the scientific programme, talked about everyday paediatric dermatology in Sweden. At the end of the meeting there was time for sightseeing in Gothenburg before participants returned home.

In the same week, one of the participants, *Dr Lyudmyla Derevyanko*, Kiev, Ukraine, also gave a highly appreciated lecture, at the Department of Dermatology, Sahlgrenska Hospital, about congenital syphilis, of which most Swedish dermatologists have limited experience. Dr Derevyanko also mentioned that she was a little early for the 300-year celebration of a Swedish-Ukranian coalition in 1709 during the reign of Karl XII (before the battle of Poltava).

One lasting impression is what a difference there is in the conditions for performing clinical work between our different countries, so close and yet so far apart, while at the same time many problems are similar. E-mail addresses were exchanged and, in a collegial and generous atmosphere, everyone committed themselves to future collaboration and contact.

We believe that this is a fruitful way of getting closer, learning more of, and from, each other and making new friends. It is hoped that we will be able to organize similar small meetings in other fields of dermato-venereology. The meeting was organized by the SSDV Foundation for International Dermato-Venereology with economic support from the Eastern Europe branch of SIDA.

FIg. 1. From left: Sanita Sigure, Latvia; Anne-Marie Ros, Sweden; Maria Karlsson, Sweden; Volodymyr Dzyubak, Ukraine; Lyudmyla Derevyanko, Ukraine; Ewa Voog; Sweden; Matilda Bylaite, Lithuania; Gunnar Nyman, Sweden; Ann Broberg, Sweden; Ama Lehtmets, Estoni; Terje Kukk, Estonia; Marcis Septe, Latvia; Sara Oldberg Wagner, Sweden; Ramune Jurciukonyte, Lithuania; Mårten Walhammar, Sweden. Not in the picture: Maria Böhme, Torbjörn Egelrud, Ylva Linde, Filippa Nyberg and Karin Rosén, Sweden.

Impressions from the International Investigative Dermatology 2008 Meeting in Kyoto

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Anders Vahlquist was one of many dermatologists from the Nordic countries to visit the International Investigative Dermatology Meeting in Kyoto. This is his impressions of the meeting.

Every 5 years, the dermatological research societies in America (The Society for Investigative Dermatology; SID), Europe (European Society for Dermatological Research; ESDR) and Japan (The Japanese Society for Investigative Dermatology; JSID) co-organize a large scientific meeting, International Investigative Dermatology (IID), which this year was held in Kyoto. The meeting attracted almost 2000 participants from all over the world. Over four days and in numerous satellite symposia nearly 1400 scientific contributions were presented, including many invited guest lectures. Since it is impossible to cover all aspects of the meeting here, my report will focus on itch, chronic allergic inflammation and genodermatoses.

News on itch

At the start of the symposium on itch, *Dr Martin Schmelz*, the German discoverer of the histamine-sensitive itch-selective neuron, covered the neurophysiological aspects of itch. The idea of two separate neuronal systems for pain and itch is in accordance with the antagonism that scratch-induced pain

can abolish itch, and analgesic opioids can generate itch. However, the distinction between pruriceptive and nociceptive stimuli is not as simple as it may at first appear. For example, histamine injected into skin in high doses will provoke pain rather than itch. Furthermore, numerous itch mediators other than histamine (e.g. prostaglandin E2 (PGE2), thromboxane and various proteases) explain itch associated with eczema, polycytemia vera and psoriasis, whereas external itch associated with cowhage (Macuna pruriens) depends on release of intensely prurigenic enzymes by the spicules of the plant. Moreover, neuropathic changes in the peripheral nerves can be linked either to pain (as in post-herpetic neuralgia) or to itch (as in brachioradialis pruritus).

Dr Glenn Giesler, Minnesota, USA, discussed central nervous system (CNS) perception of itch signals, which are processed in the spinothalamic tract (STT). Surprisingly, their results indicate that almost entirely separate populations of STT neurons code for pruritic responses to histamine and cowhage, respectively. The pruritic responses of several neurons were inhibited by scratching the receptive field, suggesting that the reduction in itch sensation produced by scratching results from inhibition of pruriceptive STT neurons.

Dr Paul Bigliardi, Lausanne, Switzerland, discussed the role of opioid receptors in the skin and CNS on pruritus. Based on clinical observations and experiments on opioid receptor knockout (KO) mice, they were able to redefine the role of opioid receptors in skin as regulators of chronic itch. Epidermal hypertrophy caused by chronic irritation and the amount of epidermal nerve endings in KO mice were significantly decreased compared with wild-type controls. Furthermore, KO mice scratched significantly less than wild-type controls. These results are supported by double-blind placebo-controlled studies in man using topically applied opioid antagonist and established the clinical relevance of the cutaneous opioid receptor system in itch control (independent of histamine and mast cells). It also underlines the importance of the interaction between skin cells and the peripheral nervous system in both itch and pain sensation. In addition, opioid receptors can regulate the transmission of the itch signal to the CNS and modulate the sensation in the brain. It seems that opioid receptors activate inhibitory circuits in the CNS and regulate the extent of intensity and quality of perceived itch.

Dr Akihiko Ikoma, Kyoto, Japan, discussed itch in patients with atopic dermatitis who are generally itch-sensitive, meaning that they easily feel itch by various non-itchy stimuli. It has been demonstrated that even painful stimuli, which normally suppress itch, also induce itch in patients with atopic dermatitis. Itch sensation makes algogens, such as bradykinin, work as pruritogens, indicating that countless inflammatory mediators might have to be targeted in anti-puritic therapies of atopic dermatitis.

In an extension to this, *Dr Gil Yosipovitch*, Wake Forest, USA, showed interesting positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) data from humans. In chronic itch, they demonstrated significant differences in brain imaging of non-sensory cortical area involved in itch between patients with atopic dermatitis and healthy subjects. New studies were presented assessing the effects of

Fig. 1. The 5th joint meeting of JSID, SID and ESDR in Kyoto.

the fundamental behaviour response to itch, i.e. scratching, on brain activity. Defining neuron networks responsible for chronic itch in the brain will identify potential therapeutic targets and thus is of great clinical relevance.

News on chronic allergic inflammation

As a nice complement to the symposium on itch, Dr Hajime Karasuyama, Tokyo, Japan, gave a lecture on the responsible cells and causative agents in chronic cutaneous allergic inflammation. He has recently shown that basophils play an important and non-redundant role in vivo and are responsible for the development of IgE-mediated chronic allergic inflammation, independently of T cells and mast cells. A single subcutaneous injection of multivalent antigens elicited not only immediate- and late-phase ear swelling, but also delayed-onset (starting on day 2 post-challenge) ear swelling with massive eosinophil infiltration in mice sensitized with antigen-specific IgE. Mast cells and T cells were dispensable for the delayed phase, which was inhibited by cyclosporine but not by anti-histamines. The treatment of mice with basophil-depleting monoclonal antibodies completely abolished the development of the delayed-onset inflammation and suppressed the on-going dermatitis. In response to the antigen stimulation, basophils secreted a panel of cytokines that stimulated other cells to produce chemokines necessary for recruitment of inflammatory cells such as eosinophils and neutrophils. These findings indicate a novel mechanism of development of chronic allergic inflammation that is induced by basophils through the interaction of antigen, IgE and FceRI. This also implies that basophils could be good therapeutic targets in chronic allergic inflammation such as atopic dermatitis.

Hyper IgE syndrome (HIES, also called Job's syndrome) is a rare congenital immunodeficiency syndrome that combines severe eczema with recurrent staphylococcal skin infections that lack the features of typical inflammation and therefore are called "cold abscesses". The clinical manifestations in HIES extend over multiple systems in the body including the immune system, skeletal/dental system and soft tissues. The Japanese group has recently identified tyrosine kinase 2 (Tyk2) as a gene causative of the autosomal recessive form of HIES and signal transducer and activator of transcription 3 (STAT3) as a gene causative of the autosomal dominant and sporadic forms of HIES. Both Tyk2 and STAT3 are involved in the signal transduction for multiple cytokines including IL-6, IL-10 and IL-23. Thus, Tyk2 and STAT3 mutations found in HIES patients result in defects of multiple cytokine signals, accounting for complex clinical manifestations in HIES patients. It is fascinating to see how under-function of the STAT-pathway explains Job's syndrome, whereas over-activation of this pathway is typically found in psoriasis.

News on genodermatoses

A significant part of the contributions was devoted to recent discoveries about the aetiology and treatment of genodermatoses. First on the agenda was pachyonychia congenita (PC), a rare disease characterized by thick nails and mucocutaneous problems. Despite the name of the disease, patients with PC often suffer more from painful calluses and blisters of the feet than from thick nails. PC was ventilated in a satellite symposium arranged by a consortium, headed by *Ms Mary Schwartz* and involving many top scientists in the field of keratin research. Dominant negative mutations in keratins K6a, 16 and 17, normally implicated in wound healing, underlie this disorder. Intriguingly enough, the disease-causing allele can be specifically silenced by small interfering RNA (siRNA) probes, which bind to the mutated mRNA sequence without affecting the wild-type allele, thus preserving an intact function of the keratin in question. The first human trial of siRNA ever performed in a skin disease was reported by *Dr Sancy Leachman*, Salt Lake City, USA, who intradermally injected RNA probes specific for the most common K6a mutation, a procedure which reduced hyperkeratosis and pain of the treated foot lesion. Time will tell whether the siRNA approach is also safe and efficient in the treatment of more extensive skin lesions, in PC and other dominant negative genodermatoses. In the meantime, more readily available symptomatic treatments should be considered. For example, injection of botulinum toxin (Btx) to prevent sweat-induced worsening of foot blisters associated with PC and epidermolysis bullosa simplex (EBS), also caused by a dominant keratin mutation, appears to be very effective. Our own 7 years of experience with Btx-injections repeated 2–4 times yearly in 14 patients with PC or EBS were reported at the meeting. Approximately 70% of patients have a marked reduction in foot pain and blistering, but regional anaesthesia and deep intradermal injections of Btx are needed to obtain good results (Swartling et al., forthcoming).

In a splendid plenary lecture, *Dr Irvine McLean*, Dundee, UK, reviewed the pathogenic role of keratin mutations and discussed new approaches to therapy of these disorders, such as natural compounds from broccoli (!), which can up-regulate complementary keratin expression. He also described the "filaggrin story", which has relevance not only for the understanding of ichthyosis vulgaris, but also opens up new horizons in the understanding of atopic dermatitis and dry skin. In many populations worldwide, 1 out of 7 persons carries at least one mutated profilaggrin allele (i.e. they are heterozygous for a mutation inherited from one of the parents). This is associated with a 40% lifetime risk of developing eczema, probably due to a partially deficient skin barrier, which enables allergens to penetrate the skin, and to a dry skin due to a lack of filaggrin breakdown products (the

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

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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