Eyesight is fundamental as one of our five senses to see our surroundings. Vision involves our eyes working in coordination with our brain to interpret and interact with the world around us. Critical thinking, scientific discovery and progress all require vision.

With our eyes on the keratins, a similar vision is required to more completely understand the structure and function of these proteins. Keratin 3 (KRT3) and Keratin 12 (KRT12) come to the forefront, both playing a special role in the eye as cornea-specific keratins and implicated in corneal dystrophies.

In the March 2016 issue of *Human Molecular Genetics*, Allen and colleagues sought to further investigate the pathomechanism of Meesmann epithelial corneal dystrophy (MECD) and shed light on the eye-specific keratins. They generated and phenotypically characterized a knock-in humanized mouse model carrying the severe MECD-associated K12-Leu132Pro mutation. While no alterations in corneal opacity were detected by slit-lamp examination, disorganized corneal epithelium with cell fragility and rupture of epithelial cysts at the corneal surface were revealed. Interestingly, the K12-Leu132Pro mutation caused an altered keratin profile with up-regulation of KRT6, KRT16 and KRT14 consistent with the stress response to compensate for decreased integrity of the cytoskeleton. In contrast to the human MECD cornea, KRT5 expression is decreased in the mouse genome, hypothesized to be due to a lack of a KRT3 equivalent.

Within the classical group of dominant-negative genetic disorders, Meesmann epithelial corneal dystrophy has been a focus for the development of allele-specific therapeutic siRNA. In the 2011 publication of *PloS One*, Liao and colleagues adapted the siRNA sequence walk methodology to design a potent siRNA against the mutant allele K12-Leu132Pro.

Furthermore, in the 2014 publication of *Investigative Ophthalmology & Visual Science*, Courtney and colleagues confirmed the siRNA approach as a viable treatment option within the context of an effective delivery vehicle.

True vision is key to fully realize the potential of RNA interference therapeutics for the prevention of Meesmann epithelial corneal dystrophy in addition to other keratinopathies including Epidermolysis Bullosa Simplex and Pachyonychia Congenita.

**References:**


TOPICAL SIROLIMUS UPDATE

We are pleased and excited to officially announce that topical sirolimus (TD201) for PC patients will be advancing towards its next human clinical study. TransDerm has recently partnered with Palvella Therapeutics, a Philadelphia-based company focused on relentlessly and selflessly serving individuals suffering from rare diseases (Palvella, in Finnish, means “to serve”), to rapidly advance the program. Palvella’s core competencies involve developing and commercializing novel rare disease therapies in the US, Europe, and other geographies. Many of you will have the opportunity to hear more about Palvella and meet their leadership team in the months to come.

Consistent with the goals of any initial study of an experimental therapy in a rare disease, the Phase Ib study of topical sirolimus elucidated several key learning points about the potential for this therapy in PC. The study met its primary objective of demonstrating the safety of topical administration of sirolimus cream for the treatment of painful plantar keratoderma in PC. Topical sirolimus demonstrated an excellent safety profile: there were few local and systemic adverse events, no serious adverse events, and overall the topical sirolimus cream was well tolerated.

The path forward for topical sirolimus in PC will now involve the Palvella and TransDerm teams working closely together to build upon the novel formulation developed at TransDerm and explore the potential to optimize that formulation for the benefit of PC patients. Once that analysis is complete and the FDA has been properly engaged on the status and plans of the program, topical sirolimus will be poised to enter its next clinical study, which will more thoroughly evaluate therapeutic efficacy.

Thanks to all of you for your engagement over many years to advance this promising therapy for PC patients. Success going forward will again necessitate the same extraordinary level of collaboration, and we will again aim to harness the collective wisdom and expertise to design and enroll the next clinical study.

Workshop on Rare Skin Diseases, October 20-21

The Foundation Ramon Areces has organized a workshop on Rare Skin Diseases in Madrid on October 20-21 covering five main topics:
- Keratinization Disorders
- Diseases of Dermo-Epidermal Fragility
- DNA Repair Diseases
- Ectodermal Dysplasias
- Vascular Diseases (genetic origin cancer and clinical aspects)

Registration is free. For additional information contact Fernando Larcher, PhD at fernando.larcher@ciemat.es

PC Project to Host Meetings in Madrid and Edinburgh in Oct 2016

Following the Rare Disease conference, PC Project will host a meeting for patients and researchers in Madrid, Spain. Beginning with a dinner on Friday, October 21 at the NH Naciontal Hotel, patients and researchers will enjoy presentations and discussion on Saturday, October 22 from 9am to 4pm. If interested, please email info@pachyonychia.org

The 2016 PC Patient Support Meeting will be held in Edinburgh for patients and researchers. The event begins with a dinner on Friday, October 28 with presentations from major leaders in PC research throughout the day on Saturday and one-half day on Sunday. Registration is required. If you are interested in attending, please email info@pachyonychia.org.
RECENT PUBLICATIONS


suggested a link between skin blistering and atopic disease. J Allergy Clin Immunol. 2016 Jun
15


Cindy Byers Atha is a Healthcare Executive with a 26-year history of Commercial experience in a series of increasingly responsible Sales and Marketing roles at Atossa Genetics, Depomed, Inc., and Amylin Pharmaceuticals, innovative biotech/biopharmaceutical companies, as well as AstraZeneca, one of the world’s leading pharmaceutical companies. She most recently was the Vice President of Sales and Marketing at Atossa Genetics where she led commercialization efforts for pharmacogenomic testing and medical devices for Breast Health. Previously, she was Vice President of Managed Markets and Trade with Depomed overseeing Managed Care Sales and Marketing, Pricing, Contracting, Trade, and Distribution. While at Depomed, her team was recognized by Healthcare Distribution Management Association (HDMA) as 2014 DIANA Winner for Best Manufacturer and while performing a similar role at Amylin, her team was twice recognized for “Best Marketing Programs and People” for a small manufacturer and achieved the 2012 DIANA Award for best new product introduction. Ms. Atha began her pharmaceutical career in field sales with Merck & Co. and then moved to AstraZeneca where she advanced into Senior Sales Leadership. She was the recipient of more than 16 sales awards for exceptional individual and group performance and AstraZeneca’s highly prestigious “Leadership Excellence Award” and "Global Challenge Award." She helped bring over 16 new pharmaceutical products to market. Early in her career, she was recognized by several key healthcare clients as the best account representative in the industry. She gained formative experience as an Account Executive with Scientific Technologies, promoting the sale of research and medical equipment to leading biotechnology companies and medical centers.

Ms. Atha also serves on the Board of Directors for Operation of Hope, a non-profit organization that provides facial reconstructive surgeries to poor children around the world. She is a member of the Academy of Managed Care Pharmacy and a volunteer mentor for BoomStartup. She received her Bachelor of Science in Zoology from North Carolina State University in Raleigh, North Carolina. She and her husband William reside in Salt Lake City, UT.

**PC ADVOCATES TRAINING**

Beginning with eight patients in the USA, PC Project has begun a program to educate, inspire and involve patients as advocates in their own communities.

Ten patients from England, Finland, France, Germany, India, Spain, The Netherlands and Wales are completing webmeeting training sessions and will meet in Edinburgh just prior to the Patient Support Meeting for an in-person training session with IPCC leaders.