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ABSTRACTS

Editors:

P. ARENBERGER, C. M. BETTS, D. BREITKREUTZ, J. McMILLAN, F. PRIGNANO, S. STÄNDER, K. WOZNIAK, W. MUSS

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[1]Department of Dermatology, Keio University School of Medicine
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[1]Experimental Pathology Department, Bologna University, and [2]Department of Dermatological Sciences, Florence University, Florence, Italy

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J Dahlqvist[1], J Klar[1], I Hausser[2], I Anton-Lamprecht[2], M Hellström Pigg[1], T Gedde-Dahl Jr[3], A Ganemo[4], A Vahlquist[4], N Dahl[1]
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Footnote:

1 **The whole Final Programme can be found at:**
http://orgs.dermis.net/content/e04scur/e03meetings/e775/e985/index_ger.html
or visit http://www.scur.org **and click "Meetings" and the sublink: >Previous Meetings<**

ORAL PRESENTATIONS

O 1

Cell adhesion and apoptosis after γ-rays in human skin

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Skin is a target organ for crucial side-effects of routine radiotherapy. The pathophysiology of the cutaneous radiation reaction is for many aspects still unknown and the early effects on epidermal compartment remain to be fully elucidated. Organotypic cultures of normal human breast skin can help in defining the immediate radiation response otherwise difficult to study in human volunteers. Using this experimental model, we reported a significant inhibition of epidermal proliferation 24 hours after the exposure to a single dose of ionising rays (Donetti *et al.*, 2005). In the present study we evaluated the early radiation effect on intercellular adhesion and apoptosis. Bioptic fragments ($n = 8$) were obtained from cosmetic surgery of young healthy women, cultured epidermal side up in Transwell, and harvested 24 or 48 hours after exposure to a single 2 Gy dose of γ-rays. Samples were processed for transmission electron microscopy and immunofluorescence to investigate desmoglein (Dsg1) and p53 expression. Throughout the epithelial compartment, Dsg1 distribution pattern was similar in all non-irradiated and irradiated samples. Preliminary observations indicated that no desmosomal ultrastructural modifications occurred, suggesting that intercellular adhesion is not yet affected. At 24 hours, in both irradiated and non-irradiated samples p53 immunofluorescence was similarly detected in scattered positive keratinocytes in the spinous layer. At 48 hours, p53 was expressed starting from basal layer, with a slight p53 staining increase in irradiated samples. Our results can help in improving the knowledge of regulatory processes as a major prerequisite for radiobiological rationale effective interventions.
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O 2

Inducible activation of the hedgehog pathway by Gli-1 or Gli-2 expression in the human keratinocyte line HaCaT, growing in skin-organotypic coculture

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Transcription factors of the hedgehog (Hh) pathway like Gli-1 and Gli-2 are involved in basal cell carcinoma (BCC) formation (deriving mainly from hair follicles). To elucidate the role of Gli-1 and Gli-2, human keratinocytes (HaCaT-cells) were transfected with inducible vectors harboring either factor (Tet-on system). In conventional culture these HaCaT-variants over-expressed either Gli-1 or Gli-2 upon tetracycline (tet) treatment. In both tet-induced cultures proliferation increased and differentiation was repressed, abolishing the markers keratin 10 (K10) and filaggrin (immuno-fluorescence, IF). Mimicking skin physiology, cells were grown in three-dimensional skin-organotypic coculture (with dermal fibroblasts). Without Gli-induction stratified, regularly differentiated epithelia developed (IIF) like in normal HaCaT-controls. Upon Gli-induction epithelial thickness was largely reduced initially, though cells, densely packed, increased in number (nuclear staining), while epidermal differentiation was blocked. Accordingly, K10 was largely and loricrin completely absent, filaggrin appeared weak and irregularly distributed. Conversely, the 'simple epithelial-type' keratins K8/18 were strongly upregulated by both Gli-factors. Components of the basement membrane zone (nidogen, laminin, integrin α6β4) revealed no visible differences (IIF). With a pronounced delay (four weeks) some invasive growth (mainly Gli-2 mediated) into the 'dermal' part of cocultures was observed, suggesting crosstalk with the fibroblasts. This was underlined by matrix metalloprotease 1 (MMP1) expression which revealed a complete shift of MMP1 mRNA (*in situ* hybridization) from the basal HaCaT-cells to adjacent fibroblasts, individually presenting also myofibroblast markers. Collectively, epidermal differentiation is repressed by activation of the Hh pathway, resembling a BCC phenotype, and the enforced Gli-expression may provoke invasive growth in these 3D-cocultures.
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O 3

Immunohistochemical and ultrastructural studies in a patient with a Kindler syndrome-like disorder

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Kindler syndrome is an autosomal recessive genodermatosis characterized by trauma-induced acral skin blistering from infancy, photosensitivity, generalized poikiloderma, and diffuse cutaneous atrophy. Mutations in the *KIND1* gene that encodes for the focal contact-associated protein kindlin-1 have been identified in several patients although the spectrum of clinical abnormalities is protean and genetic heterogeneity is plausible. A 32-year-old Japanese male, born to consanguineous parents, presented with acral skin blistering, cutaneous atrophy, palmoplantar thickening, finger contractures, absence of dermatoglyphics, and nail dystrophy. He also had leukoplakia of the tongue but did not report photosensitivity or show signs of poikiloderma. A biopsy taken from bullous atrophic skin on the dorsal surface of his left hand showed sub-epidermal blistering, vacuoles within basal keratinocytes and immunohistochemical evidence of basement membrane reduplication. Intensity of Kindlin-1 expression in patient skin was indistinguishable from that in normal skin. Electron microscopy demonstrated multiple tubulo-vesicular structures and electron dense amorphous keratinocyte-derived material immediately below the dermal-epidermal junction. Mutational analysis of the *KIND1* gene failed to identify any pathogenic mutation(s). Although this patient's clinical and skin biopsy features appear to match the clinico-pathological criteria for a diagnosis of Kindler syndrome, no mutation in *KIND1* was detected. This suggests genetic heterogeneity in this genodermatosis or perhaps the existence of a subset of patients that have a distinct but currently unclassified related inherited disorder. Identification of similar patients and characterization of this Kindler-like syndrome is expected to provide new insight into clinical disorders associated with structural pathology within the cutaneous basement membrane zone.
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O 4

Merkel cell carcinoma diagnosed by EM on formalin-fixed tissue

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A 56-year-old woman was referred to us for treatment of a skin tumor involving her right lower leg with a 2-year history of tumor growth. A nodule on her right lower leg which developed two years before gradually enlarged. The nodule was red to black coloured and measured approximately 3 cm × 3 cm × 1 cm. Biopsy of the lesion showed proliferation of small and round cells with numerous scattered mitoses, indicating malignancy. Patient otherwise was healthy, and neither physical examination nor systemic investigations including laboratory tests and CT scans of the body revealed any signs of lymphnode or distant metastasis. The lesion then was excised with a resection margin of 2 cm with the defect covered by skin graft. Pathologic examination of routinely stained sections revealed that the dermis was invaded by a tumoral proliferation made up of round, uniform cells with large, hyper chromatic nuclei with surgical margin negative. Immunohistochemically, tumor cells were positive for CD56, VS38c, Ki-67, MIC2 and vimentin. But the stains by AE1 + AE3, CK20 chromogranin, synaptophysin and neuronspecific enolase were negative. Since these results were not enough to reach a diagnosis, an electron microscopic study was performed from formalin-fixed tissue specimens. It showed dense core granules in the cytoplasm and cell surface projections. The diagnosis of merkel cell carcinoma was finally confirmed by electron microscopic study. The patient received adjuvant local radiation therapy. Formalin-fixed tissue yet to be embedded in paraffin still keeps a good ultrastructure and we would like to emphasize the importance of EM study in diagnosing cases undetermined by immunohistochemistry.
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O 5

Cutaneous Metatypical Carcinoma

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Metatypical carcinoma (MTC) is a controversial entity that presents itself as a microscopic pathway of both basal and squamous cell carcinoma. We recognized two types of histopathological patterns: a mixed and an intermediary one. The mixed type is composed of different cells: basaloid cells, which are larger, paler and more rounded of the cells of a classical basal cell carcinoma; squamoid cells with copious eosinophilic cytoplasm; in some cases it is possible to find some areas composed of cells presenting an intermediate differentiation. The intermediary type is composed of nests and strands of cell maturing into larger and paler cells. As a distinctive feature, there is a large amount of spindle-cells. Peripheral palisading is often lost, and the stroma is prominent. The World Health Organisation's (WHO) histologic classification of skin tumours (Geneva, 1980) was the first to classify this new nosologic variety of skin carcinoma, which is typically located on the face, and often resembles clinical features of basal cell carcinoma (BCC) but tends to be more aggressive with the possibility of lymph node or distant metastases. We presented a retrospective study to better define the clinical and histopathological feature of this neoplasm.
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O 6

A recycling endosome marker Rab11 is associated with epidermal lamellar granules

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Epidermal lamellar granules (LGs) are specialized organelles that transport and secrete various molecules, including lipids, proteases, protease inhibitors and structural proteins, thereby providing a protective barrier against the environment. Abnormalities in LG-related molecules result in severe skin diseases, but their transport mechanisms are poorly understood. We studied the distribution of Rab11, a common GTPase in recycling endosomes, in normal human epidermis. Confocal laser scanning microscopy detected Rab11 immunoreactivity in differentiated epidermal keratinocytes. Staining was strong at the apical side of each cell, a pattern commonly seen in LG-associated molecules. Around the nuclei, Rab11 was colocalized with TGN46, a trans-Golgi network marker. Rab11 was also colocalized with known LG-molecules, namely LEKTI, corneodesmosine, cathepsin D and glucosylceramides. Immunoelectron microscopy revealed that Rab11 was widely distributed along TGN and tubular-vesicular structures containing different LG molecules. The present results suggest that Rab11 plays a role in the intracellular trafficking of various types of LG-molecule from the TGN to the cell surface. Based on the structural similarity between LGs and recycling endosomes in other cells and the present demonstration of strong Rab11 expression around LGs, we hypothesized that LGs are modified recycling endosomes specifically developed in the epidermis.
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O 7

A genetic and ultrastructural study of Tietz syndrome

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Tietz syndrome is an extremely rare genetic disorder characterized by generalized hypomelanosis and complete nerural deafness. Only two families were reported so far and mutations in the microphthalmia-associated transcription factor (MITF) gene have been described in each family as a cause of the disease. A 24-year-old Japanese female, who was a product of non-consanguineous Japanese parents, was referred to our hospital for evaluation of generalized hypopigmentation, and pigment flecks. She had a congenital hearing loss. Her skin was white and small pigment flecks were seen on sun-exposed area that began to develop at the age of three. Her hair was gray and her eyes were blue. Nystagmus and other ocular abnormalities were absent. A dopa reaction test using hair bulb was positive. A skin biopsy from the hypopigmented region revealed that melanocytes were present in normal density and distribution but adjacent basal keratinocytes contained little melanin. Electron microscopy of the melanocytes showed stage I to IV melanosomes with irregularity in size and shapes. The direct sequencing of the MITF gene of the patient revealed heterozygous 3-bp in-frame deletion in exon 7 leading to a single amino acid deletion, delR217, which was identical mutation to that of a previously reported family. Our study indicates that, out of the two major roles of MITF, the development/maintenance of melanocytes and the regulation of melanin biosynthesis, the latter role may be more sensitive to the abnormality of MITF protein in Tietz syndrome.
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O 8

Melanoma cells circulating in peripheral blood

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Monitoring of melanoma cell levels in peripheral blood of melanoma patients is a promising method for haematogenous melanoma distribution. The method enables us to detect early metastasis and to better stratify candidates for adjuvant immunotherapy procedures. Inconsistent data on the sensitivity and clinical relevance of this method have been previously reported by several groups. In the present work the development of multimarker real-time RT-PCR for quantification of 5 melanoma markers could be shown. Following markers were detected: Melan-A, gp 100, MAGE-3, MIA and tyrosinase. In the described prospective study 65 patients with resected cutaneous melanoma stage IIB-III were screened. Samples of peripheral blood were collected every 3 months for the following 18 months and circulating melanoma cells were examined and compared with clinical staging methods. In 18 patients a relapse during the trial was observed and members of this subgroup showed different types of melanoma progression. In all of these patients statistically significant tumor marker elevation in the period from 0 to 9 months before the disease progression was measured. MAGE-3 was here the most sensitive progression marker. In patients with progression 3 concordant positive markers in 39 percent of cases, 2 concordant positive markers in 28% and finally 1 marker in 33% was observed. The present study describes a multiple marker real-time RT-PCR which is able to provide quantitative data on melanoma markers in the peripheral blood of melanoma patients. Quantitative measurement of the studied molecular markers represents an excellent prognostic factor and a useful and reliable method for early detection of metastasis and treatment response of melanoma subjects.
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O 9

Ultrastructural and molecular study in two patients with bullous congenital ichthyosiform erythroderma

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We report two sporadic cases with bullous congenital ichthyosiform erythroderma presenting different courses of the disease. First patient is a 16-months-old girl born in full term from non-consanguineous healthy parents who presented at the birth generalized blisters and erosions accompanied by Nikolsky's sign. At the beginning of the third month of life the patient developed slight hyperkeratotic plaques on erythematous base localized on extensor surfaces of the forearms and calves and on the lower abdomen. While patient was 6-months-old she developed hyperkeratotic plaques and prominent palmoplantar keratoma (PPK) whereas blisters appeared occasionally. After 15-months of life blisters stopped to appear and hyperkeratotic scales dominated in the clinical picture. Second patient is a 24-month old girl born in full term from non-consanguineous healthy parents who presented at birth with disseminated blisters and erosions which ceased at the age of 16 months of life. At the beginning of third month of life the patient developed hyperkeratotic plaques on erythematous base localized on extensor surfaces of the forearms and on the lower abdomen. PPK has never been observed. Histopathology performed in both patients showed hyperkeratosis, acanthosis and the presence of numerous cells in the upper part of stratum spinosum with large keratohyaline granules, whereas electron microscopic study disclosed keratin clumps reflecting the disturbances in the keratin assembly process. Molecular analysis of the proband with PPK showed a mutation N188K in the exon 1 of *KRT1* gene encoding keratin 1 resulting in an asparagine-to-lysine substitution, whereas in probands without PPK the mutation (g>a467) in the hot spot within the 1A domain of gene *KRT10* encoding keratin 10 was found resulting in an arginine-to-histidine substitution. Our study confirms previous observations concerning strong association between mutations in the *KRT1* gene and PPK in patients with bullous congenital ichthyosiform erythroderma.
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O 10

Cellular retinol binding protein-1 expression in skin tumors

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Retinoids play a relevant role in growth and differentiation of epidermal cells. Cellular retinol binding protein 1 (CRBP-1) is a 15,000 Da cytosolic chaperone-like molecule that regulates the pre-nuclear phase of retinoid signalling. CRBP-1 expression also influences the uptake and subsequent esterification of retinol and its intracellular bioavailability. We analyzed the expression of CRBP-1 in normal and abnormal epidermal differentiation, actinic keratosis, squamous and basal cell carcinomas by immunohistochemistry and *in situ* hybridization. CRBP-1 immunodetection was low in the basal layer of normal epidermis, with increased expression in granular layer keratinocytes; CRBP-1 was completely absent in the stratum corneum. CRBP-1 expression was also strongly expressed in skin adnexal structures. In psoriatic lesions, a hyperproliferative condition of the skin, an increased epidermal expression of CRBP-1 was also observed. In basal cell carcinomas, CRBP-1 expression was low expression of CRBP-1 was present in actinic keratosis and well-differentiated squamous cell carcinomas, whereas it was reduced in less differentiated tumors. In general, CRBP-1 transcript in situ detection is well aligned with protein expression. *In vitro*, Western Blotting demonstrates that mouse epidermal-derived cell lines maintain a variable CRBP-1 expression according to their phenotype. The treatment with *all-trans* retinoic acid induced an increase of CRBP-1 expression in human keratinocytes. Investigation of regulatory mechanisms of CRBP-1 expression may help to elucidate physiopathological changes occurring in keratinocytes during hyperproliferative and oncogenetic processes. CRBP-1 immunodetection appears also as an adjuvant marker of keratinocyte differentiation.
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O 11

Melanocytes' differentiation: what happens to the stem cell?

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Melanoblasts migrate in the skin and in other organs following a selective commitment; the activation of specific cytoplasmic and membranous receptors is mandatory for life, proliferation, migration and pigmentation of these cells. Melanosomes' organization is linked to a sophisticated intracellular secretory mechanism which gives the melanoblast/melanocyte a peculiar functional autonomy. The terminal differentiation of the melanocyte ends up in the skin and is affected by numerous cytokines, some with a pleiotropic activity such as interleukin-1 (IL-1), interleukin-6 (IL-6) and interleukin-8 (IL-8) and some others including stem cell factor (SCF) and microophthalmia-associated transcription factor (MITF) with a high specificity for melanocytes differentiation. The specific terminal differentiation marker of melanocytes is the melanosome. In some pathological conditions such as metastatic melanoma, vitiligo and other hypomelanosis, the melanocyte looses its specific differentiation markers and this is due to a ''differentiation process''. Melanocytes, after many passages in vitro, progressively loose melanosomes and many markers of melanocyte lineage as HMB-45, Melan-A, S-100 etc. reproduce in vitro what happens in some pathological conditions. A better knowledge of what happens to the stem cell of the melanocyte lineage (an autocycling cell with the ability to produce differentiated cells) would have both a biological and therapeutic relevance.

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O 12

Cutaneous extrarenal rhabdoid tumor: a case report

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Extrarenal rhabdoid tumors are rare neoplasms distinguished by a conspicuous morphological phenotype characterized by large epithelioid cells with abundant eosinophilic cytoplasm and paranuclear inclusions of intermediate filaments. Controversy exists as to whether the extrarenal rhabdoid tumor is a distinct clinicopathologic entity or merely a shared phenotypic expression of histogenetically divergent tumors. Although originally described in tumors from pediatric kidneys, the rhabdoid phenotype has since been described in a variety of patient ages and extrarenal sites. Primary presentations in the skin are exceedingly rare. Extraordinarily, the rhabdoid phenotype has emerged in cutaneous neoplasms, either as a pure extrarenal rhabdoid tumor or a composite phenotype coupled with another malignancy. In the skin, isolated case reports and small series have demonstrated the rhabdoid phenotype in conjunction with melanomas, squamous cell carcinomas, epithelioid malignant peripheral nerve sheath tumors, and rhabdomyosarcomas. Regardless of the clinical setting, the rhabdoid phenotype is uniformly associated with aggressive biological behavior. We report the findings from a rare and very aggressive primary extrarenal rhabdoid tumor of the skin.

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O 13

Specific cutaneous lesions in course of mantle cell lymphoma

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Mantle cell lymphoma (MCL) is a type of non-Hodgkin's lymphomas. The neoplastic cells derive from B-lymphocytes in the mantle zone of lymphoid follicles. The disease most often occurs in older patients. The diagnosis is usually established at the stage of generalized lymphadenopathy, splenomegaly and dissemination to the bone marrow and the blood. Skin involvement occurs rarely. We report a case of a 63-year-old woman who was admitted to the Department of Dermatology because of massive infiltrated erythemas with hyperpigmentation on the face, on nasal conchae and the nape. The lesions appeared 6 months before admission. Additional findings were dryness of nasal cavity, difficulties in speaking, increasing dyspnoea and generalized lymphadenopathy for several months. Laboratory results revealed leucocytosis 24×10^9/l with lymphocytosis 75% and normocyte anaemia (Hgb 7.7 g/dl). The biopsy of skin lesions taken from the ear showed very massive dermal lymphoid infiltrations. In the trepanobiopsy of bone marrow there were infiltrations of lymphoma presenting more than half of texture of marrow of bone. In immunophenotypic studies of the bone marrow the neoplastic cells were positive for markers: CD5+ (91%), CD20+ (93%), DR+ (96%), Lambda+ CD19+ (87%). Final diagnosis of MCL was established on the basis of immunophenotypic study of lymph node, where cells were found positive for CD20+, CD43+, CD23−, CD10−, C-myc-, tdt- and MIB (in about 50% of the cells). CT scans of the neck and chest were made and revealed a tumor mass protruding into larynx lumen from aryepiglottic fold together with enlarged lymph nodes on both sides along cervical vessels and enlarged lymph nodes in the mediastinum. The patient was transferred to an oncology department where CHOP chemotherapy (cyclophosphamide, doxorubicin, vincristine and prednisone) was administered. Improvement of general condition, with decrease of facial skin infiltration and relief of breathlessness was observed.

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O 14

Immunocytochemical and genetic proof of *Anaplasma*, *Borrelia* and *Bartonella* spp. in cutaneous and heart manifestation of Lyme disease

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The purpose of this work was to assess the presence of pathological agents of cutaneous and heart manifestation of Lyme disease. Rickettsiales are known to be present in tick vector and in reservoirs (rodents, wild and domestic mammals) individually or as co-infection of *Borrelia burgdorferi* s.l. The human monocytic and granulocytic ehrlichiosis (HME, HGA) was described recently in animals and humans in the USA and Europe. The group of patients with erythema migrans (EM) comprised 49 patients and with heart manifestation of lyme carditis (LC) after EM 36 patients. The probands were examined clinically by specialists using histological, EKG, ECHO, RGF and other methods. The skin and 9 heart biopsies were taken together with blood for electron microscopical (ISEM), genetic (PCR, RT-PCR) and serological evaluation with ELISA C6 (Focus), Western blot (Biowestern Ltd., CZ). Direct immunosorbent (ISEM) methods were performed from glutaraldehyde (Sabatini) fixed materials with monoclonal antibodies (Mabs) or with hyper-immune sera against mentioned pathogens. Observations were made with a JEOL 200CX electron microscope on negative stained or Epon embedded sections. Amplification of specific DNA and sequence analysis was performed with *recA*, *gltA 16S rRNA* primers by the Real time PCR with a LightCycler (Roche) and CEQ 2000 LX sequencer. The *Borrelia* strains were isolated from 6 skin, 2 heart biopsies and 2 blood samples in BSK-II medium and strains were characterized phenotypically with Mabs using WB and ISEM. Isolation of *Anaplasma, Ehrlichia* and *Bartonella* spp. in HL60 cells and Vero cells was not successful but 3 blood and 2 skin biopsies were PCR and ISEM positive. Analysis of partial gene sequences showed presence of *B. afzelii, B. garinii* and *B. burgdorferi* in the skin and heart samples. *Anaplasma phagocytophilum* (HGA) was proved in 1 heart and 2 skin biopsies with RT-PCR and amplicons were sequenced. *Anaplasma, Rickettsia* sp. and *Bartonella* spp. were detected in PCR positive skin and heart samples also electron microscopically. *Borrelia* were around the vessels and inside collagen fibers far from inflammation. In contrast to *Borrelia* other pathogens were inside cell inflammation i.e., neutrophils, monocytes and macrophages. Co-infections with mentioned agents can directly affect inflammation and caused different clinical feature of borreliosis.

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O 15

Kallikrein 8 is involved in skin desquamation through cleaving desmoglein 1 and corneodesmosin

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Kallikrein type serine proteases have been implicated in desquamation of epidermal keratinocyte. KLK8, one of the tissue kallikreins, is known to regulate epidermal differentiation and proliferation. However, its underlying mechanism remains largely unknown. In this study, we compared with KLK8−/− mice and wild type (WT) mice for kallikrein expression levels and skin morphology after TPA application. The KLK8−/− skin showed increased numbers of stratum corneum cell layers than the WT epidermis. KLK8 mRNA was upregulated along with KLK6 and KLK7 mRNA after TPA application in WT mice. KLK8−/− mice showed minimal increases in KLK6 and KLK7 transcripts, in protein expression levels and enzymatic activities. The inefficient cleavage of corneocyte adhesion molecules desmoglein 1 and corneodesmosin in KLK8−/− skin contributes to a delay in corneocyte shedding, resulting in the hyperkeratosis phenotype. In electron microscopic findings, the density of corneodesmosomes in KLK8−/− mice was increased compared to WT mice. We suggest that KLK8 could be a key enzyme involved in desquamation.

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POSTERS

P 1

Vogt-Koyanagi-Harada Disease: a novel ultrastructural study

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Vogt-Koyanagi Harada (VKH) disease is a multistep autoimmune disorder which affects melanocytes in the skin, ocular, auditory and central nervous system. The pathogenesis is thought to be related to an aberrant T-cell mediated immune response directed against self-antigens present on melanocytes. We studied a VHK patient who had developed the disease many years prior to our consultation. Electron microscopy (EM) and immunohistochemistry using S-100 protein, HMB-45 and Tyrosinase was performed on skin biopsies from photo-exposed and non photo-exposed skin from the VHK patient, since the white lesions almost totally covered the body area. Only S-100 protein was positive. At EM, no melanocytes were observed in non photo-exposed skin. Many clear cells (CC) were present within the epidermis at basal and suprabasal levels, containing various large mitochondria with irregular crests or matrix swelling and almost devoid of crests. Most CC were Langerhans cells (LC) containing clear Birbeck granules, although some showed vesicles, lysosomes and indented nuclei. No melanosomes were observed within keratinocyte cytoplasm. The photo-exposed skin showed increased thickness of the basal membrane with a deposition of electron-dense material. Many LC presented irregular nuclei, electron-dense chromatin and a cytoplasm rich in large and irregular mitochondria. No melanosomes were observed within this biopsy. The patients' small daughter also presented small vitiligo-like lesions mainly on her legs. Altogether these data suggest that in this illness there is an alteration of the mitochondrial system, which may also affect the antigen presenting cells.
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Autosomal recessive congenital ichthyosis: Mutations in *ichthyin* associated with structural abnormalities in the granular layer of epidermis

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Autosomal recessive congenital ichthyosis (ARCI) is a heterogeneous group of skin disorders. Several mutant genes are identified in ARCI but the association between genotype and phenotype is poorly understood. In search for genotype-phenotype correlations in ARCI we selected 27 patients from 18 families with specific ultrastructural features of the epidermis. The electron microscopy (EM) picture was characterized by abnormal lamellar bodies and elongated membranes in stratum granulosum classified as ARCI EM-type III. DNA samples from a subset of the affected individuals were screened for homozygous genomic regions and a candidate gene region was identified on chromosome 5q33. The region coincides with the ichthyin gene, previously reported as mutant in ARCI. Mutation screening of ichthyin revealed missense or splice site mutations in 25 out of the 27 individuals (93%) with specific EM characteristics of type III. In a control group of 18 ARCI patients without EM findings consistent with type III one individual was found homozygous for a missense mutation in *ichthyin*. Our findings indicate a strong association between ultrastructural abnormalities in the granular layer of epidermis and *ichthyin* mutations. The results also suggest that EM provides a tool for specific diagnosis in a subgroup of ARCI patients.
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Severe transglutaminase-1-negative lamellar ichthyosis in a 9-year-old boy

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A 9-year-old boy presented with a generalized cornification disorder consisting of dirty-brown adherent scales. The face was less severely involved, palms and soles showed accentuation of markings. Ear helices were thickened and deformed, and the external auditory canals were filled with cerumen and keratoses compromising hearing. Mental and physical development seemed not impaired. The parents and the older brother were unaffected. Histology of a skin biopsy showed pronounced orthohyperkeratosis and focal hypergranulosis without signs of epidermolytic hyperkeratosis. On ultrastructural examination, the markedly thickened stratum corneum was composed of up to 90 lamellae and contained polygonal clefts. On cryostat sections, epidermal transglutaminase activity was completely absent. Based on clinical, ultrastructural, and immunohistological data a provisional diagnosis of lamellar ichthyosis (LI) caused by transglutaminase-1-deficiency was made which could be confirmed by detection of two different mutations in the gene encoding transglutaminase-1 (TGM1). Reduction of hyperkeratoses was achieved by urea-containing preparations and baking soda baths. There are at least 6 different types of LI which can only be distinguished genetically but not clinically. Among them, LI with underlying transglutaminase-1-deficiency, as demonstrated in our patient, is the most common type accounting for about a third of cases.
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Future SCUR MEETINGS

- **35th SCUR Meeting May 17th – May 19th 2008 (JOINT Meeting with the Society for Skin Structure Research (SSSR), Otsu Prince Hotel, JAPAN.**
- The **organization of the 2008 meeting in Japan** will be organized under the steering committee headed by Y. Kitajima (meeting president), H. Shimizu (president SSSR), T. Hashimoto (General Secretary), M. Amagai (chair-man of program committee), A. Ishida-Yamamoto and their team.
- **The meeting will take place directly after the IID-meeting in Kyoto. The SCUR will provide travel grants for young scientists to enable attendance of this meeting (see:** http://orgs.dermis.net/content/e04scur/e03meetings/e121/e823/Application_FormSCUR.pdf)
- **For detailed information visit:** http://www.cs-oto.com/sssr_scur2008/welcome.htm 2nd Announcement and Call for PAPERS, more detailed information on congress site -1- (PDF 2MB) 2nd Announcement and Call for PAPERS, more detailed information on congress site -2- (PDF 2MB)
- **36th SCUR Meeting June 2009: "SCUR meets Florence"** – Francesca Prignano and her team invites us to the 36th SCUR meeting in Italy