar/CIE.

The Foundation Offers Resource and Educational Materials

Call the National Office to order the resources that are made available for you, your child's caregivers and teachers. Materials can also be ordered through the website. Visit www.scalyskin.org and click on Kiosk to place a credit card order.

- Ichthyosis: An Overview
- Ichthyosis: The Genetics of its Inheritance
- Ichthyosis: A Guide For Teachers
- Ichthyosis: Questions Kids Ask
- Release the Butterfly: A Handbook for Parents & Caregivers of Children with Ichthyosis
- Life with Ichthyosis: A Teenage Perspective, DVD

the enzyme transglutaminase-1 that helps to build the cornified envelope, which is a barrier in the skin that protects against heat loss, water loss, and infection. The epidermis, the outer layer of the skin, consists of four different layers. From innermost to outermost, they are the basal, spinous (spiny), granular, and cornified (horny) layers. Skin cells mature as they move from the basal layer outward until they die and form the cornified layer. The transglutaminase-1 enzyme builds the cornified envelope in the upper granular layer as skin cells are changing from granular layer cells to cornified layer cells called keratinocytes. Therefore, healthy keratinocytes possess a cornified envelope.

When there are mutations in the *TGM1* gene, the transglutaminase-1 enzyme stops working properly and the cornified envelope does not develop. Enzymes are complex molecules that perform different jobs in our cells. Most enzymes, including transglutaminase-1, are proteins, which are made up of many small parts called amino acids. Sometimes mutations cause a change in one amino acid to another which prevents the enzyme from working properly. Many different mutations in the *TGM1* gene are associated with ARCI and have been reported in the scientific literature. Most (71%) of the mutations in the *TGM1* gene, which cause ARCI, result in changes of a single amino acid to a different amino acid. Our lab recently reported on 23 new mutations found in patients who were registered with the National Registry for Ichthyosis and Related Skin Disorders. Our novel mutations brought the total number of distinct mutations to 115.

The job of the transglutaminase-1 enzyme is to create a bond, called a cross-link. This cross-link holds together structural proteins, including involucrin, loricrin and filaggrin, all of which are building blocks of the cornified envelope. After these proteins are cross-linked, they are deposited on the inside of the skin cells' membrane, like insulation deposited on the inside of a house. Calcium initiates this cross-linking activity. Most (54%) of the *TGM1* mutations reside in the functional part of the enzyme that is known as the catalytic core. The other parts of transglutaminase-1 are more structural in nature. Some skin cells, which have these mutations in their *TGM1* gene, have had their transglutaminase-1 cross linking activity measured experimentally. The keratinocytes from ARCI patients with *TGM1* mutations all showed transglutaminase-1 enzyme cross-linking activity below 10% that of transglutaminase-1 enzymes taken from the cells of healthy patients.

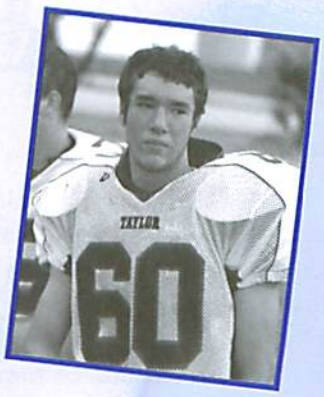
There is a lot of clinical variation in patients with mutations in *TGM1*. For instance, patients who have lamellar ichthyosis (LI) have dark plate-like scales, and patients who have NBCIE have whitish scales and erythroderma (redness). Most people with *TGM1* mutations fall into one of these two categories of ARCI. Others have variants on these two categories, one of which is called bathing suit ichthyosis (BSI), where scales develop only on the trunk and scalp. Some people are born with another variant of ARCI known as self-healing collodion baby (SHCB). These babies have a collodion membrane, which is quickly shed, and develop healthy or minimally ichthyotic skin. Mutations in *TGM1* have not been reported in patients with harlequin ichthyosis (HI), the third class of ARCI, which is associated with large dark scales that restrict movement and breathing and results from too little ABCA12 transporter (see page 8.) All of these types of ichthyoses can be inherited and first appear at birth.

In addition to reporting and classifying 23 new mutations and reviewing previous literature, we created a database, where we deposited our new mutations and those previously reported. We used the Leiden Open (source) Variation Database (LOVD) to create our own *TGM1* database. LOVD has the goal "to provide a flexible, freely available tool for Gene-centered collection and display of DNA variations" (http://www.lovd.nl/2.0/). LOVD is available to all investigators and is considerably easy to use. Patients with *TGM1* mutations can be entered into our database completely anonymously. This will allow future investigators who discover *TGM1* gene mutations to deposit them in a comprehensive list.

Finally, our group built a computer-generated three-dimensional model of the transglutaminase-1 enzyme. This model is a well-educated guess at the actual structure and was based on the known structure of a similar enzyme, factor XIIIa. The model allowed us to view the enzyme on the computer and assess the enzyme's different parts, which are called domains, including the catalytic core. With this model, we observed that a lot of the mutations that cause amino acid changes occur at the boundaries between the different domains of the transglutaminase-1 enzyme. Most of these mutations changed the amino acid arginine to another amino acid.

In summary, we investigated ARCI by reporting mutations in *TGM1*, reviewing the published literature, creating a *TGM1* database, and modeling the enzyme. Further investigations on human skin cells and animal models, which mimic ARCI, will elucidate the cellular events that lead to this rare type of ichthyosis. Classification of mutations will also help with prenatal diagnosis. Greater understanding, achieved through these types of studies and others, may lead to novel treatments.

Ichthyosis Awareness



At F.I.R.S.T., we try to cast a wide net of awareness throughout the country. We rely on our members and friends to spread the word about ichthyosis to their local communities. From time to time, affected persons are featured in their hometown newspapers, which not only educates the local readers, but shares their triumphs despite having ichthyosis. This is the case with Matt Land, a Florida teenager.

When Dave Scholl, F.I.R.S.T.'s president, was contacted by his sister in Daytona, he was excited to learn that she just read an article in the Daytona Beach News Journal about a young man with ichthyosis.

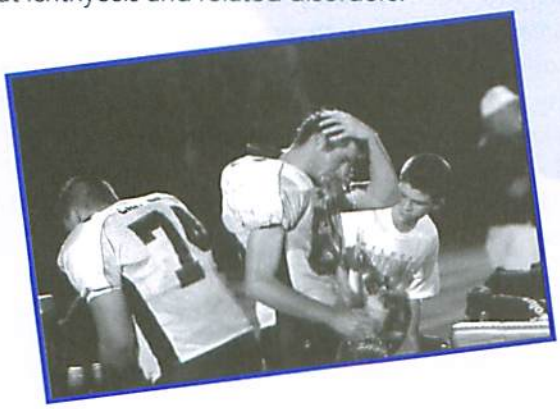
Matt Land is a senior in high school. He is a defensive lineman for the Taylor High School Wildcats. He is popular in school. He has CIE.

As a four year old, Matt was aware that he looked different from the other kids. If any of those others kids would tease him, he would tell his mother, "Mom, they're the ones with the problem, not me." As he grew, Matt approached his ichthyosis almost as a blessing. It let him know who his true friends are. Now as a senior, Matt is an active leader on his football team and looks out for the underdog.

In addition to football, Matt also holds a first-degree black belt in Martial Arts.

When Matt first started playing for Coach Doug Pettit, the Taylor High football coach, Pettit would become concerned when Matt's face reddened. He was worried that Matt was over exerting himself. The coach now understands that the overheating is part of Matt's condition and can be monitored. Matt cools down just by pouring water over himself during breaks. When he was younger, he wore a cooling vest to keep cool, but found it too constrictive.

With the completion of Ichthyosis Awareness Week, stories like Matt's remind us of the importance of creating awareness in our communities. News articles such as this are important steps toward informing the public about ichthyosis and related disorders.



A Survey About How Ichthyosis Affects Your Life!

Conducted by Emory University

In 2007, the Foundation was pleased to fund Dr. Suephy Chen, MD, MS, Principle Investigator along with Co-Investigator Mary K. Spraker, MD, for their project titled, "The Economic Burden of Cutaneous Disease in Ichthyosis Patients and Families." In fulfilling one of the aims of the project, the dermatology clinical research unit at Emory University is conducting a research study to measure quality of life and the economic impact of skin disease in ichthyosis. If you or your child has ichthyosis and would be interested in participating in the survey, please visit F.I.R.S.T.'s website, www.scalyskin.org. Click on the link "A survey about how ichthyosis affects your life!" The login ID for all study participants is "skin" and the password is "survey." Please enter your (or your child's) age during login to gain access to an age-appropriate ichthyosis survey. By your completing the survey Emory University will be provided valuable information for the ichthyosis community.

The Foundation thanks all of the generous donations that many of you have contributed over the past years. The donations are crucial for investigators to continue their important research work in the area of ichthyosis.

(Editor's note: F.I.R.S.T. awarded Dr. Traupe and Dr. Chen with grants in 2007.)

News & Notes

Insure Kids Now!

Insure Kids Now! is a national campaign to link the nation's uninsured children from birth to age 18 to free and low-cost health insurance. Many families simply don't know their children are eligible. Insure Kids Now! puts families in direct contact with their own state's children's health insurance program. Link on to their web site, www.insurekidsnow.gov/about.asp, or call the toll-free hotline 1-877-KIDS-NOW. This program is sponsored by Health Resources and Services Administration, an agency of the U.S. Department of Health and Human Services. If you have specific questions about health insurance for your children, please contact your state directly by calling 1-877-543-7669 toll-free or by going to your State Children's Health Insurance Web site.

Free Vaseline® Petroleum Jelly!

Unilever, the makers of Vaseline®, is offering a program through the Vaseline® Skin Fund. They will provide two-13 oz jars of Vaseline® Petroleum Jelly free to F.I.R.S.T. members, supplies are limited. F.I.R.S.T. will send you a preprinted postage-paid postcard; simply complete the information on the card, and mail it to the address provided. You will receive your free Vaseline® Petroleum Jelly in the mail within 24 days.

If you would like to participate in this opportunity, please call the F.I.R.S.T. office at (800) 545-3286 or e-mail us at info@scalyskin.org and we will send you the postage paid postcard.

There is a limited supply and the promotion ends on December 31, 2008 – so please hurry!

The 411 on Disability Disclosure: A Workbook for Youth with Disabilities.

The National Collaborative on Workforce and Disability for Youth (NCWD/Youth) is offering a workbook designed for youth, and adults working with them, to learn about disability disclosure. This workbook helps young people make informed decisions about whether or not to disclose their disability and understand how that decision may impact their education, employment, and social lives. Based on the premise that disclosure is a very personal decision, the Workbook helps young people think about and practice disclosing their disability.

The workbook does not tell a young person what to do. Rather, it helps him/her make informed decisions about disclosing disability, decisions that will affect educational, employment, and social lives. Download the complete guide at http://www.ncwd-youth.info/resources_&_Publications/411.html or call 1-877-871-0744.

Shade Structure Grant Applications Available

The American Academy of Dermatology's (Academy) Shade Structure Program is grant awards ($8,000 each) for the purchase of permanent shade structures designed to provide shade and ultraviolet (UV) ray protection for outdoor areas. The Academy also provides a permanent sign to be displayed near the shade structure promoting the importance of sun safety. The Academy receives support for this program from Johnson & Johnson Consumer Products Company. The deadline for the 2009 Shade Structure Program is April 10, 2009. Eligible Applicants must be 501(c)(3) organizations that serve children and teenagers, ages 18 and younger. To be considered, applicants must be sponsored by an Academy member dermatologist, demonstrate a commitment to sun safety within their organization, and agree to meet the timeline outlined on the website. Visit the link http://www.aad.org/public/sun/grants.html for an application and detailed information. Or call the AAD at 866-503-SKIN (7546).

Medical & Scientific Advisory Board

F.I.R.S.T. would like to thank the following members of the Medical and Scientific Advisory Board for the dedication and commitment they have shown to the Foundation. The Foundation is fortunate to have an elite group of nationally and internationally recognized experts in the field of dermatology on its board of medical advisors. This group of dermatologists and researchers meets annually in conjunction with the American Academy of Dermatology, serves as a referral source for members, edits publications, supplies and edits articles for the quarterly newsletter, The Ichthyosis Focus, and keeps F.I.R.S.T. and its members abreast of current research and state-of-the-art treatments for ichthyosis.

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Gaithersburg, MD
GeneDX, Inc.

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San Francisco, CA
University of California

Albert Yan, MD
Philadelphia, PA
Children's Hospital of Philadelphia

Camp Is Not Only For Kids continued from Page 10

Camper Lists Favorites about Camp Horizon

My name is Ryan Balog and I'm eleven years old from Pittsburgh, PA and I have CIE. I have been attending Camp Horizon for the past three years. I go to Camp Horizon to meet new friends and counselors with whom I communicate year round by e-mails.

I also like the idea of having my independence like when I fly without my parents or not having to shower or brush my teeth everyday (just don't tell my parents).

The following is what keeps me returning to camp year after year. These are my top favorites:

- Archery
- Fishing
- Paddle boats
- Basketball
- Riding horses
- Swimming
- Playing baseball
- Texas Hold em cards
- Rock climbing
- Arts & crafts
- Arcade room
- Knoebels Park
- Crazy hat day,
- All the kid foods like pizza and hot dogs

These are reasons I love Camp Horizon!

Editors Note: *Camp Horizon is one of the camps under the umbrella of Camp Discovery. Camp Discovery offers campers the opportunity to spend a week among other young people who have similar skin conditions. Many of the counselors have serious skin conditions as well, and can provide support and advice to campers. The camp is supervised under the expert care of dermatologists and nurses. For additional information visit the site: www.campdiscovery.org*

Donate through the United Way or Combined Federal Campaign Programs

Donating to the Foundation through the United Way or Combined Federal Campaign is an easy and convenient way to support the important work of the Foundation. A small deduction of $5.00 per paycheck can add up to over $200 per year for the Foundation. It's simple, convenient, and can really make a difference.

The United Way of America is the national organization dedicated to leading the United Way movement in making a measurable impact in every community across America. The United Way movement includes approximately 1,400 community-based United Way organizations. Each is independent, separately incorporated, and governed by local volunteers. The Foundation for Ichthyosis is the recipient of funds from many of the United Way community-based organizations. Through the Donor Choice Program, you can designate all or a portion of your donation to the Foundation. Simply write in "Foundation for Ichthyosis & Related Skin Types" on the Donor Choice Option form, and your gift will be sent to our office. Be sure to include our mailing address and phone number, 1364 Welsh Road, Suite G2, North Wales, PA 19454, 215-619-0670.

Combined Federal Campaign

The Combined Federal Campaign (CFC) is the annual fundraising drive conducted by federal employees in their workplace each fall. Federal employees and military personnel raise millions of dollars each year through the CFC to benefit thousands of non-profit charities. The Foundation is the recipient of funds from many CFC organizations throughout the country. The Foundation's CFC code is 10322, which is listed in the charitable organizations directory.

Contact your Human Resources Department to find out how you can support the Foundation using United Way or Combined Federal Campaign.

F.I.R.S.T.
Foundation for Ichthyosis and Related Skin Types

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North Wales, PA 19454

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