so-called "natural moisturizing factors"). One person in 90 is homozygous for the profilaggrin mutations and has a nearly 90% risk of developing atopic dermatitis, in addition to having ichthyosis vulgaris. The implications of these findings are huge, especially as heterozygous profilaggrin mutations can work as a disease modifier in many other conditions where the skin barrier is at stake.

Epidermolysis bullosa (EB) is a research field of intense activity, not the least since the report in 2006 from an Italian group about successful gene therapy in a patient with junctional (non-Herlitz) EB. In an excellent lecture, *Dr Leena Bruckner-Tuderman*, Freiburg, Germany, discussed disease mechanisms, particularly in the context of dermal atrophy in dystrophic EB and Kindler's syndrome, nicely demonstrating the importance of cross-talk between epidermal and dermal cells.

Dr Jouni Uitto, Philadelphia, USA, after receiving the prestigious Al Kligman Award, which he generously donated to dermatological research, subsequently dissected the importance of connecting molecules in and around the basal membrane zone, which are not only incriminated in various forms of EB but can also be antigens targeted in autoimmune blistering diseases.

Autosomal recessive congenital ichthyosis (ARCI) was the focus of many poster presentations, especially concerning the possibility of recapitulating disease mechanisms in vitro using various knock-down models and siRNA probes against the candidate gene. These models will enable new therapies to be tested in vitro without having to expose patients to potentially risky drugs.

Last, but not least, at a very memorable occasion during the meeting our Danish colleague, *Professor Kristian Testrup-Pedersen*, was awarded honorary membership of the ESDR for his lifetime contribution to dermatological research. Congratulations Kristian!

We are now all looking forward to the next IID meeting, which will be held in Edinburgh in 2013.

International Investigative Dermatology Meeting in Kyoto, Japan, 14–17 May 2008

Sirkku Peltonen
Department of Dermatology, University of Turku, Finland. E-mail: sirkku.peltonen@tyks.fi

Sirkku Peltonen gives some of her views from the International Investigative Dermatology Meeting in Kyoto, Japan.

Sister societies, the European Society for Investigative Dermatology (ESDR), the Society for Investigative Dermatology (SID) from the USA, and the Japanese Society for Investigative Dermatology (JSID) held their fifth joint meeting in the Kyoto International Conference Center, on 14–17 May 2008. The centre is famous for the Convention on Climate Change and Kyoto Protocol, which was signed in the main hall. At first sight the conference building, which has an unusual hexagonal framework and few vertical walls or columns, reminded the youngest conference participants of a science fiction film; however, it proved a most convenient venue to host a meeting of 1530 participants and 1350 posters. The conference centre is beautifully located alongside the small lake Takaragaike and a creek running from the lake. Reflecting ponds for swan, ornamental carp in various colours and turtles lie alongside the stairs of the building. Although the cherry blossom season was over, azaleas with pink and fuchsia-coloured flowers still lined the paths. The weather was sunny and warm, with the promise of a hot and humid summer season to come.

A vast meeting always has numerous interesting simultaneous symposia to choose from. The best parts of this meeting were in my opinion however, the special lectures of each Society. The series of special lectures opened with the JSID Tanioku Kihei Memorial Lecture, given by *Paul Khawari* from Stanford University, USA, entitled: Multi-functional genetics in human tissue: an emerging experimental paradigm for experimental dermatology. In his talk Khawari defined the term multi-functional genetics to mean the introduction of multiple genetic elements into primary human cells. According to him, primary human cells with defined genetic alterations made by genetic engineering have the potential to answer specific questions

Fig. 1. The fifth International Investigative Dermatology (IID) meeting took place in the Kyoto International Conference Center, which opened in 1966. The building has few vertical walls or columns.

about cell function better than widely used, immortal cell lines, which often differ widely genomically, have missing or amplified pathways, and thus may give contradictory or false results. His model of primary human keratinocytes cultured on top of fibroblasts would allow more than eight simultaneous genetic alterations. The cell culture system of grafting artificial skin in mice also provides a rapid system for testing antibodies, drugs and RNAinterference (RNAi) oligos, compared with the time-consuming construction of genetically engineered mouse models. According to Khawari, there are six recognized cardinal cancer processes, which include Ras/ erk, G1 CDK and MAPK. He has shown that one gene is sufficient to induce all the cardinal features of basal cell carcinoma in human skin, and only two or three genes are needed to induce squamous cell carcinoma and malignant melanoma. Using known genetic elements it is possible to produce cancers, for example, basal cell carcinoma, squamous cell carcinoma or melanoma, from normal primary cell lines. The critical steps of cancer treatments should target the known critical signalling pathways, cellular biosynthesis, mitosis and cell-matrix interactions.

The SID Albert M. Kligman/Philip Frost Leadership Lecture was given by *Jouni Uitto* from Thomas Jefferson University, USA. His topics included the structure and function of the skin, lessons from heritable diseases, and leadership in dermatology. Epidermolysis bullosa (EB) served as his model disease. The picture of EB appears to be complete, since mutations in ten different genes are known to cause this condition. A total of 783 distinct mutations in 1008 families have been characterized at Thomas Jefferson University. Now that the molecular basis of EB has been elucidated, it is time to concentrate efforts on finding therapies for these diseases. Uitto reviewed various gene therapy options that have been attempted in EB. These approaches included culturing of keratinocytes, followed by skin transplantations, gene correction using viral vectors and protein replacement therapy, which means introducing missing protein component into cells. For example, the laminin beta 3 chain imported into the cells is incorporated into laminin molecules by the cells. Cell-based therapies using fibroblasts have been tried in recessive dystrophic EB. The most recent newcomer is hematopoietic stem cell therapy. These modalities are discussed in more detail in the conference report from the Scandinavian EB congress in this issue. In his talk Uitto also touched on the issue of leadership in education, pointing out the importance of mentoring residents, research fellows and research juniors in the laboratory. He showed an impressive "Olympic march" of the research fellows who have been working in his laboratory over the past decades.

The ESDR Rudi Cormane lecture was given by *Leena Bruckner-Tuderman* from Freiburg, Germany, on the topic of skin fragility. She emphasized the two roles of the dermal-epidermal junction: structural function and signalling functions. The structural function is well known, while the signalling functions includes constant cross-talk between epidermis and dermis over the basement membrane via messengers that are soluble or bound in the basement membrane or extracellular matrix. Fibroblasts can also differentiate to myofibroblasts and communicate with the epidermis. Alterations in this relationship lead to consequences seen in the bullous diseases: poor wound healing, fibrosis, hair defects, atrophy, and mucosal involvement. Studying and observing the clinical phenotypes also helps in understanding these mechanisms. Leena Bruckner-Tuderman used Kindlin syndrome and type VII collagen mutations as examples. More detailed information is given in the conference report from the Scandinavian

EB congress. Knowledge of the molecular disease mechanisms and of normal physiological functions are essential in the search for therapeutic targets and design of biologically valid treatments. She also stressed the importance of international collaboration in the search for therapies.

The SID Eugene M. Farber Lecture, Psoriasis co-morbidity and chronic inflammation, was given by *Enno Chistophers* from Kiel, Germany. Psoriasis has been recognized as a potentially severe disease with various associated illnesses. An increased risk of myocardial infarction is associated with psoriasis, independent of other known risk factors such as metabolic syndrome. Accelerated atherogenesis is known to be associated with inflammation and magnitude of inflammation, e.g. in arthritis, correlates with the number of inflamed joints. The concept of inflammation-driven atherogenesis, especially in combination with obesity, may be true also in psoriasis. Some of the mechanisms have already been revealed: triglyceride overload leads to cytokine production. Exposure of vascular endothelial cells to increased cytokine concentrations IL-1, IL-6, and TNF-α results in dysfunction of the endothelium. Losing weight leads to decreased IL-6 and TNF-α levels. Important players in the process seem to be Th17 cells, which are responsible for secreting the cytokines, especially IL-17 and IL-22. IL 22 is mitogenic for keratinocytes and IL17 activates early phase reactants, such as C-reactive protein (CRP). It was shown recently that impaired Th17 cells are almost absent in subjects with hyper-IgE syndrome.

Many psoriasis patients carry two types of risk factors: traditional risk factors, such as obesity; and non-traditional risk factors, cytokines, that facilitate the atherosclerosis. Together, the risk factors lead to insulin resistance, hyperinsulinaemia and hypertriglyceridaemia and, furthermore, to atherosclerosis.

The ESDR Renee Tourane lecture, The filaggrin pathway – journey from the keratins to atopic dermatitis, was given by *Irwin McLean* from the University of Dundee, UK. He reviewed present knowledge about keratins, their genes and keratinizing diseases. To date, 54 keratins are known and 22 of them have been linked to genetic disease. McLean's research group has recently concentrated on filaggrin and its mutations. Filaggrin is a filament-aggregating protein in epidermal keratinocytes. It is synthesized as an over 400 kDa profilaggrin, which is processed to 37 kDa filaggrin. The filaggrin gene is a large and highly repetitive gene on 1q21.3, which was difficult to clone. Since its cloning, mutations in filaggrin gene have been found in patients with ichthyosis vulgaris and atopic dermatitis. According to McLean, up to 1 in 7 people of European origin carry one filaggrin null mutation, meaning that they have only 50% of the normal amount of filaggrin. This leads to dry skin and/or mild ichthyosis vulgaris, and a high risk of atopic dermatitis. Of those persons with one filaggrin mutation, approximately 40% have atopic dermatitis, while persons with two filaggrin mutations have over 95% penetrance of atopic dermatitis. Almost 40 loss-of-function mutations have been found so far, and studies on atopic dermatitis have shown that approximately half of the 262 atopic children studied carry one or more of the known filaggrin mutations. Thus, in the background of atopic dermatitis barrier defect, sensitive immune system and environmental triggers overlap.

The programme book of the International Investigative Dermatology (IID) meeting, containing abstract titles, is available at: http://www.esdr.org/pdf/IID2008program.pdf.

The abstracts have been published in the Journal of Investigative Dermatology (JID): http://www.nature.com/jid/journal/v128/n1s/pdf/jid200893a.pdf.

Fig. 2. The start of the outdoor conference dinner. Ponds with carps, turtles and swans lie next to the stairs of the conference centre.