**ONGOING RESEARCH PROJECTS**

**SKIN CANCER**

**Skin cancer in organ transplant recipients**

The high risk of skin cancer after organ transplantation is a major clinical challenge. Taking advantage of a high-quality national cancer registry, we have studied long-term changes in the risk of cutaneous squamous cell carcinoma after organ transplantation in Norway.

PhD project: Syed Mohammad Husain Rizvi. Main supervisor: Petter Gjersvik.

**Fractional laser-assisted daylight photodynamic therapy for multiple actinic keratoses of the scalp in organ transplant recipients: a randomized half-side comparative trial**

Organ transplant recipients (OTRs) are at high risk of skin cancer, especially squamous cell carcinoma (SCC). SCC often develops in the area of field cancerization, areas exposed for chronical sun damage and multiple actinic keratoses (AK). It is of high clinical value to treat precancerous lesions such as AK among OTRs. In order to evaluate more effective treatment of AKs/field cancerization in OTRs we set out a randomized half-side comparative trial to investigate the effect of pre-treating the skin with ablative, fractional carbon dioxide laser before daylight PDT.

Project leader: Syed Mohammad Husain Rizvi. Others: Gro Mørk, Petter Gjersvik, Per Helsing.

**Folliculotropic mycosis fungoides**

Folliculotropic mycosis fungoides (FMF) is a variant of mycosis fungoides (MF) with distinct clinical and histopathological features. Folliculotropism may suggest that antigen-stimulation by particular antigens present in the hair follicle contribute to the pathogenesis.

PhD project: Patty Mantaka. Main supervisor: Jan Delabie. Co-supervisor: Petter Gjersvik. Collaborator: Department of Pathology, OUS Radiumhospitalet.

**Validation of staging systems for cutaneous squamous cell carcinoma: a population-based, nested case-control study**

In this study, we aim to determine the rate of metastasis in cutaneous squamous cell carcinoma (cSCC) in Norway, by using high-quality population-based data. Also, we aim to assess the impact of reported risk factors for metastasis and to externally validate three existing current cSCC staging systems for their reproducibility and practicality.

Project leader: Ingrid Roscher. Others: Petter Gjersvik, Per Helsing. Collaborators: Department of Pathology, Oslo University Hospital, Oslo, Norway; Cancer Registry of Norway; Oslo Centre for biostatistics and epidemiology, Oslo University Hospital, Oslo, Norway

**SKIN INFLAMMATION**

**Keratinocyte stress responses and inflammation**

The relationship between keratinocyte stress responses and inflammation in human skin is not well known. In this study, we explore the effect of various stress conditions on keratinocyte immune function with special emphasis on interleukin-33 and its regulation by osmotic stress.

Project leader: Olav Sundnes. Collaborators: Guttorm Haraldsen, Department of Pathology, K. G. Jebsen Inflammation Research Centre.

**Early gene expression changes as predictors of therapeutic response to narrow-band UVB in atopic dermatitis**

Atopic dermatitis (AD) is a common, chronic inflammatory skin disease with increasing prevalence. There is a large unmet need for better treatment modalities, and the therapeutic repertoire when compared to that of psoriasis is appalling. UV-treatment is an effective and safe treatment modality, yet we know surprisingly little about the exact molecular mechanisms driven by this type of treatment. A better understanding of this could shed light on the pathophysiology behind AD and lead to more efficient treatment protocols in the future.

PhD-project: Astrid Lossius. Main supervisor: Jan-Øivind Holm. Co-supervisors: Teresa Løvold Berents, Olav Sundnes, Guttorm Haraldsen. Collaborators: Department of Pathology, K. G. Jebsen Inflammation Research Centre.

**Atopic dermatitis and skin barrier function in infancy and early childhood**

The overall aim of this project is to investigate established and potential risk factors for the development of atopic dermatitis in early life, especially the role of skin barrier dysfunction, *filaggrin* mutation status, upper airway colonization of *S. aureus*, excessive weight-for-length and vitamin D levels.

PhD-project Teresa Løvold Berents. Main supervisor: Petter Gjersvik. Co-supervisor: Karin Lødrup Carlsen, Department of Pediatrics and Pål Aukrust. Collaborators: ORAACLE

**Skin and amniotic fluid microbiome and atopic dermatitis**

In the recent years, skin microbiome studies are emerging, and there is increasing evidence of a lower microbial diversity in the atopic skin. It is still uncertain if a dysbiosis occurs before the development of atopic dermatitis or if it is a consequence of it. New sequencing methods are suggesting a unique microbiome also in the amniotic fluid that resembles the placenta and the infants’ meconium. In this PhD project of PreventADALL, we will investigate both the microbiome of the amniotic fluid as well as that in the skin in relation to early development of atopic dermatitis.

PhD-project: Eva Maria Rehbinder. Main supervisor: Karin C. Lødrup Carlsen. Co-supervisor: Linn Landrø. Collaborators: PreventADALL.

**A NORwegian multicentre trial assessing the effectiveness of tailoring infliximab treatment by therapeutic DRUg Monitoring (NOR-DRUM)**

Biological treatment with cytokine-neutralizing antibodies such as the anti-TNF antibody infliximab (INX) is highly effective for treatment of a wide range of auto-inflammatory diseases, including inflammatory bowel disease, rheumatoid arthritis and psoriasis. However, optimal response to INX treatment may depend on individual dosage. Furthermore, several patients eventually develop anti-drug antibodies (ADAb) against INX, making the treatment ineffective. The NOR-DRUM trial is a prospective randomized clinical algorithm study that investigates whether monitoring INX serum levels and INX ADAb leads to better treatment or not in terms of minimizing under-treatment, reduce over-treatment, prevent hypersensitivity and detect treatment failures prior to a clinical flare.

Project leader: Silje Watterdal Syversen, MD PhD. Others: Øystein Sandanger, Kristine Halvorsen Hortemo, Cato Mørk. Collaborators: Revmatologisk avdeling, Diakonhjemmet ved Silje Watterdal Syversen (prosjektleder), professor Espen A. Haavardsholm, professor Tore K. Kvien, Gastromedisinsk avdeling, Akershus universitetssykehus ved professor Jørgen Jahnsen, ogAvdeling for medisinsk biokjemi OUS-Radiumhospitlaet ved David J. Warren og Nils Bolstad**.**

**A novel mutation decreases innate immune responses**

Three siblings struggled with atopic dermatitis as well as increased tendency of warts and upper respiratory tract infections. In the process of diagnosis, exome sequencing revealed a previously uncharacterized mutation in a gene coding for a protein involved in negative regulation of inflammatory responses. In this project, we investigate the patients’ phenotype at the cellular and molecular levels in terms of cytokine profiling and protein expression of innate immune receptors. Induced pluripotent stem cells obtained from the patients and healthy controls will be a major tool. We hypothesize a gain-of-function mutation that leads to impaired innate immune responses and subsequently a Th2 bias.

Project leader: Børre Fevang, MD PhD, Seksjon for klinisk immunologi og infeksjonsmedisin og Institutt for indremedisinsk forskning, OUS Rikshospitalet. Others: Øystein Sandanger. Collaborators: Institutt for indremedisinsk forskning, OUS Rikshospitalet ved Børre Fevang, Pål Aukrust og Arne Yndestad, Seksjon for klinisk immunologi og infeksjonsmedisin, OUS Rikshospitalet ved Børre Fevang og Pål Aukrust, Avdeling for nyfødtscreening, OUS Rikshospitalet ved Asbjørg Stray Pedersen, og Norsk senter for molekylærmedisin, UiO ved Kjetil Tasken.

**PreventADALL**

This prospective multicenter birth cohort study will test if primary prevention of allergic diseases is possible by simple and low cost strategies, and secondary to assess the impact of xenobiotic exposure and microbiota in and on the body and the environment on allergic disease development.

Project leader: Karin Lødrup Carlsen. Others: Linn Landrø, Eva Rehbinder, Kim Endre. Collaborators: OUS, Karolinska University Hospital, Østfold Hospital Trust, University Hospital Lausanne, National Skin and Allergy Hospital Helsinki, Nowegian Institute of Public Health.

**Whole exome sequencing for diagnosis of inherited ichthyoses**

A gene panel applying whole exome sequencing (WES) in the routine investigation of patients with ichthyoses was introduced at the Oslo University Hospital in 2013. The diagnostic outcome of WES, including a description and evaluation of novel pathogenic mutations in a cohort of 34 consecutive patients, is now being analyzed.

Project leader: Jan Cezary Sitek. Collaborators: Department of Medical Genetics, OUS

**Keratolytic winter erythema – genetic and functional studies**

We have recently identified the genetic cause for keratolytic winter erythema (KWE) and are now pursuing functional investigations to elucidate pathogenetic mechanisms underlying the disease. In addition, we aim to define possible therapeutic approaches based on the knowledge from our investigations.

Project leader: Jan Cezary Sitek. Others: Olav Sundnes. Collaborators: Torunn Fiskerstrand, Haukeland University Hospital, Norway; Nijmegen University Hospital, The Netherlands; Michele Ramsay, University of the Witwatersrand, South Africa; and University of Halifax, Canada.

**Genetic causes for inherited ichthyoses applying next-generation sequencing**

Since 2013, patients with ichthyoses have been investigated with gene panels using next-generation sequencing (NGS) to identify the molecular cause for their disease. Approximately 20% of such patients have a negative gene test. These patients will be studied further by investigating their total exome, aiming at identifying new causes for their ichthyosis.

Project leader: Jan C Sitek. Collaborators: Department of Medical Genetics, OUS

**Treatment of genital lichen planus in women**

An investigator-initiated, double-blinded, randomized, placebo-controlled trial on perioral treatment with the phosphodiesterase 4-inhibitor aprimelast for genital erosive lichen planus in women, assessing the effect on patient-oriented, clinical and immunological measures.

PhD project (in planning): Kristin Skullerud, Olafia Clinic. Main supervisor: Anne Lise Ording Helgesen. Co-supervisor: Petter Gjersvik.

**Quality of life in women with genital erosive lichen planus**.

Using three validated questionnaires before and 6 months after vulvovaginal photodynamic therapy, quality of life in women with genital erosive lichen planus will be documented.

Project leader: Anne Lise Ording Helgesen. Others: Kristin Skullerud, Petter Gjersvik. Collaborators: Department of Obstetrics and Gynecology, Ullevål Hospital, Norwegian National Advisory Unit on Women’s Health.

**Effect of somatocogntive therapy vs treatment as usual in provoked vestibulodynia – a randomized controlled trial.**

Provoked vestibulodynia (PVD) is the most common subtype of vulvodynia comprising 65-80% of all cases and affecting around 8-12% of women in the general population. The study seeks to validate multimodal physical therapy approach for PVD, and provide further insights into the working mechanisms behind treatment outcomes and predictors of treatment success or failure.

PhD project. Main supervisor Gro Killi Haugstad, co-supervisor Anne Lise Helgesen, co-supervisor Slawomir Wojniusz. Collaborators: Department of Gynecology, Vulva Clinic, OUS, Department of Physiotherapy (HiOA).

**Study of the efficacy of early intervention with secukinumab compared to UVB in patients with new onset moderate to severe plaque psoriasis.** An international, multicenter, phase IV study

Project leader: Joar Austad. Other: Olav Sundnes. Collaborators: Novartis

**SKIN MICROSIRCULATION**

**Finger pulp blood flow in systemic sclerosis patients with digital ulcers treated with sympathetic blockade**

We aim to study impact of Botulinum toxin A (Botox®) and plexus blockade on blood perfusion of the finger, the effect of Botox as treatment on ulcer healing and recurrence. Measurements of skin perfusion are made using Laser Doppler flux immediate before treatment, and 4 weeks after treatment.

Project leader: Tone Kristin Bergersen. Collaborators: Department of Rheumatology.

**Treatment of pyoderma gangrenosum at the Department of Dermatology, Oslo University Hospital**

We aim to study local and systemic treatment of pyoderma gangrenosum in a retrospective cohort study designed as student project.

Project leader: Tone Kristin Bergersen. Others: Katrine Ness Johnsen, medical student.

**Erythromelalgia – clinical, genetic and functional studies**

Throughout the last 30 years, almost 300 patients have been diagnosed with erythromelalgia at the Department of Dermatology, Oslo University Hospital, of whom five have had limb-threatening erythromelalgi. We wish to publish this series of patients to document that erythromelalgia may lead to loss of limbs. 35 patients with primary erythromelalgia have been tested for mutations in the SCN9A gene.

Phd project: Mari S. Kvernebo. Main supervisor: Knut Kvernebo. Co-supervisors: Petter Gjersvik, Cato Mørk. Collaborators: Xenon Pharmaceuticals (genetical testing)

**Sturge-Weber syndrome**

Sturge-Weber syndrome (SWS) is believed to result from somatic mutations in endothelial cells. In this study, we search for possible causative somatic mutations by sequencing DNA from skin biopsies of port wine stains and non-affected tissues in patients with SWS.

Project leader: Olav Sundnes. Others: Jan Sitek. Collaborators: Kaja Selmer og Roar Fjær (geneticists).

**QUALITY OF LIFE/EPIDEMIOLOGY**

**High mortality of cutaneous melanoma in Norway: A population-based study of prognostic factors**

The mortality rate for cutaneous melanoma (CM) in Norway is the highest in Europe, higher than in countries with comparable incidence rates. The Norwegian Malignant Melanoma Registry (NMMR), established in 2008, enables study of prognostic factors of CM death. Using population-based data from NMMR and the national Cause of Death Registry, we aimed to study sex, age, residency, tumor location and histopathological characteristics of the primary tumor for all CM cases in Norway, and the associations between these factors and CM specific death. Knowledge from this study could help targeting secondary preventive measures towards the Norwegian population.

Project leader: Syed Mohammad Husain Rizvi. Others: Per Helsing. Collaborators: Norwegian Cancer Registry.

**A European multicenter study on depression, anxiety, quality of life and attachment among adult patients with common skin disorders**

A cross-sectional observation study of patients with common skin disorders in 13 European countries, studying the prevalence and burden of itch.

Local project leader: Jon Anders Halvorsen. Collaborators: European Society of Psychiatry and Dermatology, Florence Dalgard and 13 dermatological centres across Europe.

**Atopic dermatitis among children in Norway – prevalence and risk factors**

Based on data from the Norwegian Prescription Registry.

PhD project: Cathrine Helene Mohn. Main supervisor: Per Lagerløv, University of Oslo. Co-supervisor: Jon Anders Halvorsen.