Annual Activity Report 2021

LEO Foundation
Skin Immunology
Research Center

UNIVERSITY OF COPENHAGEN

Contents

Introduction

With a unique focus on inflammatory skin diseases and a 10-year perspective in research and educational development, the LEO Foundation Skin Immunology Research Center unravels key questions on some of the world's most widespread skin conditions.

The skin is our largest organ and the number of skin diseases is staggering, with more than 3,000 known diseases. Some are quite manageable, but remain incurable and unexplained, whereas others are serious and even life-threatening. In the US, skin disease impacts one in four persons in a given year and, in Denmark alone, up to 20% of school children suffer from atopic dermatitis. As such, skin diseases have a huge impact on individual quality of life as well as on society as a whole.

The field of dermatology – the branch of medicine dealing with the skin, its structure, functions and diseases – draws on research from immunology, pathology, microbiology, neurology and oncology. Our knowledge of skin diseases has accelerated over the past decade, and the pathophysiological basis of many of the diseases is becoming better understood. Conceptualising the skin as an immunological organ has proven very fruitful, and discoveries within immunology have paved the way for new treatments.

Despite significant progress, the pace of innovation is, however, not sufficiently high, and new treatments are slow to reach the patients. To boost our knowledge level, we established the LEO Foundation Skin Immunology Research Center (SIC) at the University of Copenhagen in 2019, based on an ambitious donation of DKK 400 million over 10 years by the LEO Foundation.

SIC focuses on inflammatory skin diseases, including psoriasis, atopic and contact dermatitis and cutaneous T cell lymphoma (the latter as a model disease), which are all characterised by a strong immunological component. SIC's aim is to integrate and advance basic and clinical scientific approaches to skin disease and develop future leaders in the field, at the same time increasing knowledge and awareness of skin and skin diseases among medical professionals, patients and the public. Our aim is to grow into a beacon for skin research in Denmark with a worldwide impact. ⟋

MISSION

To better understand, prevent and treat skin diseases for the benefit of the individual patient.

VISION

The LEO Foundation Skin Immunology Research Center will become a world-leading centre for research and education in skin and skin diseases.

DISEASE FOCUS

- Psoriasis
- Atopic dermatitis
- Contact dermatitis
- T cell lymphoma as a model

KEY RESEARCH THEMES

- Skin disease mechanisms
- Patient stratification and precision medicine
- Novel ways to attack and cure skin diseases

Group Leader and Professor Liv Eidsmo assumed responsibility as Executive Director of SIC in September 2021.

Report from the Executive Director

When I arrived at the University of Copenhagen last autumn, the SIC community was buzzing with scientific interaction in what felt like post-lockdown euphoria. This energy was a great reflection on how our past Acting Executive Director, Professor Charlotte Menne Bonefeld, who supported scientific and educational development through the challenges of the COVID-19 pandemic. As I took over the leadership from Charlotte, my most important task is to encourage a research environment where we dare to ask and pursue high-risk questions that challenges current dogmas in skin immunology. It is the perfect setting to take my own research programme in new directions, closer to the clinic.

The long-term, collaborative perspective of SIC enables us to pursue research programmes of relevance to persons living with chronic inflammatory skin diseases. Many of the investments during the first three years of SIC operations have already paid off through high quality publications, educational programmes and clinical collaborations. This year, SIC published the first paper based on the single cell sequencing technology, a technical platform that was financed though the Center. One group discovered a new mechanism of early allergic reactions in the skin. New investigators and funding to study critical questions with a translational scope are coming in. An ambitious clinical biobank was initiated with clinical collaborators, with samples from 3,000 patients with illnesses such as psoriasis and eczema. The BIOSKIN Programme will be a unique resource not only for SIC, but also for researchers around the world.

Within the Center, our biweekly internal lunch seminar series is the heart of our scientific interaction. Our postdocs have started a journal club to dig deeper into new papers to follow the movement in the field, and our Young Investigator Network has brought basic and clinical collaborators together for scientific discussions and career development activities. I have been deeply impressed with the scientific quality and discussions among all levels of scientists across the research groups, and I consider it a great honour and privilege to lead the LEO Foundation Skin Immunology Research Center.

My personal favourite moment was when SIC welcomed researchers from all over Europe to our first Summer School for three intense days of scientific discussion in the beautiful setting of the Danish resort, Hornbæk. We look forward to participants from all over the world for our next Summer School as travel restrictions are being lifted. I have also enjoyed all the outreach activities, welcoming school children to SIC and participating in the World Psoriasis Day at the top of the Mærsk Tower.

My first priority as Director has been to expand the SIC faculty and thereby our scientific platform, and it has been inspiring to see students and postdocs across the Center actively involved in the evaluation of potential future members of our community. Thank you for your commitment, bright ideas and for contributing to making SIC a thriving platform for impressive science. I look forward to another exciting year in 2022.

Report from the Dean

Ulla Wewer is Dean of the Faculty of Health and Medical Sciences, University of Copenhagen.

The LEO Foundation Skin Immunology Research Center (SIC) is resting on four key pillars in our efforts to make a difference for people with skin diseases across the world: Excellence in research, training of the next generation of skin immunologists, clinical and translational integration of research activities and outreach to patients and the general public. I am delighted to conclude that SIC in 2021 made significant progress within all four focus areas.

With the commencement of Professor Liv Eidsmo as Group Leader and Executive Director, SIC not only has four growing and active basic research groups interacting at the headquarters on the 12th floor of the Mærsk Tower, the Center also has its permanent leadership in place to set the scientific direction for the coming seven years. Since its inauguration, the Center has doubled in size and substantially broadened its field of expertise, allowing us to become truly interdisciplinary and fast-forwarding us toward our vision of becoming a world-leading centre for inflammatory skin diseases. More new groups are on their way. In 2021, I supported a meticulous recruitment process for new research leaders to join our vibrant community, and I am thrilled by the opportunities this brings to SIC.

In 2021 alone, SIC held its first Summer School, a three-day learning experience targeting international PhD students and postdocs within the field, and introduced an introductory course in skin immunology for secondary school students aimed at sparking an interest in research careers and skin health and disease. SIC's educational portfolio now includes high-level training opportunities ranging from secondary school to postgraduate level, and I am impressed with the wide scale of training opportunities SIC offers to our next generation of skin immunologists.

The initiation of the Copenhagen Translational Skin Immunology Biobank and Research Programme (the BIOSKIN Programme) was a major achievement this year and one that will become a cornerstone in the translation between basic biology and clinic observations at SIC. With a DKK 40 million add-on grant from the LEO Foundation, SIC will now establish a first of its kind biobank with skin tissue and blood samples from 3,000 patients with illnesses such as psoriasis and eczema and an associated research programme of six PhD studies.

Lastly, new research results, new educational activities and the BIOSKIN Programme provided many excellent opportunities to disseminate the importance and relevance of skin disease research among peers, patients and the general public as part of SIC's outreach programme. I am pleased to see the dynamic communication platform SIC has built, and how it manifests itself in interactions with stakeholders across the world.

T Cell Biology and Skin Inflammation

The T Cell Biology and Skin Inflammation Basic Research Group investigates T cell development, activation, differentiation and effector functions as key factors in the development and treatment of inflammatory skin disease. The group is headed by Group Leader and Professor Charlotte Menné Bonefeld.

In our group, we investigate several aspect of T cell biology in connection with the skin: 1) The interplay between the skin, thymus and T cell development; 2) how different factors (e.g., vitamins, cytokines and hormones) affect T cell activation and differentiation, and how this affects T cell responses in the skin; 3) the development and regulation of different subsets of epidermal T cells in healthy and inflamed skin, and 4) the immune response to contact allergen, both to single allergens and mixtures of allergen.

In 2021, the focus of our group has been on how vitamin D affects immune responses in humans, the role of local versus global T cell memory in contact allergy, and how allergens affect expression of stress molecules on keratinocytes.

We have identified and characterised a family with a new mutation in the DNA-binding region of the vitamin D receptor (VDR). The mutation strongly affected the subcellular localisation and abolished the transcriptional activity of the VDR. In heterozygous carriers of the mutation, vitamin D-induced gene regulation was reduced by ~ 50%, indicating that the expression level of wild-type VDR determines vitamin D responsiveness in T cells. Surprisingly, by studying the course of COVID-19 and the immune response to SARS-CoV-2, we further demonstrated that vitamin D signalling was dispensable for mounting an efficient adaptive immune response against SARS-CoV-2 in this family. Although these observations might not directly be transferred to the general population, they question a central role of vitamin D in the generation of adaptive immunity against SARS-CoV-2.

We have analyzed how vitamin D affects the production of IL-22 in T cells and characterised how vitamin D inhibits IL-22 production through a novel repressive vitamin D response element in the IL-22 promoter.

In addition, we have investigated differences between local and global memory responses to contact allergens. During the sensitisation phase, contact allergen-specific memory T cells are formed. Two major forms of memory T cells are generated: Tissue-resident memory T cells and circulating memory T cells. Tissue-resident memory T cells

PROFESSORS
- Charlotte Menné Bonefeld
- Carsten Geisler

ASSOCIATE PROFESSOR (EXTERNALLY ASSOCIATED)
- Beatrice Dyring-Andersen
- Marianne Bengtson Løvendorf

ASSISTANT PROFESSORS AND POSTDOCS
- Helen Vaher
- Mandy Menzel
- Martin Kongsbak-Wismann
- Mia Hamilton Jee

PHD STUDENTS
- Anders Boutrup Funch
- Fatima Abdul Hassan Al-Jaberi
- Kelvin Yeung
- Veronika Mraz

BACHELOR, MASTER AND ERASMUS+ STUDENTS
- Leila Gharehdaghi
- Mette Aagaard
- Salome Marine Astreé Havard-Guibert

LAB MANAGERS AND TECHNICIANS
- Julie Weber Friis
- Louise Mørk
- Rebecca Kitt Davidson Lohmann

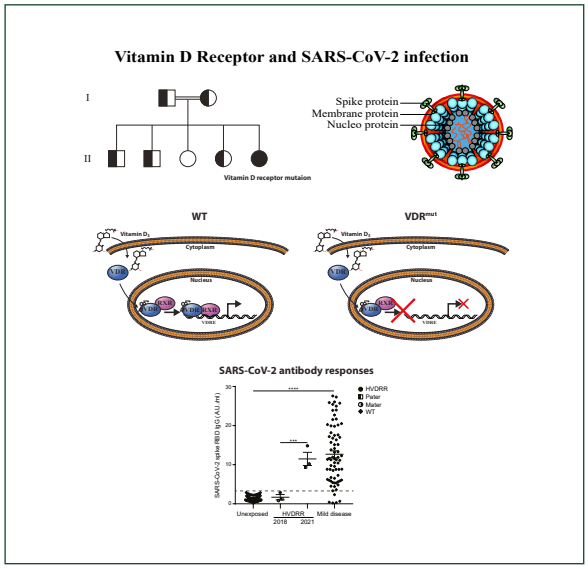


Figure showing a normal immune response against SARS-CoV-2 in a family with a mutation in the vitamin D receptor.

localise in the skin area exposed to the allergen, whereas circulating memory T cells will be in the circulation where they can be recruited to the skin upon re-exposure to the allergen. Whether these two subsets of memory T cells induce different challenge responses to contact allergens was not known. We found that tissue-resident memory T cells induce a rapid response mediated by a massive recruitment of neutrophils, something that was not seen in memory responses mediated by circulating memory T cells. During the coming years, we will investigate these mechanisms further to determine if this is a general difference between local and global immune responses to contact allergens, or if the mechanisms are allergen-dependent.

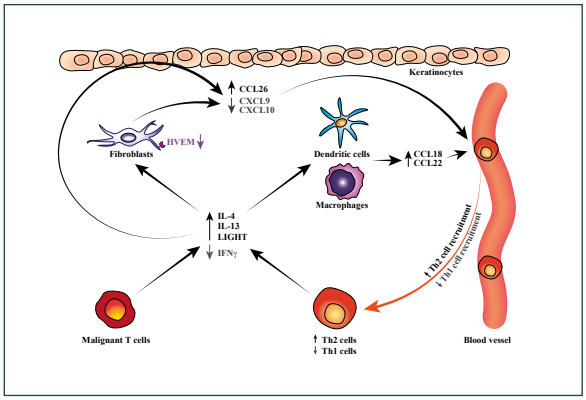
Finally, during recent years, we and others have shown that epidermal-resident memory T cells are rapidly activated after challenge with specific antigen. In general, it takes 1-3 days to re-activate a memory T cells, and it is therefore interesting that epidermal-resident memory T cells can be re-activated within hours after being challenged. It is well known that different stress molecules can be up-regulated on keratinocytes within hours after exposure to antigen and/or danger signals. However, it is not known whether these stress molecules are up-regulated in the response to con-tact allergens, or if they play a role in the rapid re-activation of epidermal-resident memory T cells. We have investigated this using both in vitro and mouse models, and we have found that exposure to contact allergens directly induces up-regulation of stress molecules on keratinocytes. Furthermore, our preliminary data suggest that these molecules play an important role in immune responses to contact allergens. We are now in the process of determining the role of stress molecules in the rapid activation of epidermal-resident memory T cells.

Skin Inflammation and Cancer

The Skin Inflammation and Cancer Basic Research Group focuses on elucidating the interplay between immunity, skin cells and the microbiota in order to understand what drives disease progression and resistance to treatment. The group is headed by Group Leader and Professor Anders Woetmann.

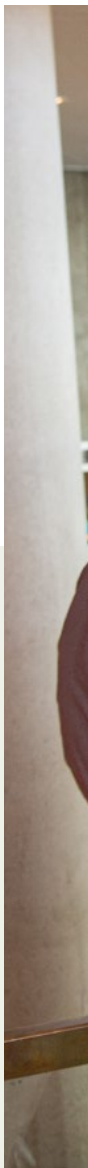
In 2021, one of our aims has been the molecular characterisation of T cells in both benign and malignant inflammatory skin diseases. A specific focus area of our research has been aimed at investigating cutaneous T lymphoma (CTCL) cells' heterogenicity and their response to staphylococcal enterotoxins by single cell RNA sequencing. Our hypothesis is that heterogenicity of malignant cells in CTCL prevents effective therapy. A deeper understanding of disease heterogenicity will likely pave the way for new therapeutic interventions. Furthermore, we have continued our work aimed at identifying new T cell subpopulations in benign inflammatory skin disorders. Using single cell RNA sequencing, we have confirmed the existence of these novel subsets of T cells, giving us a deep and valuable insight into the characteristics of these populations and their role in skin immunity and inflammatory skin diseases.

In addition, we have investigated the significance of crosstalk between malignant T cells and skin stromal cells. Here, the focus has been on both the role of cytokines and exosomes produced by malignant cells, and how they affect the keratinocyte transcriptomics, skin barrier and local microbiome composition. Our hypothesis is that cytokines and exosomes produced by malignant T cells directly affect the skin barrier and dysbiosis, and thereby aggravated disease.



Crosstalk between malignant T cells, benign immune cells, keratinocytes and skin stromal cells in cutaneous T cell lymphoma.

We continue focusing on unravelling the complex crosstalk between skin microbiota and cutaneous immunity. The microbiota has developed a symbiotic network with a skin innate immune system, and its disruption can lead to skin inflammation.



PROFESSORS
- Anders Woetmann
- Niels Ødum

ASSOCIATE PROFESSOR
- Thorbjørn Frej Krejsgaard

ASSISTANT PROFESSORS AND POSTDOCS
- Emil Marek Heymans Pallesen
- Katrine Baumann
- Morten Orebo Holmström
- Nicolai Skovbjerg Arildsen
- Tea Kirkegaard Nielsen
- Terkild Brink Buus

PHD STUDENTS
- Chella Krishna Vadivel
- Cheng Chi
- Eileen Donohue Wedge
- Katharina Wörzner
- Lisa Harth
- Maria Gluud Grøndahl
- Maria Teresa Martin Monreal
- Marina Ramírez Galera
- Martin Rich Javadi Namini
- Shayne Lavondua Ford

RESEARCH ASSISTANT
- Anders Lykkebo-Valløe

BACHELOR AND MASTER STUDENTS
- Mariana Bronze
- Ziao Zeng

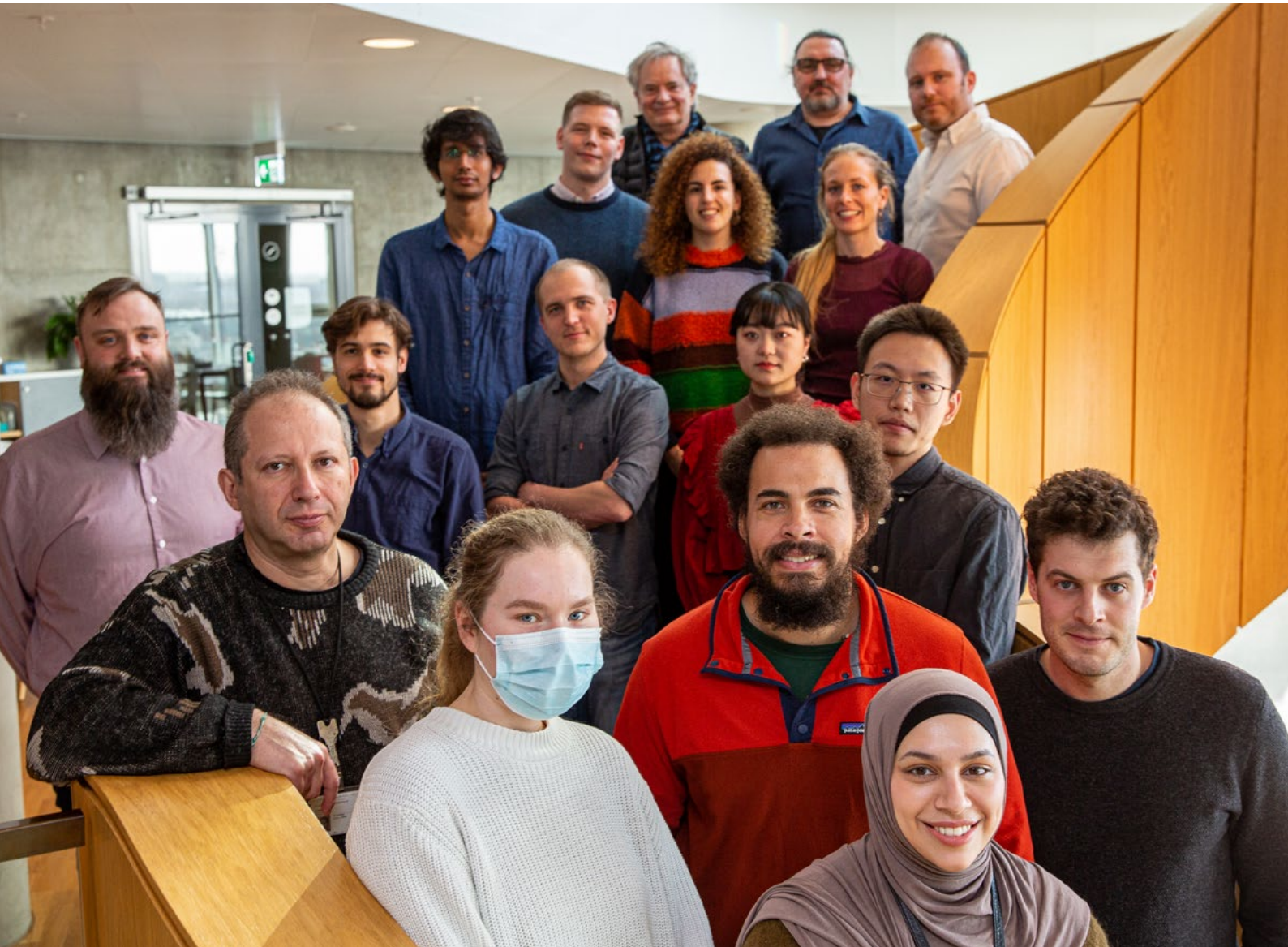
LAB TECHNICIAN
- Sana Ahmad

We have now established that bacterial metabolites have a selective modulatory effect on the innate immune system, and we are currently working to understand the molecular mechanisms behind the effect of selected bacterial metabolites. Our goal is to understand how they contribute to maintaining skin homeostasis.

Lastly, we have continued working with adipose stem cells which interestingly have an anti-inflammatory phenotype when exposed to pro-inflammatory cytokines. Now we are working on meticulously characterising these cells through several methods, and we are examining how they affect different elements of innate and adaptive immune system.

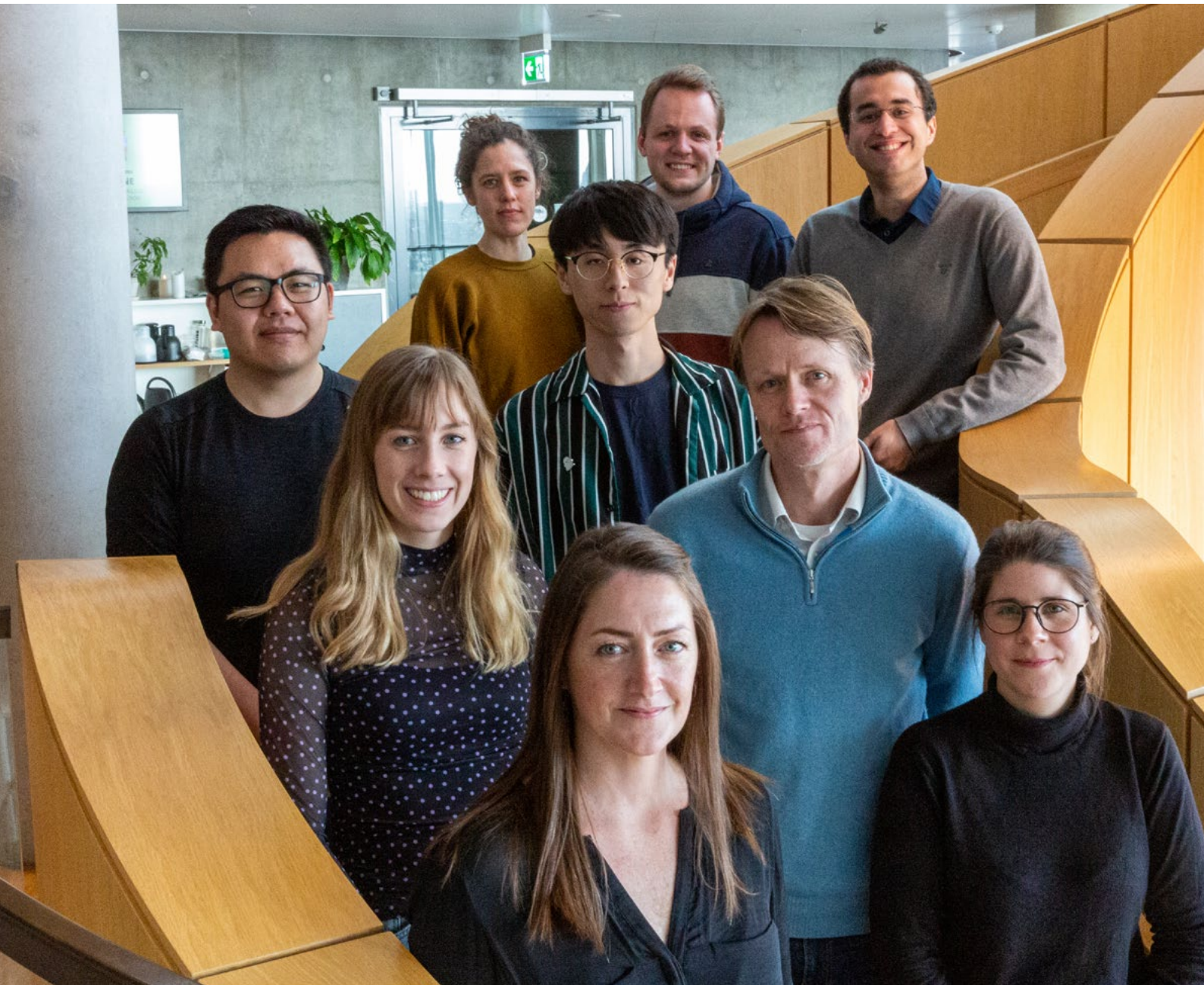
We have achieved several important results this year. We have discovered how unusual, activated and localised JAK3 regulates the proliferation and survival of malignant T cells in the skin. Targeting this pathway might open for new therapeutic intervention. We have also successfully optimised multimodal single cell analysis of the whole transcriptome, immune receptor cloning, surface protein expression, using sample multiplexing (hashing), and deep targeting of individual genes.

In collaboration with Sergei Koralov at the New York University Medical School, we have discovered that malignant and inflammatory T cells display a unique transcriptomic profile in lesional skin compared to peripheral blood, indicating that the skin lesions provide a very special and stimulating tumour microenvironment in CTCL. Moreover, we have technically improved the use of hatching antibodies to obtain more sensitive and robust responses.
In other collaborations, we have made a series of new discoveries concerning the pathogenesis of CTCL, including identification of (i) TXNIP as a novel tumour suppressor, potentially linking deregulated growth to disturbances in tumour cell metabolism, (ii) B cells as important players in the tumour microenvironment, and (3) a novel role of specific miRNAs in deregulated proliferation of malignant T cells, and how bacteria can induce expression of oncomiRs in malignant T cells. Finally, we have characterised the importance of mitochondrial metabolism for activated T cells which has previously been considered to be solely dependent on glycolysis. We will build on these new discoveries and continue to investigate how metabolism controls proliferation and function of benign and malignant T cells.



Molecular Immunology and Inflammation

The Molecular Immunology and Inflammation Basic Research Group focuses on understanding the processes that control immune responses, with particular focus on innate immune responses. The group studies molecular mechanisms governing inflammatory signalling and other host-defence processes and has a keen interest in the ubiquitin system which plays a central role in regulating inflammation and immune responses in the skin, gastrointestinal tract and other tissues/organs. Through this, we aim to understand the molecular events which on the one hand protect against invading pathogens and tissue damage, but on the other hand contribute to chronic inflammation, autoimmunity and tumour development. The group is headed by Group Leader and Professor Mads Gyrd-Hansen who was recruited from Oxford University in 2020.



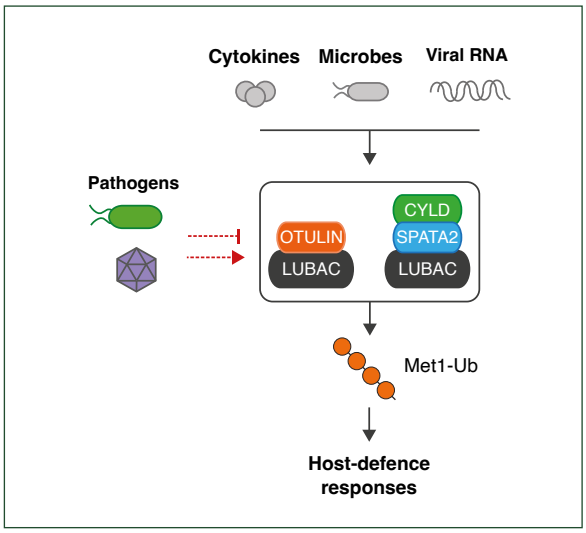
The modification of proteins with ubiquitin, termed ubiquitination, is essential for signalling by immune receptors, where ubiquitin is assembled into polymeric ubiquitin chains by ubiquitin E3 ligases and is disassembled by deubiquitinases. Depending on how they are assembled, these chains alter the function, subcellular location or stability of the modified protein. Lys48-linked ubiquitin chains cause proteasomal degradation of the modified protein, whereas Lys63- and Met1-linked ubiquitin chains function as signalling scaffolds in pro-inflammatory signalling. Met1-linked ubiquitin chains are exclusively assembled by the E3 ligase LUBAC and have emerged as hugely important in regulating inflammation and immunity in animal models as well as in humans. Genetic mutations that impact the cellular machinery which is regulating these ubiquitin chains, give rise to serious pathological inflammatory conditions, including dermatitis and cutaneous tumours. Leveraging our investigations of fundamental, regulatory mechanisms, we will explore how Met1-linked ubiquitin chains specifically affect immune responses and inflammation in the skin.

The primary objective in 2021 was to build up the newly established group at SIC, acquire the necessary equipment and transfer mouse colonies and know-how from Oxford University before the research group closed by the end of November 2021. During 2021, we welcomed several new staff members, and we also hosted Erasmus students. In 2022, we plan to recruit 1-2 additional postdoctoral fellows to bring the group size to 10 persons and further strengthen our expertise in immunology and molecular biology.

Several new research projects have been started up and, at the same time, we continue working on the projects that were started in the Oxford group. These projects are focussed on understanding how regulation of LUBAC influences the immune system under basal conditions, in the context of skin inflammation and in response to other challenges, such as bacterial infection and tumour formation. These projects rely on novel genetically modified mouse models that have been transferred from the group at Oxford University to SIC during 2021 and now are being expanded and bred. We have also initiated a project that aims to identify and characterise novel regulatory mechanisms of LUBAC by using mass spectroscopy-based proteomics available through the Proteomics Research Infrastructure (PRI) at the faculty.

The primary research outputs from the group in 2021 were the article 'Regulation of CYLD activity and specificity by phosphorylation and ubiquitin-binding CAP-Gly domains', published in Cell Reports, and the review article 'The Met1-linked ubiquitin machinery in inflammation and infection', published in Cell Death and Differentiation, in which we review the current knowledge about the role of Met1-linked ubiquitin in the host defence against invading microbes and, conversely, how pathogens derail LUBAC signalling.

A primary focus for the group in 2022 will be to advance the newly initiated research projects and to finalise research projects that were initiated in the Oxford group. ⟋



Met1-linked ubiquitin chains are important for host defence against invading microbes and is targeted by pathogens to derail LUBAC-mediated pro-inflammatory signalling.

PROFESSOR
⟋ Mads Gyrd-Hansen

ASSISTANT PROFESSORS AND POSTDOCS
⟋ Berthe Katrine Fiil
⟋ Chris Kedong Wang
⟋ John Rizk

PHD STUDENTS
⟋ Frederik Timmermann
⟋ Malin Jessen
⟋ Wenxin Lyu

ERASMUS+ STUDENT
⟋ Rebecca Mirjam Freya Sturm

LAB TECHNICIAN
⟋ Majken Kjær

Translational Skin Immunology

The Translational Skin Immunology Basic Research Group investigates the functionality, migration and new establishment of T cells in human skin. These studies address an old therapeutic dilemma in dermatology clinics, i.e., local relapse of inflammatory skin diseases. The group is headed by Group Leader and Professor Liv Eidsmo, who was recruited from Karolinska Institutet in 2021.

Modern immunomodulatory drugs that inhibit cytokines, such as TNF, IL-17 and IL-23, have revolutionised the treatment of severe psoriasis. However long-term remission after cessation of treatment is uncommon and curative treatments are still lacking. Intriguingly, previously affected, and resolved, skin is more prone to relapsing inflammation than skin that has not yet developed psoriasis. The Eidsmo group showed that disease-driving T cells poised for IL-17 production are retained and enriched in seemingly resolved skin. When these cells are activated, psoriasiform inflammation is initiated, which explains the preferential relapse in resolved sites. T cell induced molecular inflammation is a potential biomarker for treatment efficacy afterUVB treatment. These findings by the laboratory at Karolinska Institutet are currently being validated in collaboration with an industry-headed and world-wide clinical trial.

Apart from their involvement in focal inflammatory skin diseases, tissue-residing T cells contribute to local protection against pathogens and malignancies. The focus of the research programme at SIC is to explore pathways that steer the delicate balance between T cell involvement in inflammatory diseases and barrier homeostasis. As we establish the group at SIC, projects investigating T cell driven pathology in vitiligo and contact dermatitis are finalised at Karolinska Institutet. Epigenetic analysis of skin T cells with transcriptomic analysis of individual T cells in different skin compartments

SIC

PROFESSOR
- Liv Eidsmo

POSTDOC
- Ekaterina Zhuravleva

RESEARCH ASSISTANT
- Trine Schønfeldt

BACHELOR STUDENT
- Fie Bendix Thomsen

LAB MANAGERS AND TECHNICIANS
- Anne-Sofie Østergaard Gadsbøll
- Christina Agerbeck
- Maja Søberg Udsen
- Marta Madacsi

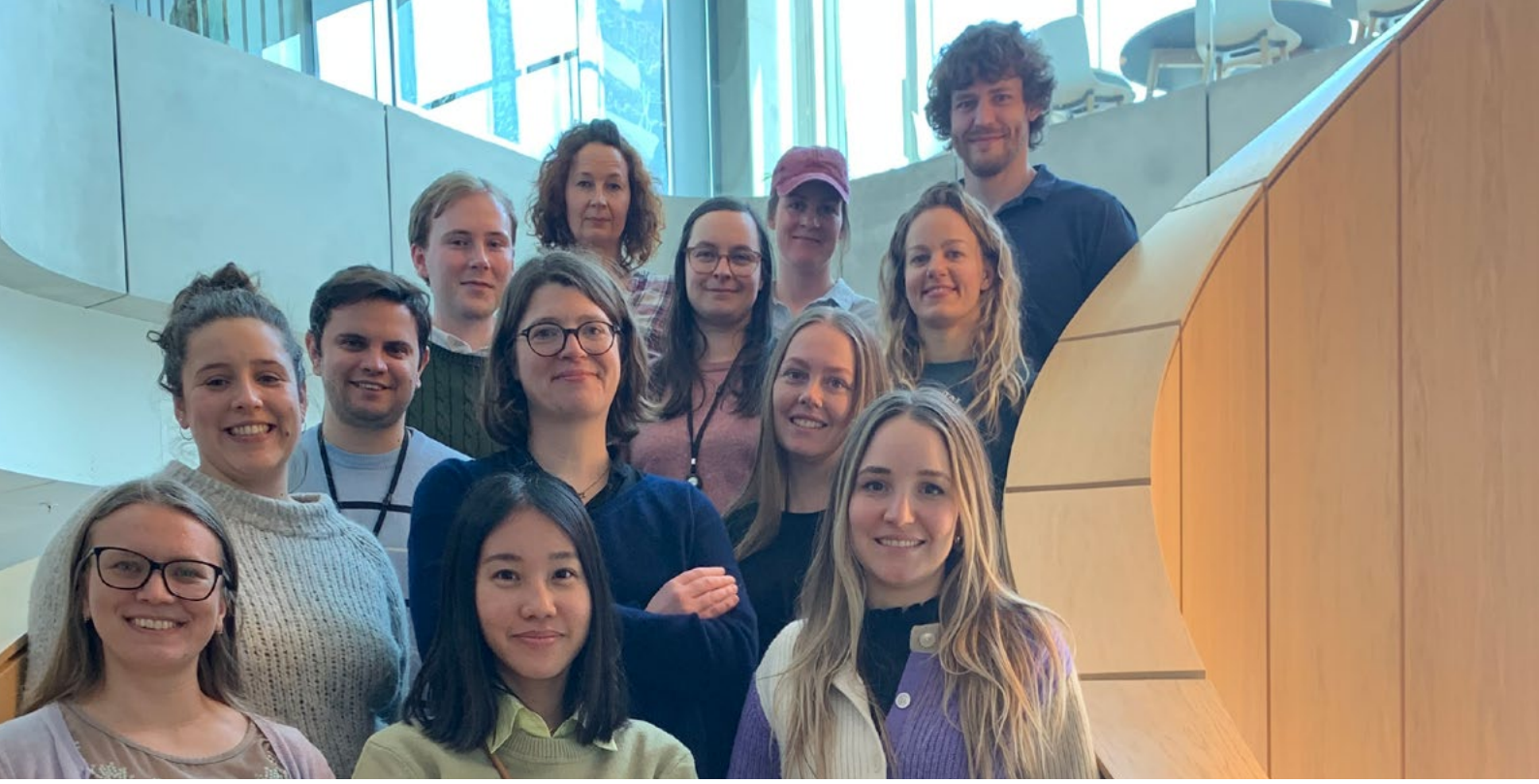
Karolinska Institutet

PHD STUDENTS
- Borislav Alyashev Ignatov
- Elena Hoffer

POSTDOCS
- Hanako Yoshioka
- Wenning Zheng

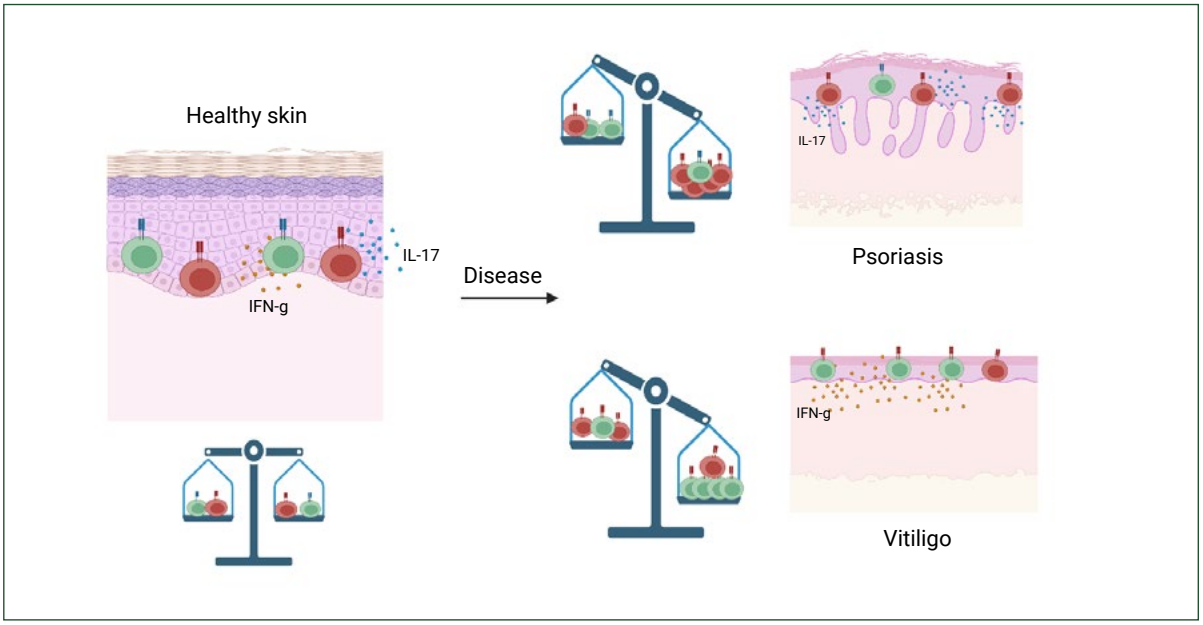
BACHELOR AND MASTER STUDENTS
- Daniel Sortebech
- Tom Geugies

COORDINATOR
- Martina Löfstedt Jalava



and blood are used to investigate how resident T cells can be seeded in new skin sites. Spatial transcriptomics is providing in depth understanding of the microenvironment surrounding resident T cells and protocol and know-how is moved from Karolinska Institutet to SIC. When gene expression analysis is performed directly on tissue sections from tissue biopsies, we can map potential environmental signals that steer T cell function in the healthy and diseased skin. Together, these projects will ultimately help us design projects aimed at normalising the balance of resident T cells in the skin.

Migrating a research programme is exciting. It also mirrors the current scientific focus in my group, when we map factors needed for T cells to establish themselves in new sites of the skin. In parallel to the science, we are getting to know a new scientific landscape together with new students and scientists recruited to SIC and the group members that move between Sweden and Denmark. SIC is a perfect platform for continuing the group's work on mechanistic projects based on clinical observations. Interactions with the local dermatology community will facilitate phrasing of hypotheses and bring our findings back to the clinic, always with the long-term goal to optimise treatment of patients.



In healthy skin, tissue resident memory T cells with different cytokine profiles are in balance. In the skin diseases psoriasis and vitiligo, the T cell balance is disturbed. IL-17 producing T cells are enriched in psoriasis, whereas IFN-g producing T cells are enriched in vitiligo.

The BIOSKIN Programme

Based on a DKK 40 million add-on grant, SIC and Herlev and Gentofte Hospital initiated the 'Copenhagen Translational Skin Immunology Biobank and Research Programme' (the BIOSKIN Programme) in 2021. The programme will establish a biobank with skin tissue and blood samples from 3,000 patients with illnesses such as psoriasis and eczema and perform unique translational research studies. The programme is headed by Clinical Professors Jeanne Duus Johansen and Lone Skov.

Chronic inflammatory skin diseases are common and represent a major health burden for society and the affected individuals. These skin diseases cause significant morbidity and strongly impact the quality of life. A major clinical obstacle to personalised treatment and prevention of these diseases is our inability to reliably distinguish between different inflammatory skin diseases and to optimise treatment by stratifying subgroups within the same disease spectrum. In addition, some – but not all – patients develop comorbidity, e.g., airway disease, arthritis or ischemic heart disease. It will be an enormous benefit if we can predict early on who is at risk of developing severe disease and/or comorbidities. This would also allow personalised treatments that address the needs of special subgroups of patients. From the immunological point of view, the main challenge to speedy transitions from novel research results in experimental models to confirmation of their clinical relevance is to secure access to a reliable source of high-quality clinical data and research material.

The aim of the BIOSKIN Programme is to intensify translational research in dermatology. The core elements of the programme are a comprehensive biobank, a set of clinical studies and state-of-the-art research technologies in skin immunology.

The programme entails unprecedented biological sampling and collection of patient data for clinical assessments, for which Denmark is the most ideal location in the world because of its linked patient registers. We will collect skin samples from diseased and healthy skin and blood, follow the patients over time to record progress of disease, response to treatments, complicating allergies, co-morbidities and quality of life. We will also take skin and blood samples from patients prior to and after new treatments. This will allow us to investigate courses of both good and poor treatment responses and identify new treatment targets. In total, we will collect samples and data over five years from 1,000 patients with the most prevalent diseases being atopic dermatitis, psoriasis and contact dermatitis, respectively. Other important – though less frequent – inflammatory skin diseases will be included for comparative purposes.

We will initiate six PhD projects to carry out the extensive sample and data collection. To utilise the collection immediately, each study will be dedicated to research objectives in early detection and intervention, identification of new treatment targets, reduced disease severity and comorbidity and personalised treatments.

CLINICAL PROFESSORS
- Jeanne Duus Johansen
- Lone Skov

HEAD OF RESEARCH
- Marianne Bengtson Løvendorf

PHD STUDENT
- Christina Yndal Erichsen

MEDICAL DOCTOR
- Lasse Balthzer Schmidt

PROJECT NURSE
- Rikke Juul Wittrup

The programme is unique in collecting high-quality clinical material and data from three common diseases in parallel, large groups of patients that will be followed over time. A particular strength of this proposed biobank is that data can be combined with the unique Danish registers and electronic patient records. The programme will strengthen the integrational approach between basic and clinical science and result in a large biobank of extremely high value, not only for SIC researchers, but also for collaborators nationally and internationally.

The programme will collect samples and data over five years from 1,000 patients with the most prevalent diseases being atopic dermatitis, psoriasis and contact dermatitis, respectively.

Translational and clinical research

SIC is strongly committed to integrating the basic research groups at the SIC headquarters with translational and clinical research forces at Danish and international hospitals and with the life science industry. On these pages, we highlight two new translational projects that have emerged from the 'Team Science Concept', as adapted by basic and clinical researchers at and associated with SIC. This approach translates basic discoveries to the patients, and it ensures that observations and questions arising in the clinic are referred back to the laboratory. Both projects are funded by the BRIDGE Translational Excellence Programme.

BRIDGE – TRANSLATIONAL EXCELLENCE PROGRAMME

The postdoctoral BRIDGE fellowships in translational medicine are funded by the Novo Nordisk Foundation and offered to selected researchers working on translational research projects at the University of Copenhagen. Fellows apply new discoveries and technologies from biomedical research to the clinical environment or to the life science industry, thus bridging the gaps between research and medical treatment.

DEEP PHENOTYPING OF PATIENTS WITH CHRONIC SPONTANEOUS URTICARIA – A QUEST FOR NOVEL BIOMARKERS RESULTING IN PERSONALISED AND OPTIMISED TREATMENT

Chronic spontaneous urticaria is an overlooked skin disease despite affecting nearly 1% of the world's population. It can have detrimental effects on the patients' quality of life due to the spontaneous occurrence of itchy wheals and/or angioedema, which is believed to be driven by activated skin mast cells, but the exact pathomechanism is still unknown. Patients are currently stratified into two groups, but the high number of refractory patients indicates that more subgroups exist and, thus, better insights into the underlying pathomechanisms and novel diagnostic strategies are needed to improve the life of patients with chronic spontaneous urticaria.

This project aims to advance our understanding of the disease by studying relevant cell types, primarily mast cells and basophils, from chronic spontaneous urticaria patients compared to healthy controls. Furthermore, we wish to identify novel biomarkers to enable robust patient stratification in order to facilitate highly personalised treatment, thereby enhancing the therapeutic outcome. This will be achieved through characterisation of the >500 patients currently included in the Bispebjerg Hospital Dermatology Department patient database together with approximately 150 patients referred to the clinic during the first year of the study. Blood and serum samples from a subset of the patients will be analysed at RefLab, a small biotech company providing allergy and chronic spontaneous urticaria diagnostics, to identify potential novel biomarkers by correlating clinical and paraclinical data. Skin biopsies, which will be obtained from a selected group of the newly referred patients, will be studied at SIC using spatial transcriptomics to map out

differences in mast cell profiles between lesional/non-lesional chronic spontaneous urticaria skin and healthy controls.

BASIC MENTOR
Professor Anders Woetmann
SIC

CLINICAL MENTOR
Professor Simon Francis Thomsen
Bispebjerg and Frederiksberg Hospital

LIFE SCIENCE INDUSTRY MENTOR
Professor Per Stahl Skov
RefLab ApS

Katrine Baumann obtained her PhD at SIC before taking on the position as postdoctoral fellow in the BRIDGE Programme in September 2021 to study pathomechanisms of chronic spontaneous urticarial.

Photo: Jannick Boerlum Photography

REVERSION OF LOCAL IMMUNE SUPPRESSION IN PANCREATIC CANCER

The project aims at identifying new targets for therapeutic cancer vaccination in patients with pancreatic cancer. The immunosuppressive cytokines interleukin (IL)-10 and transforming growth factor-beta (TGFb) are upregulated in pancreatic cancer and inhibit tumour-specific T cells. Several other immunoregulatory mechanisms are targets of specific T cells. We aim to identify if T cells specific to IL-10- and TGFb-derived epitopes can recognise and kill immunosuppressive cells, as this will revert the local immune suppression in pancreatic cancer. Additionally, we wish to elucidate differences in the transcriptome between tumour-specific T cells isolated from healthy donors and patients with pancreatic cancer.

The project will use basic immune-cellular assays such as ELISPOT and flow cytometry for identification of immunogenic epitopes in IL-10 and TGFb. More advanced assays, such as co-culture assays, will be used to determine the ability of TGFb- and IL-10-specific T cells to target regulatory and immunosuppressive cells. Murine vaccination models using both orthotopic and non-orthotopic tumour models will be used to assess the ability of IL-10- and TGFb-directed vaccination to induce tumour regression and changes in the tumour microenvironment. T cells specific to KRAS oncoprotein will be isolated using tetramers, and single cell RNA sequencing will reveal transcriptomic differences between healthy donors and patient T cells.

The project will establish the preclinical rationale for anti-regulatory therapeutic cancer vaccination in pancreatic cancer and thereby allow us to go directly into a phase I clinical vaccination trial, testing the safety and efficacy of such vaccines. Thus, our project has the potential to establish anti-regulatory T cell vaccines as a new treatment modality in pancreatic cancer. Identification of dysregulated mechanisms in tumour-specific T cells in pancreatic cancer will identify additional mechanisms that may be targeted in order to enhance the tumour-specific T cell responses in pancreatic cancer.

BASIC MENTOR
Professor Niels Ødum
SIC

CLINICAL MENTORS
Professors Julia Johansen and Mads Hald Andersen
Herlev-Gentofte Hospital

MD, PhD Morten Orebo Holmström was recruited as a postdoctoral fellow in the BRIDGE Translational Excellence Programme in September 2021 to investigate new targets for therapeutic cancer vaccination in patients with pancreatic cancer.

Photo: Jannick Boerlum Photography

Education and career development

SIC invests heavily in the training of the next generation of immunologists in an ambitious learning environment. On these pages, we present SIC's new and established educational activities that aim to prepare students for auspicious international careers within academia and the life science industry. We also highlight four of our accomplished third-year PhD students and their projects.

MASTER OF SCIENCE IN IMMUNOLOGY AND INFLAMMATION

The Master of Science in Immunology and Inflammation was established at the University of Copenhagen in 2017. The Master's programme is unique as it is the only programme taught in English in continental Europe, making it a highly coveted international programme. Each year, approximately 30 students from more than 10 nationalities are enrolled. The students receive mandatory training in advanced immunology, involving infectious immunology, tumour immunology and immunological diseases. In addition, the students can select between various elective courses. The last year of the programme is spent in the laboratory where the students prepare their master thesis project. SIC Group Leader and Professor Anders Woetmann leads the programme as Head of Studies.

MASTER'S COURSE IN SKIN IMMUNOLOGY

The elective course in skin immunology was offered to students at the Master in Immunology and Inflammation programme for the first time in 2021 and continues to be an opportunity for students to learn and understand the immunology of the body's largest organ. A broad range of PhD students, postdocs and faculty members at SIC contribute to the course together with several clinical collaborators, thus enabling the course to cover both basic and clinical aspects of skin immunology and experimental methods in the study of skin immunology. The course is a mixture of lectures, case studies and student interactive teaching. Students are taught immunology of healthy and diseased skin, including the responses to infections and allergens, in autoimmunity and upon wounding of the skin.

GRADUATE PROGRAMME IN IMMUNOLOGY AND INFECTIOUS DISEASES

At the postgraduate level, the majority of SIC's PhD students are enrolled in the Immunology and Infectious Diseases Graduate Programme, where many of SIC's researchers provide high-quality teaching and supervision. Students choose training courses within the area of immunology. The students also receive training in research methods and techniques, such as microscopy, flow cytometry, cell sorting and laboratory animal science that are needed to conduct their concurrent and independent thesis projects. Every year, the programme hosts an annual meeting with Danish and international speakers. At the end of their three-year programme, the students defend their thesis to be awarded the PhD degree.

IN 2021, SIC RESEARCHERS

- Delivered 146 teaching hours
- Conducted 259 exams at bachelor's and master's degree level
- Supervised 25 PhD students

TOP THREE TEACHING PROGRAMMES

1. Immunology and Inflammation
2. Medicine
3. Human Biology

SIC provides training in basic and advanced immunological skills, covering a range of educational programmes within health and medical sciences. SIC's researchers also host and supervise students who are working on their thesis, at both bachelor's and master's degree level.

PhD degrees awarded in 2021

MINNA TIIRIKAINEN

Thesis: *Ex vivo culture approach for inflammatory skin diseases for use of pharmacological testing and investigation of inflammatory skin disease*

Next destination: PhD Minna Tiirikainen will dedicate her time to her family for a period of time.

DANIEL VILLALBA LOPEZ

Thesis: *In vitro generation of human Th22 cells and the effects of bio-available Vitamin D3*

Next destination: PhD Daniel Villalba Lopez will continue his academic career in the Danish life science industry.

LUCAS PEIFFER

Thesis: *Characterisation of T cells in skin malignancies*

Next destination: PhD Lucas Peiffer will continue his academic career in the German life science industry.

ANNA K. OBELITZ RODE

Thesis: *Glucagon-like peptide 1 receptor expression and function in T cells*

Next destination: PhD Anna K. Obelitz Rode will continue her career in the Danish life science industry.

OLIVER KRIGSLUND

Thesis: *Development of antibody-drug conjugates with the ability to deplete tumour supporting stromal cells and potential to deliver potent chemotherapy to tumors*

Next destination: PhD Oliver Krigslund will continue his academic career in Denmark.

YOUNG INVESTIGATOR NETWORK

The Young Investigator Network was established by early-career researchers from SIC and clinical dermatological departments in the Copenhagen area in 2019. The network is a self-organising professional and social initiative that aims to expand the professional networks of its members and initiate interdisciplinary research activities with peers. Each member contributes with specialised skills, methodological expertise and unique access to data within their particular field of basic, translational and clinical skin and skin disease research. Members enjoy support from their respective PIs and departments and have an allocated budget to perform career development activities and explore the synergetic potentials in collaborations.

AS A RESEARCHER, YOU CAN JOIN THE NETWORK IF YOU ARE:

- An assistant professor, postdoc, PhD student or research assistant at SIC.
- A research active dermatologist in training in the Capital Region or Region Zealand.

New members can join by contacting
SIC@SUND.KU.DK

YOUNG SCANDINAVIAN SOCIETY FOR IMMUNOLOGY (YSSI)

In 2021, PhD student at SIC Marina Ramírez Galera and Scandinavian colleagues initiated the Young Scandinavian Society for Immunology (ySSI). The initiative aims to build a network for early-career researchers across Scandinavian countries to disseminate their research, defend their interests and support their career development as well as increase their visibility at both national and European level. The ySSI is supported by the Scandinavian Society for Immunology (SSI) and is part of the European Federation of Immunological Society's Young Immunologist Network (yEFIS).

Read more at
SCANDINAVIANIMMUNOLOGY.NU/ABOUT-YSSI

PhD student Veronika Mraz introduced the secondary school students from Gefion Gymnasium to exercises in the laboratory during the mini course in skin immunology.

MINI COURSE IN SKIN IMMUNOLOGY FOR SECONDARY SCHOOL STUDENTS

Together with the local Gefion Gymnasium in Copenhagen, SIC has organised a mini course in skin immunology for third-year secondary school students. SIC welcomed the group of students for the first time in 2021. The selected class is taught biotech which combines biology and chemistry. During the two-day course, the young people learned about the skin and immunology and grappled with quizzes and exercises in the laboratory.

Teaching students at the university enables them to get as close as possible to the research environment, The students are given a unique opportunity to be part of an authentic research environment over a period of time, and they are able to test their secondary school knowledge on actual researchers, a real, ongoing research project and relevant cases of skin disease. The collaboration also offers SIC's researchers teaching the course – many of whom are PhD students – a chance to reflect on their own research, gain insight into unforeseen angles and build concrete teaching experience, both in the form of preparation and student-teacher interaction. SIC expects to receive a third-year class from Gefion Gymnasium once a year over the next few years.

FEEDBACK FROM THE TEACHER

'The students have a deep interest in the health and natural sciences. Therefore, this meeting with the university and the research environment was essential to them and extremely motivating. It stands in contrast to their ordinary teaching. The topic – skin diseases and allergens – was new, interesting and very relevant to our students, and it constituted a new and exciting angle for us to delve into – with immunology as our starting point.'

— **Biology teacher Linda Schneider**, Gefion Gymnasium

FEEDBACK FROM THE STUDENTS

'Such a cool and insightful experience that has sparked my interest in doing research.'

'I have been filled up with a lot of new, useful knowledge on immunology and the skin.'

'I have learned how many educational opportunities actually exist within natural sciences and health and medical sciences.'

— **Third-year secondary school students,** Gefion Gymnasium

SUMMER SCHOOL 2021

After delays due to the COVID-19 pandemic, SIC was able to host young and talented researchers from across Europe at its first Summer School on 11-13 October 2021. The Summer School is an intense three-day learning experience on skin and skin disease research, offering 1:1 interaction with and feedback by leading experts from around the world.

12 EXPERT SPEAKERS

- **Liam O'Mahony**, National University of Ireland
- **Padraic G. Fallon**, Trinity College Dublin
- **Tiffany C. Scharschmidt**, University of California, San Francisco
- **John E. Common**, Skin Research Institute of Singapore
- **Sanja Kezic**, Academic Medical Center, Amsterdam
- **Cezmi A. Akdis**, SIAF, University of Zurich
- **Mads Gyrd Hansen**, SIC, University of Copenhagen
- **Muzlifah Haniffa**, Newcastle University
- **Liv Eidsmo,** SIC, University of Copenhagen
- **Bernhard Homey**, University of Duesseldorf
- **Mübeccel Akdis,** SIAF, University of Zurich
- **Niels Ødum**, SIC, University of Copenhagen

THEMES

- The microbiome and the skin
- The physical and chemical skin barrier
- The immunological skin barrier
- Therapeutic targeting the skin barriers

62 DANISH AND INTERNATIONAL PHD STUDENTS AND POSTDOCS JOINED THE SUMMER SCHOOL IN 2021. THE PARTICIPANTS REPRESENTED UNIVERSITIES AND HOSPITALS FROM NINE EUROPEAN COUNTRIES.

FEEDBACK FROM A PARTICIPANT

'The Summer School was certainly the best scientific experience I've had as a young researcher. Lots of quality scientific content, but above all I had the chance to network with researchers I admire so much. I will strongly recommend it to my colleagues.'

— **PhD student Gustavo Ferriera Alves,** University of Turin

SIC intends for the Summer School to grow into an annual flagship learning opportunity for the next generation of skin immunology researchers. The next Summer School, themed 'Immune Regulation of the Skin', will be held on 25-27 April 2022.

The three-day Summer School is held in the idyllic surroundings of Hotel Hornbækhus north of Copenhagen.

THE SKIN BARRIER AND TUMOUR MICROENVIRONMENT IN CUTANEOUS T CELL LYMPHOMA

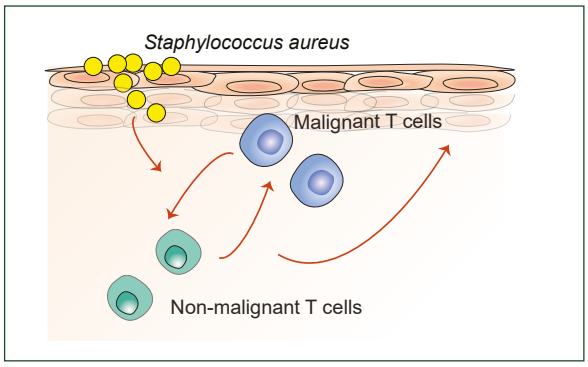
The skin is the largest organ in the body and forms the barrier protecting us from external insults. The uppermost layer of the epidermal compartment, stratum corneum, is essential for the barrier function and integrity of the skin. A competent barrier is important for avoiding infections, including staphylococcus aureus colonisation that can induce inflammatory conditions in the skin. An important component of the stratum corneum is filaggrin. Filaggrin mutations have been associated with skin diseases, including atopic dermatitis. Deficiencies in filaggrin is linked to impaired stratum corneum structure, decreased levels of natural moisturising factors, increased permeability and susceptibility to bacterial colonisation, dysbiosis and infection, thus highlighting the importance of the protein in the maintenance of optimally functional skin.

Cutaneous T cell lymphoma (CTCL) is a type of cancer – a lymphoid malignancy – characterised by accumulation of malignant CD4+ T cells residing in the skin in a chronically inflammatory environment. CTCL skin lesions cause serious symptoms that are hampering the quality of life of patients and are likely sites of infection. Severe infections are a common and potentially fatal comorbidity in advanced CTCL disease. Recent studies have shown that infections with staphylococcus aureus fuel the cancer by creating a pro-inflammatory environment inducing proliferation and survival of malignant T cells. Thus, preventing infections have a high priority for patients.

Analyses of CTCL skin have shown that the epidermal structure in lesional skin of patients is compromised. Our investigation has furthermore shown that the lesional sites often have reduced expression of filaggrin and other important skin barrier-related proteins. However, the pathophysiological mechanisms driving the epidermal changes in lesional skin of CTCL patients still need to be elucidated.

The present project aims to investigate the skin barrier in CTCL and the microenvironment in which the T cells reside, in order to gain insights into the mechanisms that are leading to defects in the skin barrier, potentially paving the way for the discovery of new therapeutic targets. The current approach is to study the cross-talk between cells in the skin microenvironment in order to identify key mediators and pathways that drive changes in the skin of these patients. The investigation is currently exploring the ability of different, clinically approved drugs to inhibit pathways responsible for inducing skin barrier defects.

As a PhD student, Maria Gluud Grøndal studies the skin barrier and tumour microenvironment in cutaneous T cell lymphoma.

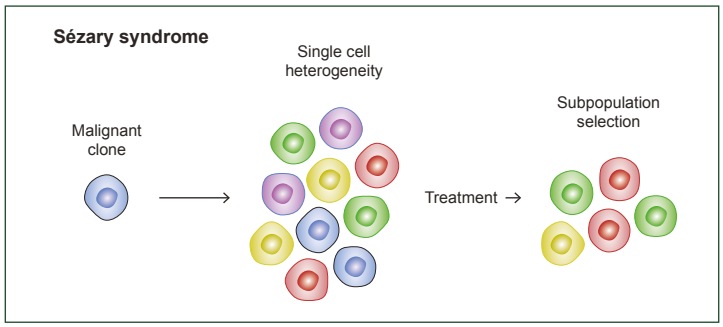


The project studies the interplay of cells in the skin (keratinocytes, malignant T cells and non-malignant T cells) and the increased bacterial colonisation of staphylococcus aureus.

The hypothesis is that a vicious cycle exists, in which the skin barrier is damaged, leading to increased bacterial colonisation that promotes inflammation which in turn exacerbates the malignant disease. Studying the interplay between different immune cells and the role of bacteria will enable us to better understand the disease progression of CTCL. The goal of the project is to provide new knowledge about the pathophysiological mechanisms in the microenvironment, potentially leading to new therapeutic interventions.

SINGLE CELL HETEROGENEITY IN CUTANEOUS T CELL LYMPHOMA

Despite their likely origin from a common ancestor cell, it is becoming increasingly clear that cancers consist of a heterogeneous collection of cells. Cutaneous T cell lymphomas (CTCL) are a group of malignancies characterised by chronically inflamed skin lesions containing skin-homing malignant T cells. Sezary Syndrome is a highly aggressive variant of CTCL that is difficult to treat and have an overall poor prognosis. Being a leukemic lymphoma, Sezary Syndrome allows regular monitoring of the cancer cells through blood samples drawn before initiation of each extracorporeal photopheresis treatment series. Originating from malignant transformation of memory T cells, Sezary Syndrome cells are known to express many surface markers related to T cell biology that are readily assayed at a single cell level using flow cytometry. We have strong preliminary data showing that several subpopulations of cells with distinct surface marker expression can be found within the malignant T cells of all investigated Sezary Syndrome patients. Our current screening experiments showed heterogeneous expression of a broad range of surface markers. Further analysis of the co-expression of a selection of these markers allowed identification of multiple subpopulations with distinct surface marker profiles. These data exemplify the heterogeneity of the malignant population in unprecedented detail and suggest that a high level of single cell heterogeneity is a common phenomenon within Sezary Syndrome patients, thus establishing that it is possible to isolate the individual heterogeneous subpopulations by fluorescence activated cell sorting (FACS).



There are many subtypes of cancer cells, but only some of them are killed by treatment. The PhD project ultimately aims to identify which drug combinations generate maximal killing of heterogeneous populations of cancer cells in individual patients.

Since multi-colour flow cytometry has some limitations, we performed single cell RNA sequencing (scRNA-seq) of malignant T cells from SS patients. Initial analysis showed good correlations with mRNA expression from bulk RNA-sequencing libraries as well as flow cytometric protein expression of the investigated surface markers. Our scRNA-seq data confirm that single cell heterogeneity can be found within all investigated patients and is reflected at both the protein and mRNA levels. We wish to verify the expression patterns of heterogeneously expressed genes by flow cytometry to solidify the findings. Furthermore, we will verify the overall gene expression levels within the malignant populations, using robust whole transcriptome RNA sequencing. We expect these studies will firmly establish the degree of single cell heterogeneity within the malignant population and provide valuable indications for the functional diversity of different malignant subpopulations.

In parallel, we will examine resistance to HDAC inhibitors (HDACi) and interferon-alpha and development of multi-resistant subsets of malignant T cells. Indeed, HDACi targets the majority of (but not all) malignant T cell subsets, favouring a relative increase of resistant subsets. Our previous findings and preliminary data indicate that JAK3 drives SOCS3 expression, and that JAK3 in some malignant T cells is resistant to inhibition by SOCS3 which, however, blocks growth inhibition by interferon-alpha, a key drug in the treatment of CTCL. Overall, we anticipate that the proposed studies will help map sensitivity/resistance to conventional and experimental anti-lymphoma drugs in subsets of malignant T cells and identify which drug combinations generate maximal killing of heterogeneous populations of cancer cells in individual patients.

PhD student Chella Krishna Vadivel studies single cell heterogeneity in cutaneous T cell lymphoma.

EPIDERMAL-RESIDENT MEMORY T CELLS RECRUIT NEUTROPHILS THAT ARE ESSENTIAL FOR FLARE-UPS IN CONTACT DERMATITIS

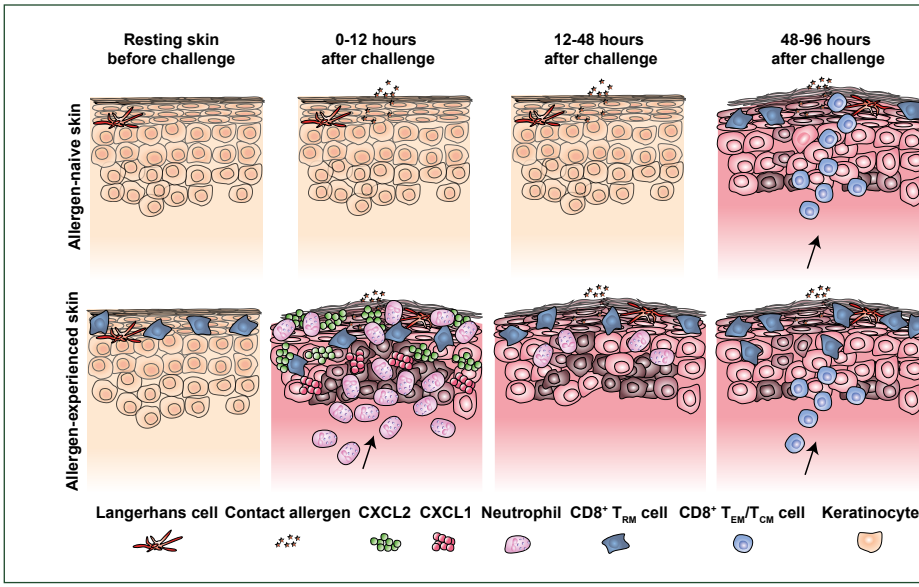
PhD student Anders Boutrup Funch studies the activation of CD8+ tissue-resident memory T cell in contact dermatitis.

Allergic contact dermatitis due to exposure to, e.g., nickel and perfume ingredients represent some of the major forms of allergic reactions seen among patients. Even though allergic contact dermatitis is classically described as a delayed-type hypersensitivity reaction some patients suffering from contact allergy develop symptoms such as rashes and itching much faster than others. Therefore, the aim of the study was to determine why some react to contact allergens much faster than prescribed, and we have succeeded in outlining an entirely new subgroup of allergic reactions which explains these early skin reactions.

The T cells in the body are responsible for delayed hypersensitivity reactions, also known as type 4 allergic reactions. But in our study conducted on mice we have shown that a subset of epidermal-resident memory T cells are formed locally and that these can to respond much faster upon re-exposure to contact allergen than previously assumed. This gives us a more complex picture of contact allergy.

The study shows that when skin area containing epidermal-resident memory T cells is re-exposed to the allergen at a later point in time, a clear inflammatory reaction is seen in the skin within only 12 hours. This indicates that T cell mediated allergic reaction probably needs to be subcategorised, giving us both the classic delayed reaction – that is, where the patient reacts 24-72 hours after exposure – and an immediate reaction, where the patient develops symptoms much faster.

The study also reveals that following exposure to an allergen, activation of the epidermal-resident memory T cells leads to massive recruitment of the most abundant type of white blood cells in the body, the neutrophils, to the affected part of the skin. Normally, neutrophil recruitment is used to fight infections, as these cells are capable of effectively eliminating microorganisms. At the same time, however, they cause intense inflammation and local tissue damage – what the patients experience as a rash. Neutrophil recruitment is not seen in connection with delayed reactions to contact allergens.



The figure illustrates the early T cell mediated inflammatory reaction upon re-exposure to the allergen.

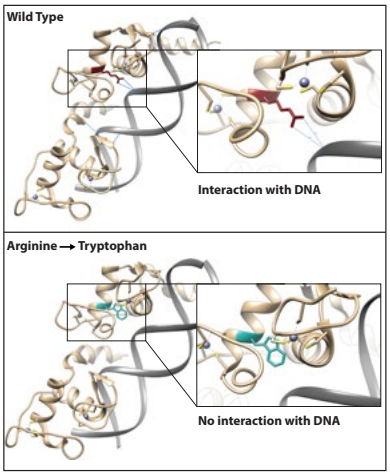
In this study, we have used the strong experimental allergen 1-fluoro-2,4-dinitrobenzene. The next step in the project is therefore to examine if this is a general mechanism of contact allergens or a mechanism only induced by strong experimental allergens. We are currently investigating the local memory response to various clinically relevant contact allergens.

NOVEL INSIGHTS INTO VITAMIN D3-MEDIATED REGULATION OF THE IMMUNE RESPONSE THROUGH CHARACTERIZATION OF A NEW MUTATION IN THE VITAMIN D RECEPTOR

Vitamin D_3 regulates numerous aspects of both innate and adaptive immune responses. Many studies also indicate that vitamin D_3 deficiency is associated with increased susceptibility to infectious diseases. However, the in vivo immunomodulatory effects of vitamin D_3 in humans is notoriously difficult to assess, since there will always be some vitamin D_3 present, even in severely vitamin D_3-deficient individuals. Vitamin D_3 exerts its biological actions through binding to the intracellular vitamin D receptor (VDR), and mutations in VDR cause a very rare genetic autosomal recessive disease called Hereditary Vitamin D Resistant Rickets (HVDRR). Such mutations are characterised by VDR loss-of-function resulting in target organ resistance to the action of vitamin D. This means that immune cells from patients suffering from HVDRR can be used as a unique experimental model to characterise the immunomodulatory roles of vitamin D_3 in humans.

In this project, we have identified a novel missense mutation in the VDR in a patient suffering from HVDRR. The mutation locates to the DNA-binding domain (DBD) of the VDR, where an arginine at position 80 is substituted with a tryptophan. Consequently, this mutation renders VDR unable to bind DNA and regulate vitamin D_3-responsive genes. In contrast, the mutation affected neither VDR's ability to bind to vitamin D_3, nor its ability to interact with the retinoic X receptor (RXR). We have shown that family members heterozygous for the mutation have an intermediary response to vitamin D_3 in vitro.

We have also investigated the functional consequences of the VDR mutation in relation to infection with SARS-CoV-2. Quickly following the onset of the pandemic, many reports suggested an important and potentially therapeutic role of vitamin D_3 in COVID-19. However, following infection with SARS-CoV-2, the patient suffering from HVDRR and the heterozygous parents only had a mild disease course. We found similar levels of SARS-CoV-2 specific memory CD4+ and CD8+ T cells and spike-protein-specific antibodies in the HVDRR patient and the parents as in control patient with a mild disease course of SAR-CoV-2. Therefore, at least in the case of infection with SARS-CoV-2 in this family, the activity of the VDR does not seem to be essential for the immune response. Although these observations might not directly be transferred to the general population, they question a central role of vitamin D in the generation of adaptive immunity against SARS-CoV-2.



The project has shown that the regulation of vitamin D-responsive genes is abolished when the vitamin D receptor can no longer interact with DNA.

Currently, we are working to clarify the role of vitamin D in eradication of Mycobacterium tuberculosis infection through regulation of the antimicrobial peptide cathelicidin. We investigate the expression levels of cathelicidin in monocyte-derived macrophages from heathy donors and family members with the VDR mutation. We have observed that in response to vitamin D_3 treatment, cathelicidin is highly up-regulated. This is, however, not the case in patients suffering from HVDRR and in heterozygous family members where only an intermediary up-regulation is observed. We are currently conducting in-depth investigations of the interplay between vitamin D_3, cathelicidin and Mycobacterium tuberculosis.

As a PhD student, Fatima Abdul Hassan Al-Jaberi studies the importance of Vitamin D_3 in regulating immune responses.

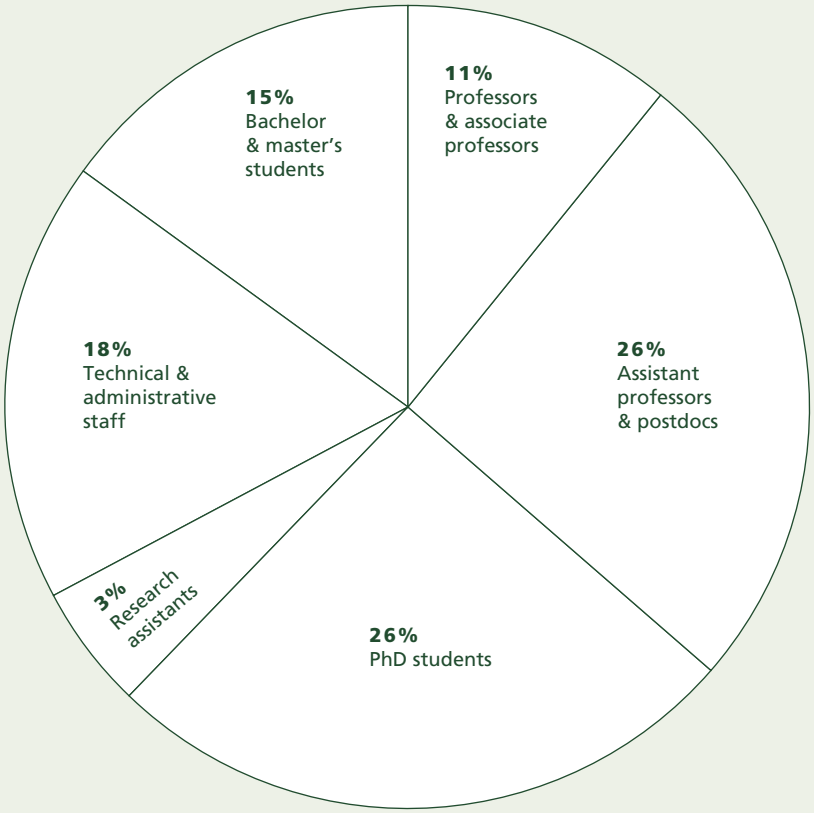
Organisation and governance

SIC is a separate organisational entity embedded in the Department of Immunology and Microbiology (ISIM) at the Faculty of Health and Medical Sciences at the University of Copenhagen. SIC's four basic research groups are based at the headquarters at the Mærsk Tower in the heart of Copenhagen. From here, scientific activities span widely, across the Faculty and across national and international clinical research units and the life science industry.

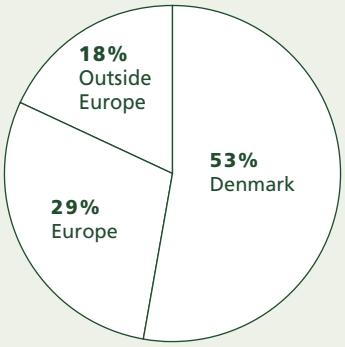
STAFF COMPOSITION

By the end of 2021, a total of 62 staff members and students of 15 different nationalities was engaged in SIC's four basic research groups.

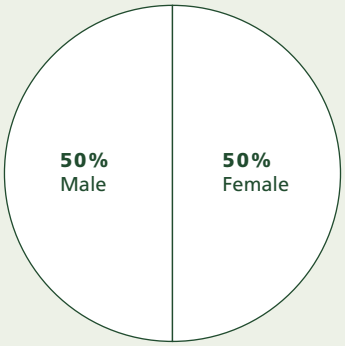
The compositional staff data presented here include visiting guest researchers, PhD students to whom SIC researchers provide main supervision and bachelor and master's students (students conducting their thesis work or completing exchange stays in SIC's laboratories). A full list of staff and students engaged in the research groups throughout the year is presented on page 39.



Distribution of staff and students by position



Nationalities of scientific staff and students



Gender distribution of scientific staff and students

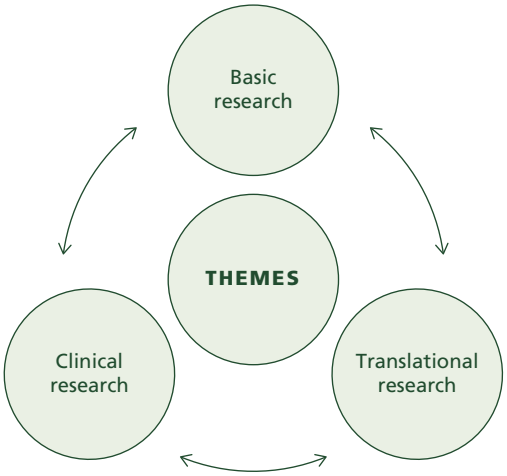
THE CORE MEMBERS

After the addition of one new basic research group in 2021, SIC now has five core members: Basic Research Group Leaders and Professors Liv Eidsmo, Charlotte Menné Bonefeld, Anders Woetmann and Mads Gyrd-Hansen and – as a representative of the translational and clinical research environment – Clinical Professor at Herlev and Gentofte Hospital, Lone Skov. The core members make up the Center Steering Committee which proposes and implements strategic scientific initiatives. The group of core members constitute the key framework behind the 'Team Science Concept'.

MANAGEMENT

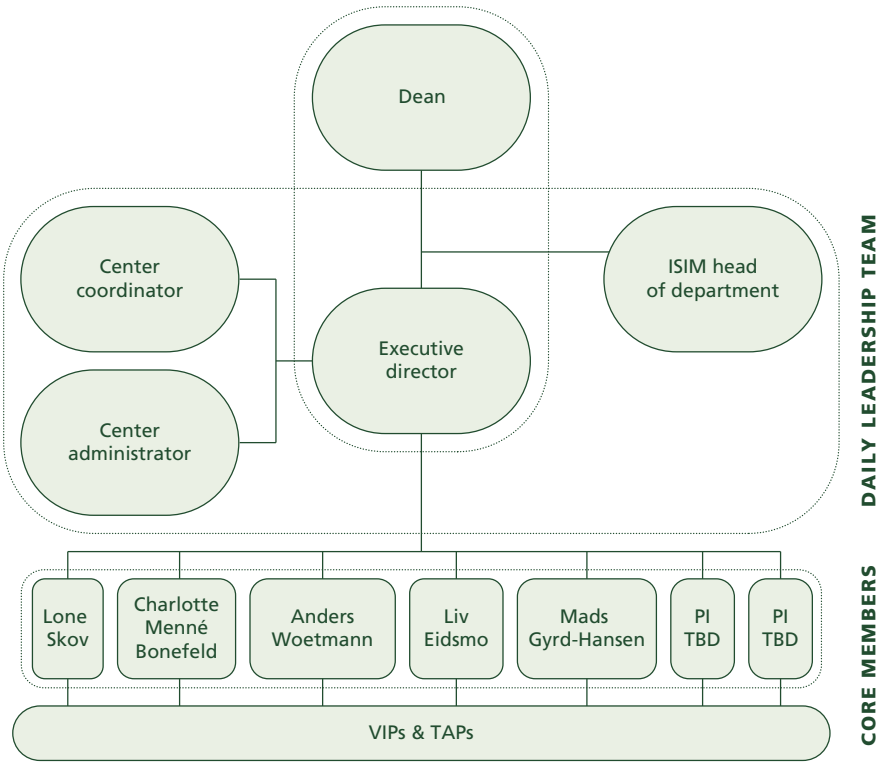
SIC's Daily Leadership Team – consisting of Executive Director **Liv Eidsmo**, ISIM Head of Department **Charlotte Menné Bonefeld**, Center Administrator **Nils Erik Samdal** and Center Coordinator **Bitten Dalsgaard** – executes and oversees the Center's day-to-day operations. The Executive Director and the leadership team meet with Dean of the Faculty of Health and Medical Sciences, **Ulla Wewer**, on a regular basis to discuss and decide strategic matters related to the continuous development of SIC. Rector of the University of Copenhagen, **Henrik C. Wegener**, is the grant holder of the SIC grant and once a year aligns with the Center Management and the LEO Foundation on strategic progress and development.

THE TEAM SCIENCE CONCEPT



SIC investigates fundamental questions within skin biology and diseases in an interdisciplinary team of scientists with core competences and insights into basic, translational and clinical skin-related research. We call this 'the Team Science Concept'.

STRATEGIC MANAGEMENT



Organisation and governance chart.

‘IN DENMARK, YOU ARE ON A FIRST NAME BASIS WITH YOUR PROFESSOR AND EAT LUNCH WITH THE EXECUTIVE DIRECTOR’

SIC aims to attract young and talented researchers from across the world to join the Center’s research environment in Copenhagen. PhD students Malin Jessen and Frederik Timmermann recently relocated from Germany and postdoc Chris Kedong Wang relocated from Canada to join the Molecular Immunology and Inflammation Group. Here, they reflect on their expectations and experiences with SIC as a workplace and their new life in Denmark.

HOW WOULD YOU DESCRIBE THE SCIENTIFIC ENVIRONMENT AT SIC?

Chris: *SIC is a young research centre with a very open environment, and we see how it evolves all the time. Everyone here takes on the responsibility of creating opportunities to interact. Working on skin immunology as our central theme leads to more collaborations across the groups than I had expected.*

Frederik: *‘Independent’ is the first word that comes to mind. The projects we do here stem from basic scientific curiosity to improve our understanding of disease mechanisms, and we have the time and place to see where our ideas can lead us in terms of future treatment for patients.*

Malin: *At the same time, it is an efficient place to be. We have excellent core facilities available, and as a newcomer, you receive thorough training, which makes it easy to get started on your experiments.*

WHAT MADE YOU DECIDE TO MOVE TO COPENHAGEN?

Malin: *To me, Copenhagen was a very attractive place to go to. It is a highly international city, and the graduate programmes here are focused and of very high quality. The immunology environment here also has a very good reputation internationally. So, when the Molecular Immunology and Inflammation Group was established, it was just the opportunity I was looking for.*

Frederik: *I knew about Professor Mads Gyrd-Hansen's work during my master's studies and hoped to eventually become a PhD student in his group. When I learned he was moving from Oxford to Copenhagen, my first thought was 'where?', but as I looked into it, I was impressed with the opportunities and how well organised everything is at SIC and the University of Copenhagen at large.*

WHAT ARE YOUR EXPERIENCES WITH LIFE AND WORK HERE?

Malin: *The housing situation in central Copenhagen is challenging, but once you find a place to live, settling into a new life here is easy. Denmark is a highly digitalised society, and Danes speak English fluently, which makes the transition very smooth. Then you just grab your bike and go meet new people.*

Frederik: *At first, I was surprised by how high housing and living expenses are in Copenhagen, but it is an expression of how little hierarchical the Danish society is. Everyone is paid fairly high wages. The low hierarchy is also practiced at work. We call our professors by their first name, and we all eat lunch next to Liv, our Executive Director, on a daily basis.*

Chris: *Everyone is as dedicated to their work here as in other places I have been. But when Danes talk about work-life balance, they mean it. We have a lot of flexibility in planning our work schedules, and we are expected to take our vacation days. It is definitely a motivational factor and contributes to a good working environment.*

Outreach and communication

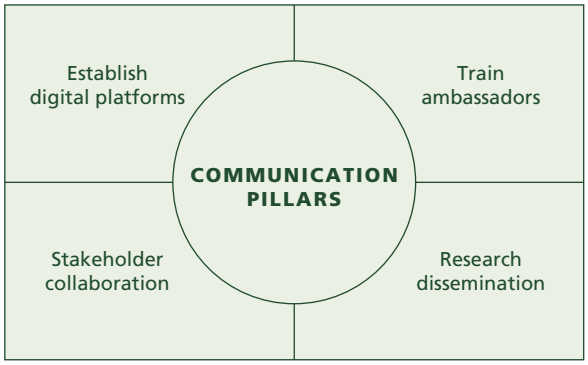
Communication efforts completed in 2021 have primarily focused on SoMe training, teaching experience as well as interaction with the public and outside world on skin related issues. The communication activities also supported the SIC's international recruitment effort to identify new group leaders for the Center.

SIC has been a visible, public voice on skin, skin diseases and immunology in 2021, primarily in the media as many physical outreach activities were cancelled due to the COVID-19 pandemic. News stories about how the body reacts to contact allergens and the establishment of a biobank with skin tissue and blood samples from 3,000 patients both performed very well and had a great exposure internationally as well as nationally. They were published both on the websites of the University of Copenhagen and on the LEO Foundation's digital platforms. Moreover, they were published in international as well as national media such as Berlingske, DR, TV2, Jyllands-Posten and Science Report.

Professor Charlotte Menné Bonefeld participated in the Danish radio show 'Sygt nok', where she talked about the evolution of the skin and discussed the immunological functions and incredible adaptiveness of human skin with Jørn Madsen, evolutionary biologist and Christian Vestergaard, chief physician in skin and venereal diseases at Aarhus University Hospital. The podcast is available at dr.dk/lyd/p1/sygt-nok.

In May, all researchers at SIC had the opportunity to join two workshops for beginners in social media. The online workshops provided hands-on training on the use of Twitter and LinkedIn and guided the participants on how to actively use their accounts to create awareness about their research and expand and engage their professional network. The workshops were tailored for SIC's researchers and clinical members of the Young Investigator Network.

During the year, SIC highlighted the new mini course in skin immunology for third-year secondary school organised together with Gefion Gymnasium and documented participants' experiences from the Summer School held at Hotel Hornbækhus. SIC further focused on communicated news of external research funding obtained by the groups, allowing the Center to conduct several new novel studies.



Find us on social media

TWITTER @skinucph
LINKEDIN LEO Foundation Skin Immunology Research Center

In May, SIC announced a call for letters of interest for group leader positions at the Center. Communication efforts supported the wide distribution of the call to reach excellent researchers and research environments across the world.

In 2022, the focus will be on communication training, offering story telling tools, SoMe and media training. There will also be focus on research dissemination via media and outreach activities, dialogue with stakeholder relations and a continuing focus on recruitment of talented researchers and students.

UPCOMING EVENTS

SIC hosts the translational networking event "From clinical observation to new mechanistic insights' at the Nordic Congress of Dermatology and Venereology 2022 on 19 April 2022.

Visit ncdv2022.org for details.

The SIC Summer School 2022 on 'Immune Regulation of the Skin' will be held from 25-27 April 2022 in Hornbæk, Denmark.

Visit embo.org/summerschool for details.

Group leader Anders Woetmann participates in the Bloom Festival from 27-29 May 2022 in Copenhagen for a scientific discussion on the relationship between regeneration and immunology.

Visit bloom.ooo for details.

SEMINARS AND WEBINARS BY INVITED GUEST LECTURERS IN 2021

Negative regulation of the inflammasome signalling

Senior Research Fellow
Jelena Bezbradica Mirkovic
Kennedy Institute of Rheumatology, University of Oxford

The extracellular matrix as a regulator of immune activity

Senior Researcher Daniel Hargbøl Madsen
Center for Cancer Immune Therapy (CCIT), Herlev and Gentofte Hospital

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Cellular stress responses: Signals, sensors and outcomes

Professor Simon Bekker-Jensen
Center for Healthy Aging, University of Copenhagen

GlycoSkin: How to use genetic engineering and 3D models in dissection of function

Associate Professor Sally Dabelsteen
Copenhagen Center for Glycomics/Department of Odontology, University of Copenhagen

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Development and function of IL-17-producing γδ T cells

Associate Professor Vasileios Bekiaris
Department of Health Technology, DTU

High-throughput high-efficiency immune cell engineering for immune therapy and functional analysis

Senior Researcher Brian Tate Weinert
Novo Nordisk Foundation Center for Biosustainability, DTU

Intracellular signalling molecules in psoriasis: New potential treatment targets

Associate Professor Claus Johansen
Department of Dermatology and Venereology, Aarhus University

The skin microbiome in health and disease

Professor Thomas Bjarnsholt
Department of Immunology and Microbiology, University of Copenhagen

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SIC actively uses digital platforms and events such as the Summer School to interact with collaborators, stakeholders and the general public.

Funding and awards

SIC was awarded DKK 400 million by the LEO Foundation for Center operations in 2019-2028, distributed on a base grant of DKK 250 million and a pool for add-on grants of DKK 150 million. The turnover from the base grant totalled DKK 17.5 million, and the turnover from the add-on grants totalled DKK 9.8 million in 2021. Also, SIC obtained a total of DKK 18.6 million in new funding from nine external research grants.

SIC'S SENIOR RESEARCHERS CONTRIBUTE TO THE DISTRIBUTION OF RESEARCH GRANTS ASBOARD AND COUNCIL MEMBERS OF THE FOLLOWING FUNDING BODIES:

- Academy of Finland
- Danish Cancer Society
- European Cooperation in Science and Technology (COST)
- Icelandic Research Fund
- Medical Research Foundation
- Nordic Dermatology Association
- Swedish Dermatology Association
- Swedish Research Council
- Wellcome Trust

EXTERNAL RESEARCH GRANTS AWARDED IN 2021

FUNDER	RECIPIENT	AWARD TITLE	AMOUNT IN DKK
Aage Bangs Fond	**Marianne Bengtson Løvendorf**	Composition of proteins in the skin - impact on identification and treatment of skin diseases	200,000
Aage Bangs Fond	**Kelvin Yeung**	The role of IL1 beta in contact allergy	270,000
Estonian Research Council	**Helen Vaher**	The role of microRNAs in the regulation of the generation and maintenance of skin resident memory T cells	715,500
European Academy of Dermatology and Venereology	**Helen Vaher**	The role of microRNAs in the regulation of the generation and maintenance of skin resident memory T cells	225,000
Lundbeck Foundation	**John Rizk**	Linear Ub deubiquitinases in Tregs (LinDeT)	2,400,000
Novo Nordisk Foundation	**Niels Ødum**	Tandem Programme — Translational research collaboration between Basic and Clinical Researchers	9,875,561
Translational Excellence Research Programme	**Anders Woetmann**	BRIDGE Fellowship	1,130,000
Translational Excellence Research Programme	**Niels Ødum**	BRIDGE Fellowship	1,130,000
Wellcome Trust (transfer from Oxford University)	**Mads Gyrd-Hansen**	Regulation of Met1-linked ubiquitin and its impact on immune function	2,670,000

Scientific output

SIC researchers authored 35 publications in peer-reviewed journals in 2021. Bibliometric data of senior scientists and publications of the year are listed here.

Sources: Scopus, Web of Science

H-INDEX OF SENIOR SCIENTISTS

RESEARCHER	NO. OF PUBLICATIONS (TOTAL)	NO. OF CITATIONS (TOTAL)	H-INDEX
Professor **Anders Woetmann**	127	4,774	39
Professor **Carsten Geisler**	200	6,643	45
Professor **Charlotte M. Bonefeld**	135	2,834	32
Professor **Liv Eidsmo**	53	3,478	24
Professor **Mads Gyrd-Hansen**	52	3,643	26
Professor **Niels Ødum**	309	10,423	55
Associate Professor **Thorbjørn Krejsgaard**	59	2,119	28

HIGH-IMPACT PUBLICATIONS 2019-2021

Number of publications in high-impact journals (impact factor >10).

2019	2020	2021	TOTAL
1	1	5	7

PUBLICATIONS

Publications are listed in alphabetical order by article name. Journal and impact factor are in bold.

A gene-centric approach to biomarker discovery identifies transglutaminase 1 as an epidermal autoantigen.

Landegren N, Ishii N, Aranda-Guillén M, Gunnarsson HI, Sardh F, Hallgren Å, Ståhle M, Hagforsen E, Bradley M, Edqvist PD, Pontén F, Mäkitie O, Eidsmo L, Norlén L, Achour A, Dahlbom I, Korponay-Szabó I, Agardh D, Alimohammadi M, Eriksson D, Hashimoto T, Kämpe O.

Proc Natl Acad Sci USA. 2021 Dec.118;e2100687118. **11.205**

Acute Experimental Barrier Injury Triggers Ulcerative Colitis-Specific Innate Hyperresponsiveness and Ulcerative Colitis-Type Microbiome Changes in Humans.

Seidelin JB, Bahl MI, Licht TR, Mead BE, Karp JM, Johansen JV, Riis LB, Galera MR, Woetmann A, Bjerrum JT.

Cell Mol Gastroenterol Hepatol. 2021 Jan.12;1281:1296. **9.225**

Applicability of Small-Molecule Inhibitors in the Study of Peptidyl Arginine Deiminase 2 (PAD2) and PAD4.

Martín Monreal MT, Rebak AS, Massarenti L, Mondal S, Šenolt L, Ødum N, Nielsen ML, Thompson PR, Nielsen CH, Damgaard D.

Front Immunol. 2021 Oct.12;716250. **7.561**

Autologous serum skin test reactions in chronic spontaneous urticaria differ from heterologous cell reactions.

Baumann K, Marcelino J, Skov PS, Santos MCP, Wyroslak I, Scheffel J, Altrichter S, Woetmann A, Costa C, Maurer M.

J Eur Acad Dermatol Venereol. 2021 Jun.35;1338:1345. **6.166**

Bacterial genotoxins induce T cell senescence.

Mathiasen SL, Gall-Mas L, Pateras IS, Theodorou SDP, Namini MRJ, Hansen MB, Martin OCB, Vadivel CK, Ntostoglou K, Butter D, Givskov M, Geisler C, Akbar AN, Gorgoulis VG, Frisan T, Ødum N, Krejsgaard T.

Cell Rep. 2021 Jun. 35;109220. **9.423**

CD8+ tissue-resident memory T cells recruit neutrophils that are essential for flare-ups in contact dermatitis.

Funch AB, Mraz V, Gadsbøll ASØ, Jee MH, Weber JF, Ødum N, Woetmann A, Johansen JD, Geisler C, Bonefeld CH.

Allergy. 2021 Jun. 77;513:524. **13.146**

Design of pyrido[2,3-d]pyrimidin-7-one inhibitors of receptor interacting protein kinase-2 (RIPK2) and nucleotide-binding oligomerization domain (NOD) cell signaling.

Nikhar S, Siokas I, Schlicher L, Seungheon L, Gyrd-Hansen M, Degterev A, Cuny GD.

Eur J Med Chem. 2021 Feb. 215;113242. **6.514**

Diagnostic Two-Gene Classifier in Early-Stage Mycosis Fungoides: A Retrospective Multicenter Study.

Nielsen PR, Eriksen JO, Lindahl LM, Wehkamp U, Bzorek M, Andersen G, Woetmann A, Iversen L, Ødum N, Litman T, Gjerdrum LMR.

J Invest Dermatol. 2021 Jan.141;213:217. **8.551**

Distinct contribution of hyperbaric oxygen therapy to human neutrophil function and antibiotic efficacy against Staphylococcus aureus.

Schwartz FA, Lerche CJ, Christophersen L, Jensen PØ, Laulund AS, Woetmann A, Høiby N, Moser C.

APMIS. 2021 Sep. 129;566:573. **3.205**

Epidermal T cell subsets - Effect of age and antigen exposure in humans and mice.

Gadsbøll AØ, Jee MH, Ahlström MG, Dyring-Andersen B, Woetmann A, Ødum N, Johansen JD, Geisler C, Bonefeld CM.

Contact Dermatitis. 2021 Jun. 84:375-384. **6.600**

Factors associated with adverse COVID-19 outcomes in patients with psoriasis-insights from a global registry-based study.

Mahil SK, Dand N, Mason KJ, Yiu ZZN, Tsakok T, Meynell F, Coker B, McAteer H, Moorhead L, Mackenzie T, Rossi MT, Rivera R, Mahe E, Carugno A, Magnano M, Rech G, Balogh EA, Feldman SR, De La Cruz C, Choon SE, Naldi L, Lambert J, Spuls P, Jullien D, Bachele, H, McMahon DE, Freeman EE, Gisondi P, Puig L, Warren RB, Di Meglio P, Langan SM, Capon F, Griffiths CEM, Barker JN, Smith CH.

Liv Eidsmo and Lone Skov contributed to the PsoProtect Study Group.

J Allergy Clin Immun. 2021 Jan.147;60:71. **10.794**

Impaired Vitamin D Signaling in T Cells From a Family With Hereditary Vitamin D Resistant Rickets.

Al-Jaberi FAH, Kongsbak-Wismann M, Aguayo-Orozco A, Krogh N, Buus TB, Lopez DV, Rode AKO, Gravesen E, Olgaard K, Brunak S, Woetmann A, Ødum N, Bonefeld CM, Geisler C.

Front Immunol. 2021 May. 19;12:684015. **7.561**

Improving oligo-conjugated antibody signal in multimodal single-cell analysis.

Buus TB, Herrera A, Ivanova E, Mimitou E, Cheng A, Herati RS, Papagiannakopoulos T, Smibert P, Odum N, Koralov SB.

eLife. 2021 Apr. 16;10:e61973. **8.146**

Inhibition of succinate dehydrogenase activity impairs human T cell activation and function.

Nastasi C, Willerlev-Olsen A, Dalhoff K, Ford SL, Gadsbøll AØ, Buus TB, Gluud M, Danielsen M, Litman T, Bonefeld CM, Geisler C, Ødum N, Woetmann A.

Sci Rep. 2021 Jan. 11:1458. **4.380**

Intestinal helminth infection transforms the CD4+ T cell composition of the skin.

Classon CH, Li M, Clavero AL, Ma J, Feng X, Tibbitt CA, Stark JM, Cardoso R, Ringqvist E, Boon L, Villablanca EJ, Rothfuchs AG, Eidsmo L, Coquet JM, Nylén S.

Mucosal Immunol. 2021 Dec. **7.313**

Investigating the Early Events after Skin-Barrier Disruption Using Microdialysis—A Human Ex Vivo Skin Model.

Baumann K, Knudsen NPH, Gadsbøll ASØ, Woetmann A, Skov PS.

Dermato. 2021 Nov. 1;47:58. **N/A**

IL-22 Ddownregulates Peptidylarginine Deiminase-1 in Human Keratinocytes: Adding Another Piece to the IL-22 Puzzle in Epidermal Barrier Formation.

Padhi A, Srivastava A, Ramesh A, Ehrström M, Simon M, Sonkoly E, Eidsmo L, Bergman P, Lysell J.

J Invest Dermatol. 2021 Aug.142;333:342. **8.551**

JAK3 Is Expressed in the Nucleus of Malignant T Cells in Cutaneous T Cell Lymphoma (CTCL).

Vadivel CK, Gluud M, Torres-Rusillo S, Boding L, Willerslev-Olsen A, Buus TB, Nielsen T, Persson JL, Bonefeld CM, Geisler C, Krejsgaard T, Fuglsang AT, Odum N, Woetmann A.

Cancers. 2021 Jan.13:280. **6.639**

Long-term Outcomes and Prognosis in New-Onset Psoriasis.

Svedbom A, Mallbris L, Larsson P, Nikamo P, Wolk K, Kjellman P, Sonkoly E, Eidsmo L, Lindqvist U, Ståhle M.

JAMA Dermatol. 2021 Apr. 157;1:8. **10.282**

Macrophages Control the Bioavailability of Vitamin D and Vitamin D-Regulated T Cell Responses.

Lopez DV, Al-Jaberi FAH, Woetmann A, Ødum N, Bonefeld CM, Kongsbak-Wismann M, Geisler C.

Front Immunol. 2021 Sep. 12;722806. **7.561**

MicroRNA-93 Targets p21 and Promotes Proliferation in Mycosis Fungoides T Cells.

Gluud M, Fredholm S, Blümel E, Willerslev- Olsen A, Buus TB, Nastasi C, Krejsgaard T, Bonefeld CM, Woetmann A, Iversen L, Litman T, Geisler C, Ødum N, Lindahl LM.

Dermatology. 2021 Apr. 237;277:282. **5.366**

Multimodal single-cell analysis of cutaneous T-cell lymphoma reveals distinct subclonal tissue-dependent signatures.

Herrera A, Cheng A, Mimitou EP, Seffens A, George D, Bar-Natan M, Heguy A, Ruggles KV, Scher JU, Hymes K, Latkowski JA, Ødum N, Kadin ME, Ouyang Z, Geskin LJ, Smibert P, Buus TB, Koralov SB.

Blood. 2021 Oct.138;1456:1464. **23.629**

Normal T and B Cell Responses Against SARS-CoV-2 in a Family With a Non-Functional Vitamin D Receptor: A Case Report.

Kongsbak-Wismann M, Al-Jaberi FAH, Schmidt JD, Ghanizada M, Hansen CB, Lopez DV, Woetmann A, Ødum N, Bonefeld CM, Stryhn A, Garred P, Buus S, Geisler C.

Front Immunol. 2021 Sep. 12;758154. **7.561**

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*PADI4 Polymorphisms Confer Risk of Anti-CCP-Positive Rheumatoid Arthritis in Synergy With HLA-DRB1*04 and Smoking.*

Massarenti L, Enevold C, Damgaard D, Ødum N, Garred P, Frisch M, Shelef MA, Jacobsen S, Nielsen CH.

Front Immunol. 2021 Oct. 12;707690. **7.561**

Regulation of CYLD activity and specificity by phosphorylation and ubiquitin-binding CAP-Gly domains.

Elliott PR, Leske D, Wagstaff J, Schlicher L, Berridge G, Maslen S, Timmermann F, Ma B, Fischer R, Freund SMV, Komander D, Gyrd-Hansen M.

Cell Rep. 2021 Oct. 37;109777. **9.423**

SARS-CoV-2 mRNA vaccine elicits a potent adaptive immune response in the absence of IFN-mediated inflammation observed in COVID-19.

Ivanova EN, Devlin JC, Buus TB, Koide A, Shwetar J, Cornelius A, Samanovic MI, Herrera A, Mimitou EP, Zhang C, Desvignes L, Odum N, Smibert P, Ulrich RJ, Mulligan MJ, Koide S, Ruggles KV, Herati RS, Koralov SB.

medRxiv. 2021 Aug. 04:20:21255677. **N/A**

Single-Cell Analysis Reveals Major Histocompatibility Complex II–Expressing Keratinocytes in Pressure Ulcers with Worse Healing Outcomes.

Li D, Cheng S, Pei Y, Sommar P, Kärner J, Herter EK, Toma MA, Zhang L, Pham K, Cheung YT, Liu Z, Chen X, Eidsmo L, Deng Q, Xu Landén N.

J Invest Dermatol. 2021 Sep. S0022-202X;02167:9. **8.551**

Skin T cells maintain their diversity and functionality in the elderly.

Koguchi-Yoshioka H, Hoffer E, Cheuk S, Matsumura Y, Vo S, Kjellman P, Grema L, Ishitsuka, Y, Nakamura, Y, Okiyama N, Fujisawa Y, Fujimoto M, Eidsmo L, Clark RA, Watanabe R.

Commun Biol. 2021 Jan. 4;4:13. **6.268**

Staphylococcus aureus and Antibiotics in Cutaneous T-Cell Lymphoma.

Lindahl LM, Iversen L, Ødum N, Kilian M.

Dermatology. 2021 Oct.1:3. **5.366**

Staphylococcus aureus Induces Signal Transducer and Activator of Transcription 5–Dependent miR-155 Expression in Cutaneous T-Cell Lymphoma.

Willerslev-Olsen A, Gjerdrum LMR., Lindahl LM, Buus TB, Pallesen EMH, Gluud M, Bzorek M, Nielsen BS, Kamstrup MR, Rittig AH, Bonefeld CM, Krejsgaard T, Geisler C, Koralov SB, Litman T, Becker JC, Woetmann A, Iversen L, Odum N.

Invest Dermatol. 2021 Oct. 141;2449:2458. **8.551**

The Met1-linked ubiquitin machinery in inflammation and infection.

Fiil BK, Gyrd-Hansen M.

Death Differ. 2021 Jan. 28;557:569. **15.828**

The role of interleukin-1β in the immune response to contact allergens.

Yeung K, Mraz V, Geisler C, Skov L, Bonefeld CM.

Contact Dermatitis. 2021 Oct. 85;387:397. **6.600**

Vitamin D Inhibits IL-22 Production Through a Repressive Vitamin D Response Element in the il22 Promoter.

Lopez DV, Al-Jaberi FAH, Damas ND, Weinert BT, Pus U, Torres-Rusillo S, Woetmann A, Ødum N, Bonefeld CM, Kongsbak-Wismann M, Geisler C.

Front Immunol 2021 Aug. 12;715059. **7.561**

What Basophil Testing Tells Us About CSU Patients - Results of the CORSA Study.

Marcelino J, Baumann K, Skov PS, Pereira Santos MC, Wyroslak I, Scheffel J, Altrichter S, Woetmann A, Pereira-Barbosa M, Costa C, Maurer M.

Front Immunol 2021 Sep. 12;742470. **7.561**

ZBP1 induces inflammatory signaling via RIPK3 and promotes SARS-CoV-2-induced cytokine expression.

Ruoshi Peng, Xuan Wang-Kan, Manja Idorn, Felix Y Zhou, Susana L Orozco, Julia McCarthy, Carol S Leung, Xin Lu, Katrin Bagola, Jan Rehwinkel, Andrew Oberst, Jonathan Maelfait, Søren R Paludan, Mads Gyrd-Hansen

bioRxiv. 2021 Oct. **N/A**

Full staff list

/// Funded by the SIC grant
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/ Not funded by the SIC grant

PROFESSORS

/ Anders Woetmann
/ Carsten Geisler
/ Charlotte Menné Bonefeld
/// Liv Eidsmo
/// Mads Gyrd-Hansen
/ Niels Ødum

CLINICAL PROFESSORS

/ Jeanne Duus Johansen
/ Lone Skov

ASSOCIATE PROFESSORS

/ Beatrice Dyring-Andersen
/// Marianne Bengtson Løvendorf
/// Thorbjørn Frej Krejsgaard

ASSISTANT PROFESSORS AND POSTDOCS

/ Andreas Willerslev-Olsen
/// Anne-Sofie Østergaard Gadsbøll
/// Berthe Katrine Fiil
/ Chris Kedong Wang
/// Ekaterina Zhuravleva
/// Emil Marek Heymans Pallesen
/ Helen Vaher
// John Rizk
/ Katrine Baumann
/ Mandy Menzel
/ Martin Kongsbak-Wismann
/// Mia Hamilton Jee
/ Morten Orebo Holmström
/// Nicolai Skovbjerg Arildsen
/ Tea Kirkegaard Nielsen
/ Terkild Brink Buus

PHD STUDENTS

/ Anders Boutrup Funch
/ Anna Kathrine Obelitz Rode
/ Chella Krishna Vadivel
/ Cheng Chi
/// Christina Yndal Erichsen
/ Daniel Villalba Lopez
/ Eileen Donohue Wedge
/ Fatima Abdul Hassan Al-Jaberi
/// Frederik Timmermann
/ Katharina Wörzner
// Kelvin Young
/ Laura Massarenti
/// Lisa Harth
/ Lukas Peiffer
/ Malin Jessen
/ Maria Gluud Grøndahl
/ Maria Teresa Martin Monreal
/// Marina Ramírez Galera
/// Martin Rich Javadi Namini
/ Oliver Krigslund
/// Shayne Lavondua Ford
/// Veronika Mraz
/// Wenxin Lyu

RESEARCH ASSISTANTS

/ Anders Lykkebo-Valløe
/// Lasse Balthzer Schmidt
/// Trine Schønfeldt

GUEST RESEARCHERS

// Marina Passos Torrealba
/ Sara Torres Rusillo

BACHELOR AND MASTER'S STUDENTS

/ Mariana Bronze
/ Ziao Zeng
/ Leila Gharedaghi
/ Louise Aagaard
/ Salome Marine Astreé Havard-Guibert
/ Rebecca Mirjam Freya Sturm
/ Miriam Beichler
/ Fie Bendix Thomsen

LAB MANAGERS, TECHNICIANS AND SPECIALISTS

/// Christina Agerbeck
/ Julie Weber Friis
/ Louise Mørk
/// Maja Søberg Udsen
/// Majken Kjær
/// Marta Madacsi
/// Rasmus Nielsen Klitgaard
/ Rebecca Kitt Davidson Lohmann
/// Rikke Juul Wittrup
/ Sana Ahmed

ADMINISTRATION

/// Bitten Dalsgaard
// Mette Malene Odgaard
// Nils Erik Samdal

LEO Foundation
Skin Immunology
Research Center

ADDRESS Blegdamsvej 3b
2200 Copenhagen N
Denmark

EMAIL sic@sund.ku.dk

PHONE +45 20 40 22 68

WEB sic.ku.dk

TWITTER @skinucph