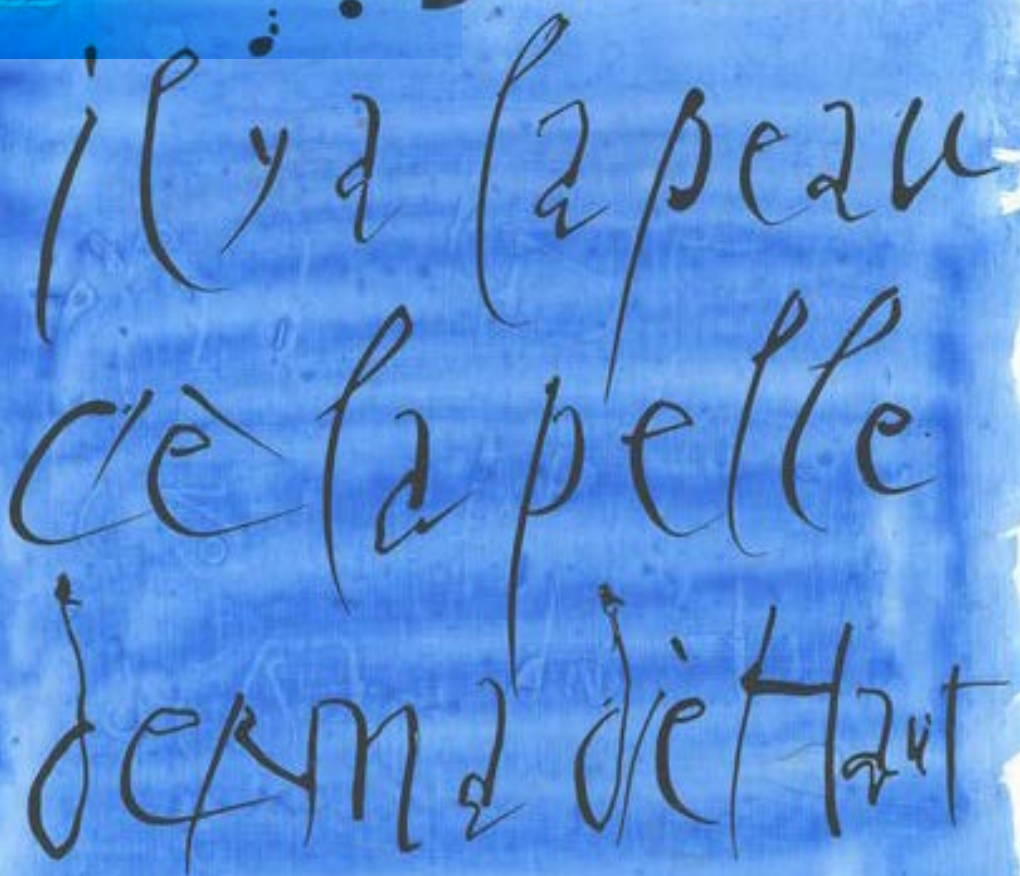


Department of Dermatology, Inselspital  
University Hospital Bern  
**Activity Report 2013–2014**

 **INSELSPITAL**

UNIVERSITÄTSSPITAL BERN  
HOPITAL UNIVERSITAIRE DE BERNE  
BERN UNIVERSITY HOSPITAL



il y a la peau  
de la pelle  
derme de haut

## Foreword

### Introduction

The Department of Dermatology of the University Hospital of Bern is pleased to provide its third Activity Report. In the past 6 years the Department has undergone substantial changes in spirit, in medical staff as well as in overall organisation. Requisite changes made then positioned the Department correctly to face the challenges imposed by the new developments in the Swiss health objectives set by the Directorate of the University Hospital. In order to achieve operational excellence, the Department has undergone, in the past two years, a critical reassessment of its processes and organisation and accordingly developed a strategic framework for the next 5 to 10 year. Furthermore, the Department successfully managed the ISO certification of its Skin Tumour Center which will be one of the players in the Inselspital's Cancer Comprehensive Center.

The overall goals remain to provide high level medical care and services in close collaboration with both other Hospital Departments and external specialists, to achieve high patient satisfaction, to carry out successful clinical and basic research and to ensure the best possible pre- and post-graduate teaching. Efficient management and optimal engagement of the various resources with improvement of the processes have emerged as crucial factors in increasing budgetary constraint as well as in both given and enforced yearly objectives. Finally, the attractive workplace and job quality give additional value.

*Professor Luca Borradori  
Director and Chairman*



*Therese Zürcher  
Chief Nurse*



### Titelbild

Ausschnitt aus:

R. Mumprecht CH 3098 Köniz

Il y a la peau 2013 Kat.Nr. emy 593

Acryl auf Pavatex 31 x 24 cm

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## Staff and collaborators

(as at 31.12.2014)

Director and Chairman	Professor L. Borradori
Vice-Chairman	Professor N. Yawalkar
Chief Nurse	Th. Zürcher
Faculty and Chiefs	Professor R. Hunger/Professor D. Simon
Research	Dr B. Favre/Professor E. Müller
Chief physician clinical ward	H.-W. Klötgen
Chief surgical unit	Dr R. della Torre
Dermatopathology sector	Dr H. Beltraminelli / Dr R. Blum
Chief administration officer	J. Peissard-Auberson
Administration officer	J. Sprecher
Director assistants	L. Bohm, M. Schenk

## Attending physicians

Dr N. Dietrich, Dr K. Kernland, Dr D. Perruchoud, Dr Z. Spanou,  
Dr M. Stieger, Dr P. Weber

## Consultants and lectors

Dr M. Adatto (Laser), Dr M. Baumgartner (Phlebology), Dr P. de Viragh (Trichology), Professor E. Haneke (Nail diseases), Professor Th. Hunziker (Vitiligo), Dr H. Nievergelt (Histopathology), Dr Dr A.-A. Ramelet (Phlebology), Dr A. Skaria (Mohs Surgery), Professor L. Naldi (Epidemiology), Professor Y. Barrandon (Epidermolysis bullosa)

## Residents

Dr K. Gadaldi, Dr S. Häfliger, Dr S. Häsler, Dr K. Heidemeyer, Dr C. Houriet,  
Dr I. Joggi, Dr I. Reber, Dr Ch. Schlapbach, Dr B. Weber

## Background

- The Department of Dermatology is part of the Inselspital, University Hospital of Bern. The Inselspital belongs to a private foundation, the Inselstiftung. The latter has an agreement with the Canton of Bern to serve as a tertiary health care centre for the population of the Canton of Bern and as a University teaching hospital.
- The Department of Dermatology within the Inselspital is a tertiary referral centre for skin and sexually-transmitted diseases. Patients are referred from all over Switzerland. More than 20% of the treated patients come from outside the Canton of Bern.

## Structural organization, medical staff and nurse team

- Our Department comprises an in-patient section with 14 beds, an out-patient section with several specialized clinics, a day hospital for the management of complex cases with emphasis on chronic wounds, a phototherapy unit, a surgical unit, a laser platform, as well as a dermatopathology unit.
- The medical staff consists of 10 senior physicians and 9 junior physicians. There are one full Professor, four associate Professors and one senior lecturer. Furthermore, there are 8 part-time board-certified consultants and lecturers. The Department regularly hosts a number of guest physicians in training as well as board-certified dermatologists from European and non-European countries for elective periods.
- The medical staff works in tight collaboration with the specialized out-patient and in-patient nursing teams. The latter take particular care in ensuring the best education and practice quality in nursing. These high quality levels and standards have been accredited for activities both in the in-patients ward and as well as for distinct out-patient activities.

## Activity and areas of expertise

Our current medical offer is focused on the evaluation and management of:

- Skin cancers including clinical evaluation, management and systematic follow-up of melanoma and non-melanoma skin cancer patients using video-microscopy and digital imaging devices
- Dermatosurgery, including Mohs micrographic surgery
- Inflammatory skin diseases, psoriasis and atopic dermatitis
- Autoimmune blistering disorders of the skin and mucous membranes
- Skin allergies and environmental dermatology
- Paediatric dermatology, inherited blistering and fragility syndromes of the skin
- Acne and hidradenitis suppurativa
- Medical lasers
- Hair and nail diseases with specific conservative and surgical treatment
- Phlebology as well as chronic wound care
- Dermatopathology

## Certification of the Skin Cancer Center

The best and comprehensive care of our patients is one of the priorities of our Department. In November 2014 we have been able to successfully finalize the certification of our Skin Cancer Center according to the «Deutsche Krebsgesellschaft (DKG)». We are now able to offer our patients with skin cancers comprehensive medical care with high standards of quality. The certification process has allowed us to further improve our collaboration with the other Departments of our Hospital as well as with specialist physicians and general practitioners in private medical practice to ensure the best possible management of patients.

## Current challenges

The structure of the Swiss health system continues to undergo substantial reorganisation. The Swiss health system is one of the most expensive in the world. Measures are being taken in an effort to reduce expenditure for both in-patient and out-patient services. This situation has put hospitals under pressure with budget cuts and rigorous budgetary control, making the implementation of cost-containment measures and the reassessment of the running of the Department including patient management and medical services essential. Since 2012 the hospital Directorate has set a number of objectives each year for each Department in the hospital to meet. The goals invariably encompass a defined budget, a given number of hospital admissions, out-patient cases, medical treatments, as well as management improvement processes and a campaign of quality projects.

## Lean and Kaizen principles: process reorganization in our Department

To ensure high quality in medical and nursing care, better process organization and, last but not least, continuous improvement of the financial results, the activities in the various out-patient units underwent, in 2012 and 2013, systematic analysis of work flow according to the «Lean» management philosophy. This focuses on the elimination of waste (overburden and unevenness) and on putting patients and referring physicians (the costumers) at the centre of interest.

Applying this specialised philosophy, the management team in the Insel Hospital (Mrs S. Radnic, Mrs S. Puliafito), acting as both consultant and teacher the various professional groups (with representatives of the medical, nurse, administrative and management staff) of the Department, held workshops to fully analyse departmental processes. The goals were to identify and eliminate waste and to cut out unnecessary steps, to simplify pathways, patient flow and administrative processes, to improve or adapt the available infrastructure to the new simplified steps, to better allocate human resources to the new defined tasks. The basic idea was to seize this challenging and critical time as the opportunity to begin a transformation of working methods with the ultimate goal of continuous improvement (Kaizen:

Kai = change, Zen = good). The results showed that the planning of patient consultations, operational planning for physicians and nurses, various administrative processes, personal management and working space and infrastructure needed to be changed and improved.

After identification to these problems we were able to progressively implement change and complete major transformation in out-patient activities. We have now implemented a «lean» and «Kaizen» board to maintain and encourage the new philosophy, to control the performance and results and to continuously improve workflow.

## Objectives

The main goals of the Department of Dermatology are

1. to provide high quality medical care and service by offering a spectrum of specialised out-patient consultations as well as appropriate evaluation and management of patients requiring hospitalisation. Respect of patients' dignity and overall ethical issues are of constant concern for patient treatment,
2. to carry out clinical, translational and basic research. The ultimate objective is to ensure best patient care, state of the art therapy and to have a better understanding of disease mechanisms,
3. to provide intensive teaching for pre-graduate and post-graduate students in medicine and biomedical sciences, residents, physicians and specialists of dermatology and venereology, as well as other specialisations.

Overall, the Department is very enthusiastic and highly motivated to share experiences in clinical evaluation, management and treatment of dermatological patients through interface with other partners within the Canton of Berne and in the rest of Switzerland. Joint ventures with focus on consultative activities for dermatological patients have been established with one of the largest emergency and primary referral out-patient centres in Bern (City Notfall) as well as with two major hospitals in neighbouring Cantons (Fribourg, Solothurn). Finally, the Department is keen on developing and carrying out clinically oriented and basic investigative research projects in collaboration with either other researchers or with pharmaceutical companies.

## Patients and technical statistics

The number of dermatological in-patients has increased to up to 650 new cases per year. The average length of stay in hospital has decreased from 6 days to 3.7 days in the last 4 years. There are up to 21,000 out-patient consultations per year, 3,800 patients are cared for at the wound care clinic, up to 6,300 phototherapy treatments and 2,300 surgical procedures are routinely performed. The dermatohistopathology sector processes and analyses 18,500 skin biopsy specimens per year and is one of the largest dermatopathology units still fully integrated within a University Hospital in Switzerland.

## Specialized nursing team

- The nursing team is headed by Mrs T. Zürcher, member of the department's directorate. The nursing team constitutes the largest group among medical personnel working in the Department of Dermatology and represents the critical backbone requisite to providing the specialized high level medical care of patients. Mrs Zürcher and her closest collaborators ( Mrs T. Gross, Mrs B. Nydegger, Mrs S. Hale) have been faced with a number of significant organizational changes and new goals over recent years.
- The most significant challenges have been to deal with a new management pathway of in-patients with a significant reduction in the length of the hospital stay and a rapid turnover of patients in the clinical ward, an increased number of out-patient surgical cases related amongst others, to the introduction of the micrographic Mohs surgery, as well as the implementation of new therapeutic approaches with related training, including UVA1 phototherapy and lasers. Furthermore, in the light of increasing budgetary restriction, the personnel pool has to be constantly adapted to needs with always the ultimate goal of increased efficiency. Finally, the nursing team is keen to maintain a high standard of care. These efforts are reflected by the regular internal and external controls meeting the quality management standards required to maintain certification.

## Strategy development: setting the goals for 2020–2025

The Department performed strategy development under the lead of Porsche Consulting GmbH. In 2013 and 2014, 14 departmental representatives, including medical, nursing, administrative and human resource staff members, participated in two intensive workshops under the guidance of two experts Porsche Consulting. Strategy was developed in 4 distinct steps according to the Porsche methods. The first step included a SWOT (strengths/weakness/opportunities/risks) analysis. Mission visions and objectives were further defined. Building on the latter, several initiatives and projects have been defined. In a second step, the results obtained by using the defined strategy and projects roadmap, were given to all members of the Department as well as to the Board of Directors of the Hospital Directorate. The third step included operational planning of initiatives and projects in order to implement the strategy and the control of that implementation. The final step includes current and constant strategy review, the analysis of ongoing results as well as the assessment of the need to adapt the various initiatives and strategy. Overall, we have defined 4 major objectives for the next 5 to 10 years: 1) strengthening and further improving distinct medical services, which represent our areas of medical expertise and strategically important domains. The latter include allergology, melanoma and non-melanoma skin tumours, surgery and Mohs micrographic surgery, autoimmune and immune mediated skin diseases, dermatopathology and patient education with specialised nurses; 2) financial profitability as an essential prerogative for the further development of the speciality; 3) attractive workplace with quality employment and quality jobs; 4) greater patient satisfaction with the provided services.

## Detailed clinical services

In the following section the specialised out-patient clinics available in our Department and specific areas of clinical and research interests are both presented.

## Autoimmune skin diseases clinic

**(responsible: Professor L. Borradori)**

- Our Department has a specific interest and expertise in the evaluation, diagnosis and management of patients with severe autoimmune blistering diseases of the skin and mucosa, such as bullous pemphigoid, cicatricial pemphigoid, epidermolysis bullosa, pemphigus and cicatricial pemphigoid, pemphigoid which is unique in Switzerland. Furthermore, we are interested in the evaluation and management of patients with cutaneous manifestations of systemic diseases, such as systemic lupus erythematosus, dermatomyositis, scleroderma, vasculitis and Adamantades-Behçet disease. In this context, our clinic is involved as tertiary referral centre for patients from the Canton of Bern as well as from all over the country.
- Besides the clinical management of patients with autoimmune diseases, we are directly involved 1) in clinical multicentre European studies to characterise the clinical course, severity and prognostic markers in affected patients; 2) in the development of diagnostic tools such as ELISA for improved diagnosis and better follow-up; and 3) in basic investigative studies to assess the immunological humoral and cellular response in affected patients (see research part).
- For correct evaluation of patients and classification of autoimmune diseases, we provide the required immunopathological analyses, such as direct and indirect immunofluorescence microscopy techniques (with various substrates), as well as immunoblot and immune-precipitation techniques using recombinant proteins. These immunopathological studies are carried out in close collaboration with the Institute of Immunology (immunopathology laboratory supervised by Dr Michael Horn). Finally, we have contributed to the development of several different novel diagnostic ELISA tests.

## Chronic wound care centre

**(responsible: Dr H.W. Klötgen)**

The management of chronic skin wounds is organised in close collaboration with the chronic wound care centre. In the whole county of Bern the wound care centre is the largest out-patient clinic specialised on the evaluation and management of recalcitrant vascular, neuropathic, tumoral and/or inflammatory skin wounds. Here we provide the entire conservative (e.g. use of novel wound dressings and matrix products) and surgical (conventional skin grafting, complex grafting procedures) treatment spectrum of wound therapy. For the management of recalcitrant chronic wounds our team frequently takes advantage of tissue-engineered skin equivalents, some of which have been developed in our clinic. The treatment and long-term management of patients is professionally supported by specialised nurses.

## Dermatopathology unit

**(responsible: Dr H. Beltraminelli, Dr R. Blum, Dr H. Nievergelt, Professor E. Haneke)**

The Dermatopathology sector deals with the processing and evaluation of 15,000 to 18,000 tissue samples per year (with >50,000 slides). Biopsy specimens are referred from our Department (30%) of the university hospital and from dermatologists from all over the country (70%).

The diagnostics cover the whole spectrum of dermatopathology, especially inflammatory, autoimmune and neoplastic skin diseases. For the most cases we use conventional histological investigations, when necessary immunohistochemistry (we have a large panel of stainings covering more than 95% of dermatopathology diagnoses) and molecular technologies (in collaboration with the Institute of Pathology, University of Bern). Our interest is specifically focused on the diagnosis of cutaneous lymphomas, melanocytic tumours and inflammatory diseases.

The team of dermatopathologists is actively implicated in post-graduate teaching courses in dermatopathology. Furthermore, it provides weekly the clinical-pathological correlation during the meetings of our clinical staff.

### International activities in the field of dermatopathology

Since 2009 there is an intense collaboration with the Regional Dermatology Training Centre (RDTC) in Moshi, Tanzania. We provide human and technical support for the development of the local dermatopathology unit and fellowship of African specialists. Moreover since 2013 we have a collaboration with the Pathology Unit at the Stellenbosch University in Cape Town, South Africa.

Since 2014 we enlarged our African project and we are now offering a dermatopathology fellowship to several Subsaharan Dermatologists coming from different African countries (Egypt, Ethiopia, Kenya, Malawi, Rwanda, Tanzania). This is possible thanks a Grant from the European Academy of Dermatology and Venereology (EADV).

In January 2015 Dr Beltraminelli organized an African Dermatopathology Conference of two days at the RDTC in Moshi, Tanzania.

Our dermatopathology sector has been officially recognised as training centre in dermatopathology by the International Committee for Dermatopathology ICDP-UEMS ([www.icdermpath.org](http://www.icdermpath.org)). Since 2009 we have hosted several guest physicians from many countries: China, Egypt, Ethiopia, India, Kenya, Rwanda, Saudi Arabia, Turkey. Since 2010 we participate to the Groupe Francais pour l'Étude des Lymphomes Cutanés (GFELC) as active members, discussing all skin lymphomas seen at our clinic.

## Dermatosurgery clinic: Micrographic surgery

**(responsible: Dr R. della Torre, Dr A.M. Skaria, Dr M. Stieger)**

Since 2008 our dermatosurgery department has been continuously developed with a growing number of patients and surgical procedures offers. A number of personnel and a better rotation of residents has been achieved. The Mohs- micrographic surgery introduced in 2008 by Dr A.M Skaria and the slow Mohs surgery technique have consequently been established. Skin cancer patients benefitted from a university-level high quality procedure in the surgery sections and a better follow-up also thanks to the achieved certified Skin cancer centre. In addition to the malignant skin process's treatment, therapy of benignant tumours or other skin diseases and malformations, such haemangioma of the childhood or condyloma, are also treated in our dermatosurgery department with multiple new devices. Our close cooperation with Professor M. Constantinescu and his team from the Department of the Plastic and Reconstructive Surgery has been further improved.

## Eczema and atopic dermatitis clinic

**(responsible: Professor D. Simon)**

Eczematous skin diseases are very common and concern over 20% of dermatologic patients. For instance, atopic dermatitis affects more than 10% of children between the ages of 6 to 7 years. Irritant and allergic contact dermatitis as well as occupational eczema is common in adults. These groups of cutaneous diseases are characterised by an acute and/or chronic inflammation of the skin and intense itch. Therefore, they have an enormous impact on the quality of life and are of medical as well as socioeconomic importance.

This specialised clinic provides all diagnostic and therapy facilities for patients with eczematous skin diseases. Diagnostic tests comprise blood and skin tests (patch test, skin prick test, atopy patch test, and provocation tests) to identify exogenous and endogenous pathogenic factors. Comprehensive management of affected patients encompasses installation of adequate anti-inflammatory topical and systemic therapies, skin care and skin protection teaching courses and practical instructions, psychological advice and support, as well as avoidance of triggers in daily life and occupational activities. Finally, we offer specific medical education courses for atopic dermatitis patients provided by dermatologists, allergists, psychologists, and nutritionists as well as practical education on topical treatment, which are unique in Switzerland. Our on-going research projects include clinical studies focusing on pathogenic mechanisms of allergic skin diseases such as atopic dermatitis and contact dermatitis, as well as eosinophilic skin diseases. Furthermore, we are involved in epidemiologic studies on hand eczema as well as contact allergy.

## Laser clinic

**(responsible: Dr N. Dietrich, Dr M. Adatto, Dr K. Heidemeyer)**

The laser clinic manages both in- and out-patients by using various laser types and light sources. Established and innovative therapies are provided under the supervision of experienced laser specialists to provide high clinical care. Dr Adatto and Dr Fritz have been directly involved in the development of laser devices in collaboration with various American and European companies.

Our laser centre is equipped with state of the art laser devices (e.g. vascular, ablative fractional, pigmented, excimer). A close collaboration with specialists from other Departments (angiology, paediatrics, and paediatric surgery) allows interdisciplinary clinical management.

Efforts are made to improve therapy algorithms by the use of lasers for a number of skin disorders, such as vascular malformations, pigmentary disorders and vitiligo, psoriasis, eczema, and inflammatory skin conditions. Furthermore, we are also involved in studies aimed at assessing the impact of laser wavelengths on tissue reaction, safety aspects, as well as aesthetic issues.

With regard to clinical research, we are currently analysing the effect of distinct lasers on pigmentation disorders (Excimer, IPL), rosacea, psoriasis (Excimer and pulsed dye laser), atopic eczema (light vaccination, multicenter trial with Optomed), and actinic keratoses (laser PDT). The clinical staff consists of Dr M. Adatto, past-President and Honorary Member of the European Society of Laser Dermatology as well as founder and medical director of Skinpulse Dermatology and Laser Centre Geneva, Dr N. Dietrich and Dr K. Heidemeyer, dermatologists, with specific interest in lasers.

## Melanoma and pigmented lesion clinic

**(responsible: Professor R. Hunger)**

The incidence of malignant melanoma is rapidly growing. The current incidence rate in Switzerland is 22 new cases per 100,000 inhabitants followed by over 200 melanoma related deaths each year. While early stages can be cured by surgical excision, late stages have a poor prognosis. To best follow up patients with malignant melanoma and to recognise these tumours at an early stage two specialised consultations are available:

### Malignant melanoma and pigmented lesions

We provide regular clinical follow-ups for our patients with atypical moles and malignant melanoma. The regular examinations are important to exclude disease progression as early as possible. Since patients with melanoma have an increased risk to develop a second melanoma, regular full skin examination is essential.

Dermoscopy/videomicroscopy. Patients with multiple dysplastic naevi and other patients at high risk for melanoma are regularly evaluated using a digital dermoscopic system (Fotofinder). This technique allows the detection of even the slightest changes in the pigment pattern of the lesions, increasing the sensitivity and specificity of diagnosis.

## Nail diseases clinic

**(responsible: Professor E. Haneke)**

In a dermatological practice, up to 15% of the patients present with nail disorders. The current knowledge in this area is not always satisfactory and management of many nail diseases has been limited due to lack of specific and effective therapeutic modalities. For example, onychomycoses that affect up to a third of the elderly still represent a problem with a complete cure rate remaining far below 50%. Furthermore, treatment of nail psoriasis is still challenging despite the availability of systemic biological treatments. Evaluation of nail diseases and their diagnoses are further hampered by the fact that few dermatopathologists and pathologists have the required experience with the interpretation of nail biopsies. Most physicians are reluctant to biopsy the nail organ. Finally, some nail diseases require a specific surgical approach, and few experts are familiar with nail surgery.

In our Nail Clinic we offer both conservative and surgical management for a variety of inflammatory, infectious, tumoral and congenital nail diseases. Our clinic provides a unique expertise in nail surgery and nail pathology throughout Europe.

## Non-melanoma skin cancer consultation

**(responsible: Dr P. Weber)**

Non-melanoma skin cancers (NMSC) such as basal cell carcinoma and squamous cell carcinoma represent a medical and epidemiological challenge in Western countries. This is related first to the significant increase of skin cancers (4–8% in Europe per year) as a consequence of the current life style (sun exposure) as well as the ageing of the population. In this context, there is a growing demand for treating these patients, and e.g. for skin surgical approaches ensuring good aesthetic results. Since the Inselspital is one of the Swiss referral centres for organ transplantation, we are also frequently involved in the evaluation and management of skin tumours in this high-risk organ recipient population. Our clinic has thus a strong commitment to management of skin tumours of peculiar complexity. A close collaboration with the Department of Plastic and Reconstructive Surgery (Chair: Professor M. Constantinescu) and with the Department of Radiation Oncology (Chair: Professor D. Aebersold) exists.



To address these issues, specific platforms and therapies are developed and performed, respectively

1. Tumour board: Interdisciplinary evaluation of patients with complex cutaneous cancers together with the Department of Plastic and Reconstructive Surgery and Department of Radiation Oncology
  2. Dermatologic surgery, with particular focus on Mohs micrographic surgery
  3. Non-invasive therapeutic approaches, such as radiation therapy, photodynamic therapy (PDT), cryosurgery, and non-invasive topical immunomodulatory therapies
- Collaboration with the Department of Nephrology for the dermatological follow-up of renal transplant patients.

## Paediatric dermatology clinic

**(responsible: Dr Z. Spanou)**

Dr Spanou, consultant in pediatric dermatology, ensures evaluation and management of children and adolescents with skin diseases. In particular, she is specialised in the evaluation of children with genetic, infectious, endocrine and allergic diseases. Patients are evaluated in close collaborations with University Children's Hospital of Bern.

## Phlebology clinic

**(responsible: Dr Dr A.A. Ramelet, Dr M. Baumgartner)**

More than 50% of the adult population in Western countries suffers from chronic venous disorders (CVD). Besides varicose veins, the most severe form of CVD, chronic venous insufficiency (CVI), occurs in up to 10% of people. CVI is responsible for and may lead to acute and/or chronic eczematous diseases, pigmentation, leg oedema, dermatoliposclerosis, atrophie blanche, and leg ulcers, resulting in high morbidity and health costs. In addition to classic vein pathologies and cosmetic impairments play a major role in the phlebology.

Our Department is specialised in the clinical evaluation, clinical investigation (cw-Doppler and colour duplex) as well as in both the conservative (compression, venoactive drugs, physiotherapy) and surgical (sclerotherapy, echo-guided sclerotherapy, surgery) treatment of CVD. There is a tight collaboration with the Department of Angiology in Bern (Professor I. Baumgartner), and the Department of vascular surgery (PD Dr M.K. Widmer) which is of fundamental importance for comprehensive and multidisciplinary evaluation of patients.

Management of chronic wounds comprises special therapeutic procedures which are provided by nurses specifically trained in wound care.

Management of small vessel problems also cosmetic aspects with sclerotherapy and vascular lasers.

## Psoriasis clinic

**(responsible: Professor N. Yawalkar)**

Psoriasis is a common inflammatory skin disease of variable severity with significant morbidity and impact on quality of life. Evidence exists indicating that psoriasis may be associated with serious comorbidities such as cardiovascular and metabolic diseases. The underlying pathomechanisms are not yet fully understood. Recent advances in our understanding of the pathomechanisms of psoriasis have opened the way for new therapeutic strategies in psoriasis, such as the use of targeted therapies with biologic treatments.

In our specialised psoriasis clinic the following services are provided:

- topical and systemic treatments including phototherapy, traditional immunosuppressive agents (methotrexate, retinoids, and ciclosporin) and biologics such as tumour necrosis factor inhibitors (etanercept, infliximab, adalimumab) and anti-IL-12/23p40 monoclonal antibodies (ustekinumab) are routinely used
- interdisciplinary medical education courses provided by dermatologists, psychologists and nutritionists are offered to affected patients and their families, an opportunity exclusive to Switzerland
- clinical research studies aimed at testing novel biologic treatments are carried out.

The clinic participates in phase 2 and phase 3 trials.

The clinic is also directly involved in basic investigative studies focused in the characterisation of the immune and inflammatory response in psoriasis (see research part).

## Rare skin disease and genodermatoses

**(responsible: Dr Kristin Kernland Lang)**

Dr Kernland Lang, consultant in pediatric dermatology, focuses on rare skin disease, mainly in children, such as the field of genodermatoses. In particular, this includes the diagnosis and management of patients with inherited skin blistering disorders, such as epidermolysis bullosa (EB).

We offer a specialized and comprehensive interdisciplinary evaluation of affected patients by the EB network at the Inselspital. Our specialized team ensures an appropriate care of wounds and addresses further problems occurring in this rare and complex disease. We focus also on information and support of affected people, as well as their family members and institutions involved. Furthermore, molecular diagnosis for a variety of congenital diseases is provided in close collaboration with the department of human genetics and various leading European laboratories. A long-standing cooperation with Professor Peter Itin, head of Dermatology, University of Basel, has been established to ensure the best-possible approach for diagnosis and management in patients with unsolved complex syndromal skin disease.

## Trichology clinic

**(responsible: Dr P. de Viragh)**

We provide a specialised evaluation and care of patients with complex and severe diseases of the scalp and hair. Expert evaluation and individualised therapy are mandatory in cases of hair loss, hair structure alteration, and scalp inflammation or scarring.

To properly evaluate patients, the following exams are carried out:

- microscopical analysis of hair samples (trichogram) to assess structural abnormalities, establish the rate of hair loss, or identify genetic influences
- scanning electron microscopy for definitive diagnosis of hereditary hair abnormalities
- stereotactic photography and computer-assisted digital imaging (trichoscan) is used to evaluate treatment efficacy objectively
- dermoscopic scalp evaluation (trichoscopy)
- scalp biopsies for examination by light microscopy and immunohistochemistry studies.

The scientific experience in the field of hair physiology and diseases of the pilosebaceous follicle is attested by numerous presentations at international meetings and publications by the involved staff, as well as by the ongoing research activities such as treatment protocols for alopecia areata and lichen planopilaris.

## Urticaria clinic

**(responsible: Professor D. Simon)**

Urticaria is a common mast cell-driven skin disease presenting with an acute onset of wheals and/or angioedema. Acute urticarial is often associated with acute infections, drugs, and allergic reactions. The diagnostic of chronic spontaneous urticarial is complex and based on the patient's history, clinical examination and laboratory tests. The triggers of inducible urticarial should be identified by provocation test. We provide all diagnostic work-up and therapy, including anti-IgE antibody and other immunomodulating therapies for those patients not responding to antihistamines.

## Vitiligo clinic

**(responsible: Professor Th. Hunziker)**

Vitiligo is a relatively frequent autoimmune pigmentation disorder affecting up to 0.5 % of the population. While diagnosis is usually straightforward, the management of vitiligo is difficult. There is no rapidly acting and in the long term well-tolerated treatment with a high rate of cosmetically satisfying, stable repigmentation. The challenge of vitiligo resides in the comprehensive management of the affected patient, in which the disease has a great psycho-social impact. In our consultation, we aim to establish tailor-made treatment schedules, which also integrate the psycho-social context. In addition to detailed information about the causes of vitiligo, its course, associated morbidities, we discuss with the affected patients the various treatment modalities available. Treatment modalities, include topical therapies, nbUVB, excimer laser as well as camouflage. Outer root sheath cell transplantation, developed at our department, is occasionally offered in severe cases.

## Service

Consultations	2011	2012	2013	2014
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### Out-patient unit

#### Number of consultations

Out-patient unit (including private consultations)	15 800	17 922	18 730	20 142
Out-patient day clinic	3 015	3 284	3 256	3 814
Surgery sector	1 980	1 975	1 998	2 290
Phototherapy sector	4 799	5 254	5 475	6 292
Corrective cosmetic procedures	1 050	697	808	353

#### Activity of the hospital In-patient unit

Number of hospitalised patients	504	538	527	649
Total of hospital days	3 068	2 866	2 466	2 423
Hospital average length of stay (days)	6.09	5.33	4.68	3.73

#### Activity of the dermato-allergology laboratory

Patch tests (number)	1 234	1 818	3 080	3 548
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#### Activity of the dermatopathology sector

Processed external biopsy specimens	11 519	11 836	11 725	12 903
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## Research and development projects

### 1. Atopic eczema and contact dermatitis

Pathogenic mechanisms of chronic inflammatory skin diseases including eczema represent an important research area in our Department. By analysing the skin infiltrating cells and cytokines as well as their regulation, we aim to better understand the pathophysiologic mechanisms of eczema. Within this research frame, our interest is specifically focused on the function of eosinophilic granulocytes. Better characterisation of their pathogenic role in eosinophilic skin diseases is expected to help the development of new therapeutic strategies.

### 2. Autoimmune blistering diseases: bullous pemphigoid and pemphigus

Our group is implicated in studies aimed at understanding the pathophysiologic mechanisms of pemphigoids and pemphigus, a group of severe autoimmune blistering diseases of the skin and mucosae. These diseases run a chronic course, are frequently difficult to treat and are associated with a significant morbidity and mortality. Overall, understanding the etiopathogenesis of pemphigus and pemphigoid may provide crucial additional insights into basic mechanisms of autoimmunity and may help to design more specific therapeutic strategies.

The pemphigoids include bullous pemphigoid, gestational pemphigoid and cicatricial pemphigoid. They are a relatively common group of autoimmune blistering disorders associated with autoantibodies directed against two proteins of the cutaneous basement membrane zone, BP180 and BP230. The current project is aimed at: 1) characterising the humoral and autoreactive T cell response to BP180 and BP230 in the disease course of the pemphigoids; 2) identifying laboratory markers predicting disease activity and outcome; 3) developing innovative diagnostic tools such as ELISAs and microarrays for the detection of patients' autoantibodies with high sensitivity and specificity.

Pemphigus is another severe autoimmune blistering disease of the skin and mucous membranes. There are two major types of pemphigus: pemphigus foliaceus and pemphigus vulgaris. There is a related disease called paraneoplastic pemphigus sharing some overlap with pemphigus. They are caused by the production of IgG autoantibodies directed against cell-cell adhesion complexes, called desmosomes. Specifically, two transmembrane desmosomal proteins are characteristically targeted by patients' autoantibodies, desmoglein 1 and desmoglein 3. Paraneoplastic pemphigus autoantibodies target several intracellular linkers of the cytoskeleton, a family termed plakins, and a novel protein identified in our laboratory, called alpha-2 macroglobulin-like 1 protein, which is an extracellular, broad range protease inhibitor.

Our ongoing project represents a joined effort of several European groups with the following long term goals: 1) analysis of the autoantibody-driven effector phase frequently involving «epitope spreading»; 2) characterisation of the molecular events

leading to intraepidermal blistering; 3) analysis of the impact of therapeutic strategies such as the monoclonal antibody anti-CD20 (rituximab) on the cellular and humoral autoimmune response in pemphigus, and 4) definition and establishment of clinical parameters as valid measurements for the extent and activity of the disease and life quality assessment in pemphigus.

### 3. Characterisation of the interactions between plakins and the cytoskeleton

Our group is primarily implicated in basic investigative studies aimed at characterising 1) the association of plakin family members, plectin, desmoplakin and bullous pemphigoid antigen 1 (BPAG1), with the cytoskeleton in epithelia and striated muscle cells; 2) the regulation of these interactions by posttranslational modifications (such as phosphorylation), and 3) the contribution of the plakins to the overall organisation of the cytoskeleton since plakins can usually interact with at least two components of the cytoskeleton, the microfilaments, the microtubules and/or the intermediate filaments, and specifically anchor these structural networks to various membrane complexes. All these connections are critical for the maintenance of the cell architecture and tissue resilience to mechanical forces. In fact, mutations in the genes coding for plectin, desmoplakin, BPAG1, and intermediate filaments cause a variety of devastating human diseases, attesting to the importance of these proteins for tissue integrity.

### 4. Cutaneous drug reactions

The main research goals are 1) to improve the understanding of the molecular interactions of drugs/chemicals with immune cells, i.e. T cells, dendritic cells and 2) to dissect the mechanisms by which these interactions stimulate and affect the immune system. These studies are planned to pave the way for improved methods to diagnose adverse drug reaction and to improve risk assessment of chemicals/drugs.

### 5. Cutaneous T cell lymphoma

Primary cutaneous T-cell lymphomas (CTCL) represent a heterogeneous group of extranodal non-Hodgkin lymphomas. Mycosis fungoides (MF) and Sézary syndrome (SS) are the most common types. Our specialists are well-connected internationally, especially with the Groupe Français pour l'Étude des Lymphomes Cutanés (GFELC) and with the Dermatology clinic in Graz, where we studied the characteristics of rare cutaneous CD4+ pleomorphic skin lymphomas and related diseases.

### 6. Hidradenitis suppurativa

Hidradenitis suppurativa (also called acne inversa) is a chronic inflammatory disorder of the apocrine gland-bearing skin. The clinical course can be devastating. End-stage hidradenitis suppurativa is disabling and has a profound impact on the quality of life. At present, the pathophysiology of this condition is still poorly understood. To better

understand its mechanisms we are currently performing studies using immunohistochemical and molecular biology methods to better comprehend the mechanisms leading to chronic inflammation. To better help these patients we have a special hidradenitis suppurativa clinic (responsible: Professor R. Hunger) at our department. At present we can offer these patients many different therapeutic options including the participation in clinical studies (i.e. biologicals, laser treatment, extracorporeal shock wave).

### 7. Human interleukin 9-producing T helper memory cells and their role in anti-tumor immune response in malignant skin disease

Human T helper (TH) cells are crucial mediators of the adaptive immune system. To respond to the myriad of infectious and non-infectious challenges, they have evolved into distinct subsets such as TH1, TH2, or TH17 cells. IL-9 producing TH9 cells have recently been proposed as a novel subset of TH cells and studies in animal models suggest a protective role for these cells in tumor immunity. However, studies of TH9 cells thus far have largely been limited to TH cells differentiated in vitro. Studies of human in vivo differentiated TH9 cells are lacking. Therefore, the existence of TH9 cells as an authentic cell type has been called into question.

Our data now indicate for the first time the existence of human in vivo differentiated TH9 cells, thus raising the possibility to investigate their true identity and functional properties. In addition, we find large numbers IL-9 expressing cells in the immune infiltrate of human melanoma, thus warranting further investigation of the role of TH9 cells in the human anti-melanoma immune response.

The overarching aim of our research is to investigate the identity and properties of human TH9 cells and their role in the anti-melanoma immune response. Based on our preliminary data, we hypothesize that TH9 cells are in fact a distinct subset and that they can be identified by a specific set of skin-homing receptors. Because of the robust tumor immunity mediated by TH9 cells in mice, we hypothesize that they can be found at higher numbers in the immune infiltrate of primary melanomas compared to metastasized melanoma, since metastasis requires immune evasion of the tumor, and that the number of TH9 cells correlates with disease prognosis.

Established immunological methods for the analysis of human T cell biology (cell culture, intracellular FACS staining, FACS sorting, ELISA, Luminex cytokine multiplex assay, RT-PCR, immunohistochemistry, immunofluorescence double staining) are used in combination with a novel method for ex vivo analysis of human tissue-resident T cells. Answering the questions raised in this project will increase our understanding of TH cell biology, lead to a thorough characterization of human TH9 cells and shed light on their contribution to the anti-melanoma immune response. Based on surprising recent findings that TH9 cells mediate superior tumor immunity in mice, it seems highly promising to investigate the biology of TH9 cells in humans; a better understanding of these cells may lead to the development of innovative T cell based immunotherapies for malignant melanoma.

## 8. Non-melanoma skin cancers

Our research is focused on epidemiologically studies on NMSC.

- We are collecting UV-exposure behavioural data of the general population
- We aim to identify patients that are at high risk for developing NMSC (and melanoma) in the setting of immune suppression e.g. due to organ transplantation. Our collaborations with the different departments of the Transplant Board of the Inselspital are constantly developing.

## 9. Psoriasis research

Our studies are aimed at investigating basic immunological mechanisms, e.g. cytokines and chemokines and their regulation through therapeutic interventions in psoriasis. As control, findings are compared to those obtained in different forms of eczema. These investigations may help to identify new targets for future therapeutic intervention.

Another field of expertise are the clinical trials with new therapeutic agents. Sonic hedgehog inhibitors are administered to otherwise untreatable basal cell carcinoma. Future projects involve the genomic, proteomic and metabolomic characterisation of highly aggressive and recurrent NMSC in heavily sun-damaged non-immunosuppressed patients and in organ transplant recipients. This kind of research will involve a collaboration with the Department of Clinical Laboratory (Chair: Professor G. Fiedler). These studies are expected 1) to be useful for the selection of high-risk patients who may benefit from more aggressive treatment and follow-up protocols and 2) to identify targets for novel pharmacological intervention.

## Results 2013–2014

### Allergies

Eosinophilic esophagitis (EoE) is often associated with atopic airway and skin diseases. More than 80% of EoE patients are sensitized to aero- and/or food allergens and immunoglobulin (Ig)E-mediated immune responses to microbes have been reported to be deleterious in connection with atopic diseases. We found that *Candida albicans* and profilins, which are cross-reactive plant allergen components, were frequent sensitizers in adult EoE patients.

In the two rare pustular skin disorders with systemic involvement, acute generalized exanthematous pustulosis and generalized pustular psoriasis, we have found that the interleukin 17A/F was highly expressed by the innate immune cells neutrophils and mast cells. Our findings provide a rationale for a therapeutic approach with modern antibodies against IL-17A/F.

The heat shock protein (HSP) 90 plays an important role in cell survival, cytokine signalling, and immune responses. Therefore, we have investigated its potential involvement in the chronic inflammatory skin disease psoriasis. Our data show that the inducible isoform HSP90 $\alpha$  is significantly up-regulated in epidermal keratinocytes and mast cells of lesional skin. Interestingly, patients treated with ustekinumab, a human monoclonal antibody neutralizing IL-12 and IL-23, exhibited a reduced HSP90 expression in psoriatic skin in parallel with clinical resolution of psoriasis. Our findings provide a rationale for a novel therapeutic approach in psoriasis with HSP90 inhibitors.

In mice, T helper type 9 (TH9) cells, which specifically produce interleukin 9 (IL-9), mediate tumor immunity and participate in autoimmune and allergic inflammation. We have characterized human TH9 cells and found that most memory TH9 cells were skin-tropic or skin-resident. Many of them were stimulated by the opportunistic fungus *Candida albicans*. IL-9 production was transient and preceded the up-regulation of other inflammatory cytokines such as interferon- $\gamma$ , IL-9, IL-13, and IL-17 by skin-tropic T cells. IL-9-producing T cells were increased in the skin lesions of psoriasis, suggesting that these cells may also contribute to human inflammatory skin diseases.

Although due to different causes, eczematous skin lesions of atopic dermatitis and allergic or irritant contact dermatitis are characterized by the same typical clinical signs. We investigated the expression of interleukin 17 (IL-17) and markers of tissue remodeling in these acute eczematous skin lesions. We found that in contrast to other cytokines, IL-17, as well as IL-21 and IL-22, were expressed in all eczema subtypes independent of their pathogenesis. There was a correlation between the expression of the tissue remodeling markers tenascin C and matrix metalloproteinase 9 with IL-17+ T cells and neutrophils, respectively, the latter responding to IL-17.

## Melanoma

The anti-tumour immune response plays an important role in the prognosis of melanoma. High numbers of circulating regulatory T cells have been associated with rapid disease progression. We found that disease-free survival and overall survival were significantly longer in patients expressing in the primary melanoma low levels of FOXP3, a transcription factor specific for regulatory T cells.

## Paraneoplastic pemphigus

Pemphigus is severe autoimmune blistering disease of the skin and mucous membranes. Among the various pemphigus forms, paraneoplastic pemphigus (PNP) is the most severe. It is a muco-cutaneous disease associated with underlying lymphoproliferative disorders and characterized by the presence of auto-antibodies and cell-mediated immune response mainly against the transmembrane protein desmoglein 3, the plakins envoplakin, periplakin, and the broad range secreted protease  $\alpha$ 2-macroglobulin-like 1 (A2ML1). In a collaborative study, we found that 69 % of PNP patients produce anti-A2ML1 autoantibodies, which could be pathogenic by reducing the adhesion properties of keratinocytes. Moreover, we participated in a study aimed at finding the best and easiest method to diagnose PNP.

## Plakins and the cytoskeleton

Plakins are intracellular proteins that interact with various elements of the cytoskeleton and critically regulate the cytoarchitecture of cells. They play a crucial role in the maintenance of the integrity of tissues such as the skin and muscles that are subjected to mechanical stress. We demonstrated that the phosphorylation of a specific serine in the carboxyl extremity of the plakin plectin has an inhibitory effect on its interaction with intermediate filaments. Furthermore, we identified two signalling pathways stimulating this posttranslational modification of plectin and two different protein kinases responsible for this phosphorylation, the cyclic AMP-dependent protein kinase (PKA) and the mitogen-activated protein kinase (MAPK)-interacting kinase 2 (MNK2). It is the first time that a link between MNK2 and the cytoskeleton has been found. We also characterized the complex interaction of plectin with several types of intermediate filaments by various approaches, including a recently developed novel and rapid binding method based on the expression of fluorescent proteins in mammalian cells (FluoBACE). Finally, we found that the plakins BPAG1-a and -b associate with the microtubule plus-end-binding proteins EB1 and EB3 and modulate vesicular transport, Golgi apparatus structure and cell migration in myoblasts.

## Postgraduate teaching courses

21.02.2013	Neues beim Laser <i>Dr M. Adatto, Dr K. Fritz, Dr N. Dietrich, Dr N. Irla</i>
30.05.2013	Seborrhoische Erkrankungen <i>Guests: PD Dr M. Müller, Basel, Dr S. Läuchli, Zürich, Dr M. Kägi, Zürich</i>
29.08.2013	Sommerquiz – interaktive Fallvorstellungen Residents of the Dept of Dermatology Bern
24.10.2013	The Yushchenko case and what we learned from dioxin poisoning <i>Guest: Professor J.-H. Saurat</i>
06.03.2014	Radiotherapie <i>Guests: Dr F. Behrensmeier, Bern, Professor R. Panizzon, Dr G. Duchini, Biel</i>
05.06.2014	Autoimmunität <i>Guests: Dr M. Hoernes, Zürich, Professor M. Seitz, Bern, PD Dr K. Scherer Hofmeier, Basel, Professor P. Villiger, Bern</i>
11.09.2014	Komorbiditäten bei Psoriasis <i>Professor N. Yawalkar</i>
15.10.2014	Dermatologie in Moshi <i>Dr H. Beltraminelli</i>
06.11.2014	Du traitement des mycoses quotidiennes comme un roman policier <i>Guest: Dr F. Baudraz-Rosselet</i>
13.11.2014	Skin barrier dysfunction and inflammation <i>Professor D. Simon</i>
27.11.2014	Gesichtsdermatosen <i>Guest: Professor H. Schöfer, Frankfurt</i>

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#### **Master thesis and PhD thesis**

Nathalie Friedli: Epithelial barrier function in eosinophilic esophagitis (Professor D. Simon); Master thesis, Pharmazie, Uni Basel

Robin Kaufmann: Dermatologische Probleme bei Organtransplantierten (Professor R. Hunger, Dr. P. Oberholzer); Master thesis

Christoph Sebastian: Sonnenschutz bei Freizeitsportlern (Professor R. Hunger, Dr. P. Oberholzer); Master thesis

Stillhard Andrea: Tumor-stroma characteristics in melanocytic lesions - Analysis of elastic fibres in regressing/fibrosing/scarring zones (Professor L. Borradori, Dr. H. Beltraminelli); Master thesis

Kseniia Poliakova: Localization and function of Bullous Pemphigoid Antigen 1 in C2.7 myoblasts (Professor L. Borradori, Dr B. Favre); PhD thesis

Jamal-Eddine Bouameur: Characterization of the interaction of plectin with intermediate filaments and its regulation by phosphorylation (Professor L. Borradori, Dr B. Favre); PhD thesis

#### **Guest doctors**

Sallam Mohammed Abdel Azeem Shahwan from Cairo, Aegypt (16.09.2011 - 15.06.2013)

Kexiang Yan from Shanghai, China (18.09.2013 - 17.09.2014)

Davide Basso from Genova, Italy (01.11.2013 - 28.02.2014)

Samson Kiprono from Kakamega, Kenya (11.11.2013 - 08.12.2013)

Simone Ribero from Torino, Italy (01.01.2014 - 31.01.2014)

Alice Amani from Kigali, Republic of Rwanda (31.03.2014 - 20.06.2014)

Workalemahu Belachew from Mekelle, Ethiopia (01.05.2014 - 31.07.2014)

#### **International recognitions and awards**

Professor L. Borradori

– Honorary member of the Hellenic Society of Dermatologie (2013)

– International invited member of the American Dermatological Association (ADA) (2014); [www.amer-derm-assn.org](http://www.amer-derm-assn.org)

– President-elect of the European Academy of Dermatology and Venereology (EADV) (2014-2016); [www.eadv.org](http://www.eadv.org)

– Vice-president International Society of Dermatology (ISD); [www.intsocderm.org](http://www.intsocderm.org)

Professor E. Haneke

– International Honorary Member of the American Dermatological Association (ADA)

– Clinical Care Award of the European Academy of Dermatology and Venereology (EADV)

Dr Dr A.-A. Ramelet

– Silver Pin (Officer) of the European Academy of Dermatology and Venereology (EADV) (2013)

– Ratschow Memorial Medal, Curatorium Angiologiae Internationalis, Deutsche Gesellschaft für Phlebologie (2014)

## Grants

Dr Ch. Schlapbach

- Novartis Foundation for biomedical research: Characterizing human interleukin 9-producing T helper memory cells and their role in inflammatory skin disease. CHF 60'000; 2013
- Bernese League against cancer: Characterizing human interleukin 9-producing T helper memory cells and their role in anti-tumor immune response in malignant melanoma. CHF 50'000; 2013
- Inselspital – Research grant: Characterizing human interleukin 9-producing T helper memory cells and their role in anti-tumor immune response in malignant melanoma. CHF 80'000; 2013

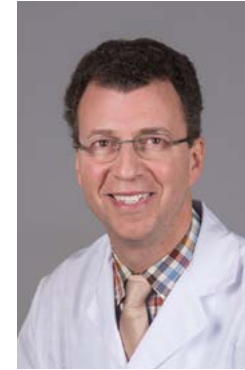
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## Consultant physicians



**Dr M. Adatto**  
(Laser)



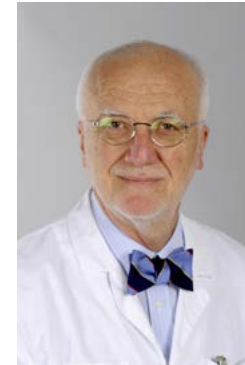
**Dr P. de Viragh**  
(Trichology)



**Professor E. Haneke**  
(Nail diseases)



**Dr H. Nievergelt**  
(Dermatopathology)



**Dr Dr A.A. Ramelet**  
(Phlebology)



**Dr A. Skaria**  
(Mohs Surgery)



Medical staff



Out-patient clinic staff



Dermatopathology staff



In patient staff



Administration staff



Head of nursing team

## **Inselspital**

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[www.insel.ch](http://www.insel.ch)

[www.dermatologie.insel.ch](http://www.dermatologie.insel.ch)

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