Annual Activity Report 2023

LEO Foundation
Skin Immunology
Research Center

Content

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Introduction

The LEO Foundation Skin Immunology Research Center (SIC) has a unique 10-year perspective to advance research and education of inflammatory skin diseases.

The skin is our largest barrier to the external environment and the number of skin diseases exceeds 3,000. In Denmark, skin diseases remain one of the most common reasons to seek medical consultation and up to 20% of school children suffer from atopic dermatitis. The knowledge of diseases mechanisms has accelerated over the past decade and discoveries within immunology have paved the way for new treatments. Despite this significant progress, curative treatments for common inflammatory skin diseases are not available yet, and these diseases come with a large impact on quality of life as well as on society as a whole. Co-morbidities in other barrier tissues are common and with rapid development of immunomodulatory treatments for psoriasis and atopic dermatitis, it is increasingly clear that dampening inflammation in the skin may lead to inflammation in other parts of the body.

The LEO Foundation Skin Immunology Research Center (SIC) was established to advance research and education in common inflammatory skin diseases 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 the common inflammatory skin diseases psoriasis, atopic and contact dermatitis but we also cover cutaneous T cell lymphoma as a model disease of T cell driven pathology in skin. SIC aims is to integrate, bridge and advance basic and clinical scientific approaches to skin disease. With new recruitments, SIC has secured interdisciplinary excellence from mucosal barriers to address the increasingly appreciated co-morbidities that occurs in common inflammatory skin diseases. Our research covers many different perspectives of fundamental research with impact with patients living with inflammatory skin diseases. Importantly, we educate future scientists with the aim to nurture the next generation of leaders in the field, and concurrently increase the 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

- Lead discoveries of mechanisms that cause and maintain skin diseases
- Be an international center of excellence for barrier tissue immunology research
- Educate the next generation of research leaders in barrier tissue immunology

KEY RESEARCH THEMES

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

Director's Corner

Executive Director of SIC, Professor Liv Eidsmo.

A Dynamic Era for Skin Immunology

My lasting impression from 2023 is the privilege to participate in truly exciting times for skin and tissue immunology! Over the last years, technical progress and new mechanistic insights have coincided with rapid implementation of new immunomodulatory drugs in the clinic. The common skin diseases psoriasis, atopic dermatitis and contact allergy are all caused by local overactivation of the immune system. Despite the impressive development of new treatments, tools to predict of disease trajectories, effective prevention of disease progression, and curative treatments are still lacking. The LEO Foundation Skin Immunology Research Center (SIC) is well positioned to explore the intersection between fundamental research and new insights from the clinic with the goal to improve lives for people living with chronic skin diseases.

Our scientific scope is enriched with exciting insights from mucosal barriers in lung and gut with the recruitment of Associate Professor Jonathan Coquet, from Karolinska Institutet, and Professor Bill Agace, from DTU and Lund University. A center that focuses on skin immunology benefits from expertise in other tissues. One example of the relevance for SIC to study different barrier tissues is the side effects of inflammation in gut and eyes that can occur during immunolodulatory treatments for psoriasis and atopic dermatitis.

As SIC grows, our interface with the international community is expanding. Our Springtime School gathers scholars and young researchers from all over the world in the quaint seaside town Hornbæk. Intense scientific discussions during our three days away have formed long-lasting scientific relationships and it is always fun to meet up with our alumni in international meetings. Our postdocs and faculty also invite international speakers to SIC to interact with the scientific community at the Department and faculty. During 2023, workshops in SIC have brought international experts together with local scientists to explore topics close to our heart, such as proteomics and how to breach the skin barrier with local therapies.

Our commitment to education and mentorship extends from high school courses, through BSc and MSc programmes to PhD courses. During 2023 we extended this commitment to a SIC PhD programme. SIC already hosts an amazing next generation of skin immunologists, and it was an absolute delight to celebrate Assistant Professor Terkild Brink Buus as our first Dr. Abildgaard Fellow.

It has been a privilege to follow the development in SIC over the past three years. I am so grateful for the contributions from each and everyone in the SIC community that shape our thriving platform for research, education, translation, and outreach. Looking ahead, it will be exciting to see how future discoveries at SIC extends concepts of skin immunology and improve the lives for individuals living with chronic inflammatory diseases.

Report from the Dean

As the LEO Foundation Skin Immunology Research Centre (SIC) enters a phase with a concentrated focus on consolidation, science, and fostering the SIC community, I am pleased that the center is fully embedded within the university structure and the Department of Microbiology and Immunology (ISIM) at the Faculty of Health and Medical Sciences (SUND).

Education is one of the core pillars of SIC's vision and mission, and this past year the educational programmes have continued to expand, including specialised courses, workshops, and mentorship opportunities. The commitment to career development is evident in the support for young researchers as they embark on their academic journeys at SIC. Empowering the next generation ensures a sustainable legacy of excellence in skin immunology research.

Environmental responsibility is an important priority for SUND. SIC has fully embraced the Laboratory Efficiency Assessment Framework (LEAF), a pioneering initiative focusing on efficiency in labs. Beyond reducing the climate impact of labs, LEAF promotes good lab practices and collaborations between groups, thereby saving both time and money. At SIC, every research group is committed to achieving a minimum Bronze LEAF certification and one group has recently renewed their Silver LEAF certification and continues the journey towards the prestigious Gold LEAF certification, symbolising the highest standard of lab efficiency and sustainability.

That SIC offers an attractive platform for research of highest quality was clear by the recent recruitment of Professor William Agace and his research group. With their expertise from DTU and Lund University, Professor Agace's team brings insights into the complexity of gut immunology with relevance for skin research, thereby opening up for new collaborations within the SIC community.

Bente Merete Stallknecht is Dean of the Faculty of Health and Medical Sciences, University of Copenhagen.

With scientists joining from various corners of the globe, SIC is a melting pot of diverse perspectives and experiences. This cultural diversity contributes to a vibrant community and enhances the creativity and innovation that define our approach to skin immunology research. To fully take advantage of this diversity, to promote truly creative research, the SIC community dedicated a day during 2023 to learn more about cultural intelligence and had a fun day of learning together.

In the past year, we've also seen significant progress in our collaboration with Herlev/Gentofte Hospital through the BIOSKIN program. The biobank has successfully reached a substantial number of patients within its first year and continues to grow. The BIOSKIN program bridges interdisciplinary partnerships to advance skin immunology research.

In conclusion, I extend my sincere appreciation to the entire community at SIC. Together, we look forward to a future where our collective efforts aim at finding better ways to tackle common skin diseases whilst adhering to principles of sustainability and inclusion.

Professor William (Bill) Agace is new Group Leader at SIC.

New Group Leader

We proudly welcomed Professor William (Bill) Agace as a new Group Leader at SIC in November 2023. Bill is also the leader of the Center for Intestinal Immune Regulations (CIIR) and will extend our research scope to gut immunology to complement our strong base of skin immunologists to SIC and the Department of Immunology and Microbiology (ISIM).

Bill and his group Barrier Immunology bring a wealth of expertise in gut immunology from murine models and primary human material, thereby elevating our understanding of immune responses across various barrier surfaces in the human body. As Executive Director Liv Eidsmo notes, "With a gut immunologist at SIC, we deepen our understanding of the complexity of the skin in regards to other barriers. It is a timely recruitment as complementary expertise can address mechanisms behind the often unexpected side-effects of novel immunomodulatory drugs that are becoming evident in the clinic."

Bill is enthusiastic about the potential of new collaborations, and the shared passion for tissue immunology among SIC and ISIM members. His group's goals involve establishing techniques for high resolution analyses of human intestinal samples, to re-establish animal models at SUND, and to foster collaborative projects with the other SIC groups to explore co-morbidities between intestinal and skin inflammatory diseases.

When asked about his personal goals as a scientist at University of Copenhagen, Bill aims to contribute to SIC's understanding of how the immune system maintains intestinal health and, when dysregulated, contributes to intestinal disease. Additionally, Bill is committed to mentoring early career scientists and fostering a positive research environment at SIC, ISIM, and SUND as a whole.

Bill presents his group Barrier Immunology in more detail on pages 12-13.

Organisation and governance

SIC operates as a center within the Department of Immunology and Microbiology (ISIM) at the Faculty of Health and Medical Sciences (SUND) at the University of Copenhagen. Situated at the Mærsk Tower in Copenhagen, SIC's research groups engage in scientific collaborations across the Faculty, national and international clinical research units, and the life science industry.

Staff composition

As of the end of 2023, the SIC community consisted of 95 members, representing 19 nationalities. The SIC community includes members of core research groups at SIC (72) and Herlev/Gentofte Hospital (23), visiting researchers and bachelor's and master's students conducting their thesis work or participating in exchange programmes.

The core members

With the addition of the Barrier Immunology research group headed by Professor Bill Agace in November 2023, SIC hosts six core groups. Affiliated Clinical Professors at Herlev and Gentofte Hospital, Lone Skov and Jeanne Duus Johansen head BIOSKIN. The core members form SIC's Steering Committee, spearheading strategic scientific initiatives and embodying the 'Team Science Concept.'

THE SCIENTIFIC ADVISORY BOARD CONSISTS OF

- Tomas Mustelin, University of Washington, USA (Chair)
- Emmanuella Guenova, University of Lausanne, Switzerland
- Johann Gudjonsson, University of Michigan, USA
- Kenji Kabashima, Kyoto University, Japan
- Mübeccel Akdis, University of Zurich, Switzerland
- Olle Kämpe, Karolinska Institutet, Sweden
- Riitta Lahesmaa, University of Turku, Finland

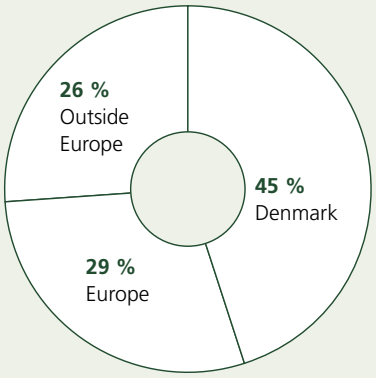
Management

SIC's Daily Leadership Team, consisting of Executive Director Liv Eidsmo, Deputy Director Mads Gyrd-Hansen, ISIM Head of Department Charlotte Menné Bonefeld, Department Administrator Nils Erik Samdal, and Center Coordinator Hannah Paludan, oversees day-to-day operations.

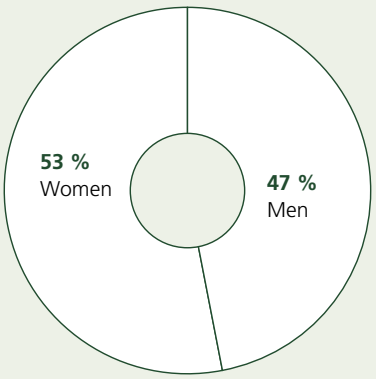
Regular consultations with Dean Bente Merete Stallknecht guide strategic decisions. Annually, Rector Henrik C. Wegener aligns with Center Management and the LEO Foundation to review strategic progress and development. The Center Management also meets annually with the LEO Foundation to present the current strategy and agenda.

Scientific advisory board 2023-2025

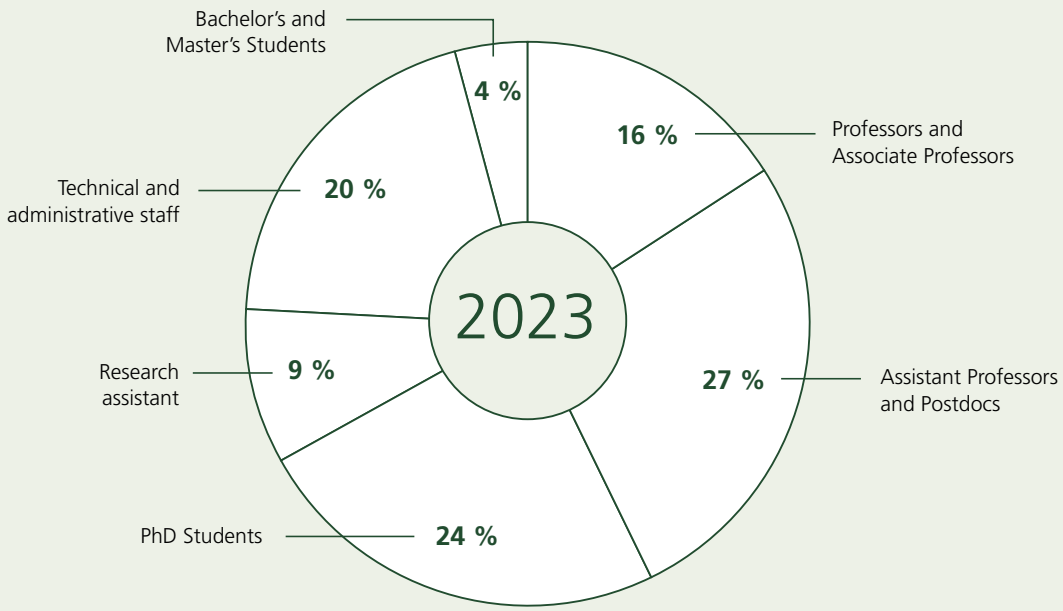
The Scientific Advisory Board (SAB) provides guidance on scientific and strategic directions that support the center's international impact.



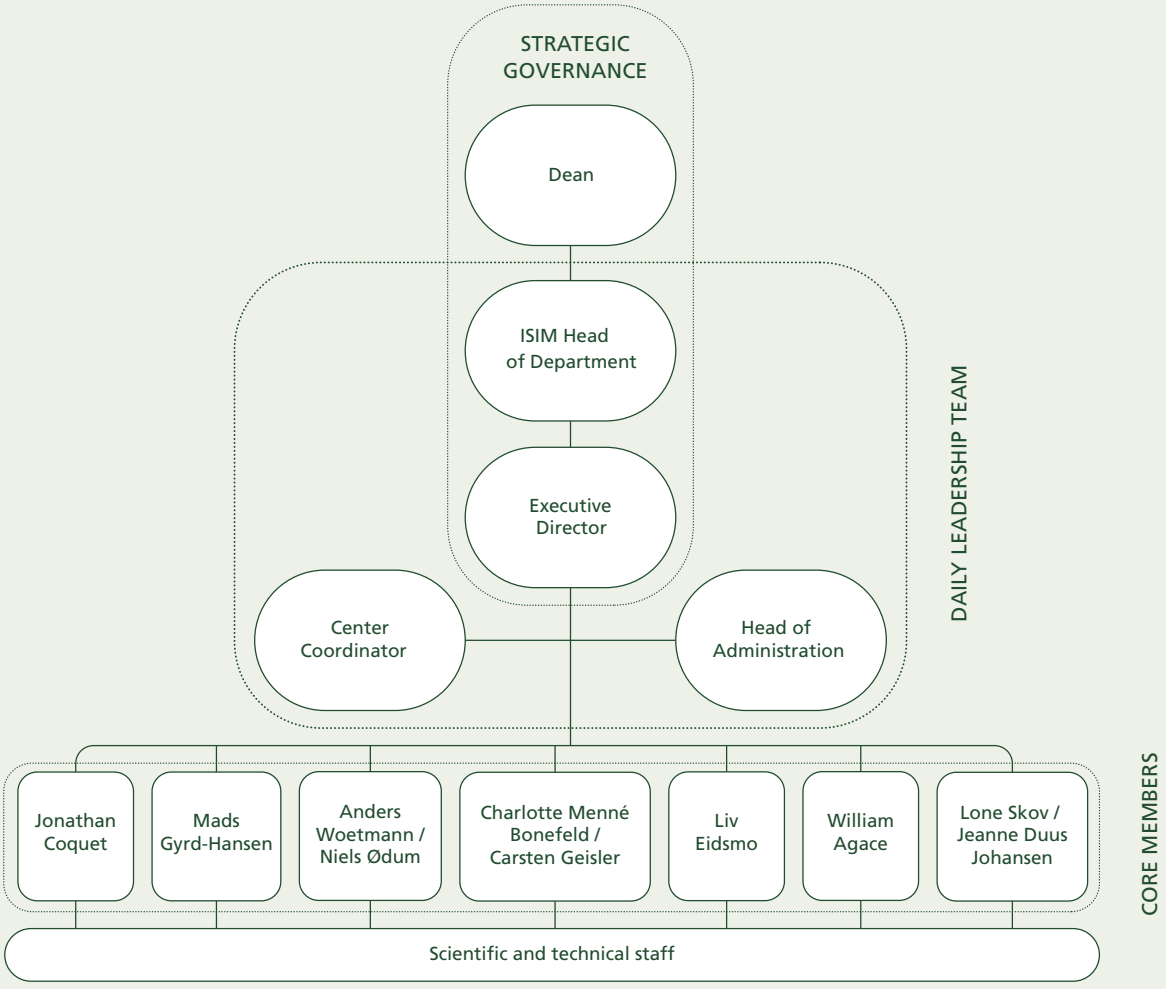
Nationalities of scientific staff and students



Gender distribution of scientific staff and students



Distribution of staff and students by position



Organisation and governance chart

Allergic Inflammation

The Allergic Inflammation Group is interested in understanding how our adaptive immune cells, commonly called T and B cells, see, and respond to allergens from our environment. The group focuses on uncovering the nature of the antigens that drive acute and chronic allergic inflammation in different organs including the lungs and the skin, and moreover, to better understand how immune responses evolve to become pathogenic. The group is headed by Associate Professor Jonathan Coquet.

In 2023, Alma Lindell, research assistant in our group did a wonderful job in setting up our lab space, making it a functional work environment by around mid-year. This allowed for the transition of postdoc Egon Urgard and PhD student Javiera Alvarez to SIC around the middle of the year. A focus for Alma and Javiera was to set up cellular analyses of small skin biopsies using the new FACS-Symphony flow cytometers.

Associate Professor
- Jonathan Coquet

Postdoc
- Egon Urgard

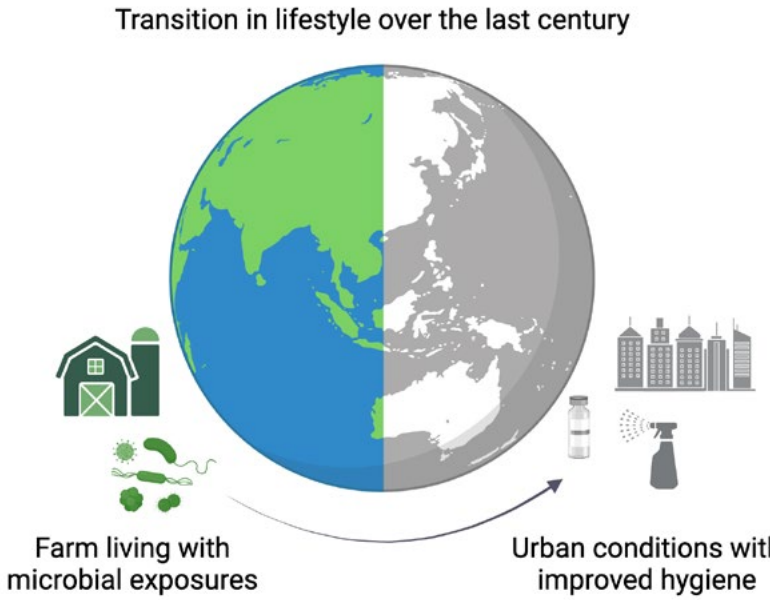
PhD Student
- Javiera Alvarez Moran

Research Assistant
- Alma Lindell

These machines allow for the analysis of over 25 protein markers on cells at once, facilitating measurements of the status and function of multiple cell populations in this limited tissue. This was achieved and the first samples from patients, in collaboration with the BIOSKIN program, was realised in the latter half of the year. Having standardised analysis techniques for such material holds us in good stead for the coming years as we continue to analyse similar samples from patients with eczema and other disorders.

A highlight for our group was the publication of our 'wildling' study in the journal, Science Immunology. Here, Egon Urgard and past lab members tested the so-called hygiene hypothesis - the concept that microbes may protect us from allergy - in a laboratory system. We compared the allergic immune response of specially-bred and highly-exposed 'wildling' mice to those of standard clean laboratory mice. Contrary to what might have been expected, we found that the allergic immune responses in these highly exposed mice was not entirely different to those of the clean mice. When looking specifically at T and B cells in mice, and at the inflammatory signs of allergic disease, we observed no obvious difference in the quality of inflammation and concluded that these highly-exposed mice showed no signs of being protected from developing allergic immune responses. Thus, our results put a question mark over the proposed role that microbial factors may play in protecting us from allergies. It is a major goal for our group to bring the wildling mouse system to SIC and we are currently working on measures to make this happen. This could be a useful resource for many arms of research at our university.

In December 2023, the group was also awarded the Carlsberg Foundation Semper Ardens Accelerate Grant, which will support our work in the field of allergy, specifically allowing us to probe why allergies occur and how allergic symptoms can come and go across our lifespan. In the coming year, the group will continue to foster new collaborations at the university and make new recruitments. In March 2024, Isabel Ulmert will commence a postdoc in our group, with more recruitments planned in the second half of the year.



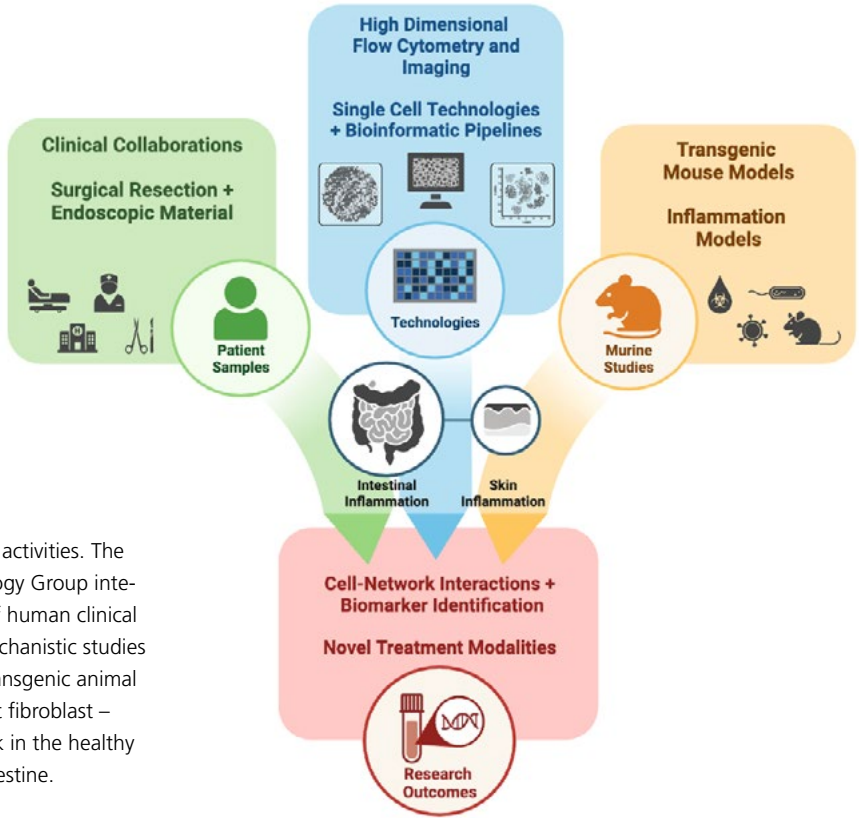
Changes in living conditions and decreased exposures to beneficial microbes are thought to be responsible for the rise in allergic diseases. We tested the impact clean and dirty living environments on responses to allergens in a study published in Science Immunology. Figure made with Biorender.com.

Barrier Immunology

The Barrier Immunology group joined SIC in November 2023 and seeks to understand the cellular and molecular mechanisms regulating immune responses at our barrier surfaces, primarily the intestine. Broadly, we are interested in determining how different cell populations and niches within barrier tissues interact to support local immune homeostasis, the environmental and tissue derived factors that regulate barrier immune function and how alterations in this crosstalk contribute to the initiation and maintenance of barrier and systemic inflammation.

The intestinal mucosa represents the largest surface area of the body that is exposed to the outside environment and is continually exposed to foreign material derived from our diet and the trillions of microorganisms residing within the intestinal lumen. The maintenance of intestinal homeostasis is dependent upon the immune system's ability to remain tolerant to such material, while retaining the ability to mount appropriate immune responses to the many viral, parasitic, and bacterial pathogens that utilise the intestine as a primary site of entry into the host. A breakdown in such mechanisms is thought to contribute to the development and maintenance of inflammatory bowel disease (IBD; Crohn's disease (CD) and ulcerative colitis). While biologics such as TNF-a inhibitors have improved the treatment of IBD, many patients do not respond to such treatment, develop intolerable adverse events or lose the therapeutic effect over time. There is thus an urgent and unmet need for new directions and approaches to disease management and treatment.

The current groups activities focus around three main themes. Firstly, based on our in-house protocols (Fenton *et al*, Immunity 2020, Jörgensen et al Nature Protocols, 2021), and as part of a Leona M. and Harry B. Helmsley Charitable Trust funded Gut Cell Atlas (GCA) consortium grant, we are generating a single cell transcriptional and proteomics atlas of immune niches in the human intestine in health and in CD. We are currently exploring these data sets to assess antigen presenting cell diversity and function as well as adaptive immune cell priming, differentiation and migration in health and CD.



Overview of CIIR activities. The Barrier Immunology Group integrates analysis of human clinical samples with mechanistic studies in in vitro and transgenic animal models to dissect fibroblast – immune crosstalk in the healthy and inflamed intestine.

A second major activity of the group is as participants of the Novo Nordisk Foundation Challenge grant funded Center of Intestinal Immune Regulation (CIIR). Here together with CIIR groups headed by Prof. Flemming Bengtsen (Hvidovre Hospital), Ass. Prof. Lars Rønn Olsen (Technical University of Denmark) and Prof. Kathy McCoy (University of Calgary) we are exploring the role of intestinal fibroblasts in the regulation of intestinal immune function in health and disease. We focus on testing two major hypotheses; Firstly, that intestinal fibroblasts play a key role in intestinal immune cell development, maintenance, and function and that this is essential for maintaining intestinal immune homeostasis. Secondly, that alterations in intestinal fibroblast-immune cell crosstalk contribute to the initiation and maintenance of IBD. To test these hypotheses, we combine CIIR's expertise in gastroenterology, mucosal immunology and bioinformatics with the analysis of human intestinal tissues, and mechanistic studies in *in vitro* models and state-of-the-art transgenic animal models (Figure). The long-term goals of CIIR are to identify novel treatment modalities for IBD as well as biomarkers of disease severity and treatment response.

Finally, within SIC we are initiating and collaborating on projects exploring potential mechanisms underlying the poorly understood co-morbidities of skin and inflammatory bowel disease. Such studies will include performing deep immunological profiling of affected skin and intestinal tissues from these patients to assess potential common inflammatory pathways and adaptive immune responses across inflamed tissue sites.

Professor
- William Agace

Postdocs
- Andrew Brown
- Luiza Moraes Holst
- Urs Mörbe

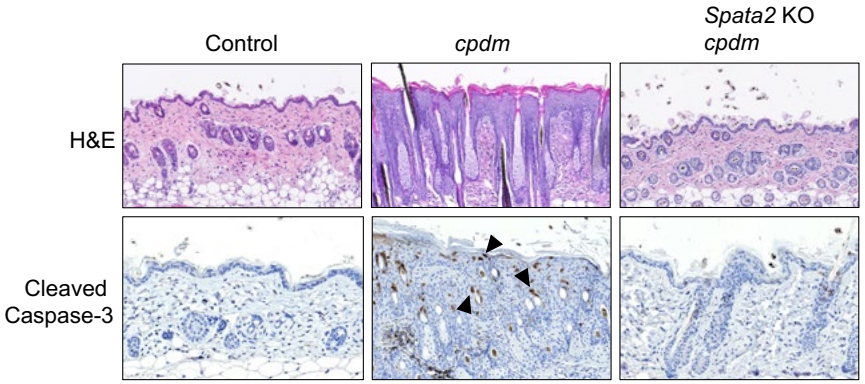
PhD Students
- Christian Ashworth
- Venla Väänänen
- Fredrik Junghus
- Mads Damsgaard Wewer

Molecular Immunology and Inflammation

The Molecular Immunology and Inflammation Group focuses on understanding the fundamental processes that control immune responses, with a particular focus on molecular mechanisms governing inflammatory signalling and innate immunity. We aim to advance our understanding of the molecular aetiology of inflammatory skin diseases and other immune disorders, which ultimately may pave the way for improved treatment strategies.

Our research has a particular focus on the ubiquitin system, which plays a central role in regulating inflammation and immune responses. 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 are disassembled by deubiquitinases. These chains, depending on how they are assembled, 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 a central regulator of inflammation and immunity in animal models as well as in humans. 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 main focus of the group is to understand how regulation of LUBAC and Met1-linked ubiquitin chains influences the immune system under basal conditions and in the context of skin inflammation or other challenges such as bacterial infection. These projects rely on novel genetically-modified mouse models that have been generated and are being extensively characterised in different experimental



H&E and cleaved caspase-3 (apoptosis) stain of mouse skin sections. Epidermal thickening and cell death characteristic of cpdm mice is ameliorated by knockout (KO) of Spata2. Data by Malin Jessen / Majken Kjær.

inflammation models. We have also initiated projects aimed at using mass spectroscopy-based proteomics to better understand the regulatory mechanisms of LUBAC and how these are altered in the inflamed skin.

During 2023, we have advanced the on-going research projects relating to the role of Met1-linked ubiquitin in immunology and skin inflammation. One of the exciting research developments relates to the role of SPATA2 in skin inflammation. We have established that SPATA2 contributes to chronic proliferative dermatitis (cpdm) in mice deficient for the LUBAC subunit SHARPIN (Figure). Molecularly, SPATA2 links the deubiquitinase CYLD to LUBAC and is responsible for recruitment of CYLD to the active TNF Receptor 1. Our data indicate that the SPATA2-dependent recruitment of CYLD "licenses" the activation of cell death signalling by TNF Receptor 1, a key driver of skin inflammation in the cpdm mouse model (Figure). We are currently investigating if this role of CYLD contributes to skin inflammation in other models.

In 2023 the group has been engaged in a number of education and research dissemination activities. Mads Gyrd-Hansen has taken over the responsibility for the MSc course "Chronic Inflammation - From Basic Research to Therapy", which runs annually in February-April. The PhD course "Mechanisms in Innate Immune Signalling" established by Berthe K. Fill and Mads ran for the second time in January 2023. Mads also co-organised the annual SIC Springtime School held in Hornbæk and together with Beatrice Dyring-Andersen organised the first "Skin Proteomics and Immunology" symposium held in the Mærsk Tower. In addition, Mads participate as a mentor in the Postdoc and Assistant Professor Mentoring Programmes offered by UCPH and Berthe is part of the organising committee for the SIC Young Investigator Network.

The focus areas for 2024 will be to submit the first manuscripts based on research projects developed at SIC on the role of Met1-linked ubiquitin in immunology and skin inflammation. In addition, the group will continue to contribute to education in molecular mechanisms of inflammation and immunology.

Professor
- Mads Gyrd-Hansen

Assistant Professors and Postdocs
- Berthe Katrine Fiil
- Chris Kedong Wang
- John Rizk
- Biao Ma
- Max Sauerland

PhD Students
- Frederik Timmermann
- Malin Jessen
- Wenxin Lyu

Erasmus+ student/Research Assistant
- Hanna Kulvicki

Lab manager
- Majken Kjær

Skin Inflammation and Cancer

In the Skin Inflammation and Cancer Group we aim to unravel the interplay between immune cells, skin cells, and the skin microbiota to understand skin immunity and what mechanisms drive benign and malignant inflammatory skin disease progression. In addition, we explore whether and how the identified mechanisms can be developed into novel therapeutic areas for inflammatory skin diseases.

In 2023, we made the unexpected but important discovery that a subset of $CD4^+$ T helper (TH) cells express hepatocyte growth factor (HGF) – a signalling molecule primarily linked to the normal development and function of the liver. HGF production was predominantly but not exclusively confined to TH1 cells and driven by a PI-3 kinases and mTOR-dependent pathway suggesting a potential role of HGF in TH1-associated pathology. Of note, T cells expressing the HGF-receptor (c-Met) have recently been linked to tissue inflammation in patients with heart disease suggesting that HGF plays a role in T-T cell communication and probably in chronic inflammation. In support, we have identified an HGF-producing T cell line derived from psoriatic skin, which is a unique novel tool for studying HGF associated T cell biology. Importantly, pharmacological compounds against PI-3/mTOR inhibited HGF release by T cells indicating that already existing drugs may be used to target HGF^+ T cell-associated pathology (Ford et al 2023).

Skin lesions with a broken skin barrier play a key role in pathology, clinical manifestations, and the risk of staphylococcus aureus colonisation and infection in patients with cutaneous T cell lymphoma (CTCL). Yet, it has been unknown what drives skin barrier deterioration during disease progression. We have now unravelled that malignant T cells trigger a disease-stage-dependent breakdown of the filaggrin barrier through the release of a series of cytokines that attack the normal function and differentiation of keratinocytes preventing the proper formation of a protective skin barrier. Importantly, a coordinated blockage of the involved cytokine receptors and their downstream effector kinase (Janus Kinase-1) almost completely reversed

Professors
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- Niels Feentved Ødum

Assistant Professor
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Postdocs
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- Emil M H Pallesen
- Maria Gluud Grøndahl
- Morten Orebo Holmström
- Pia Rude Nielsen

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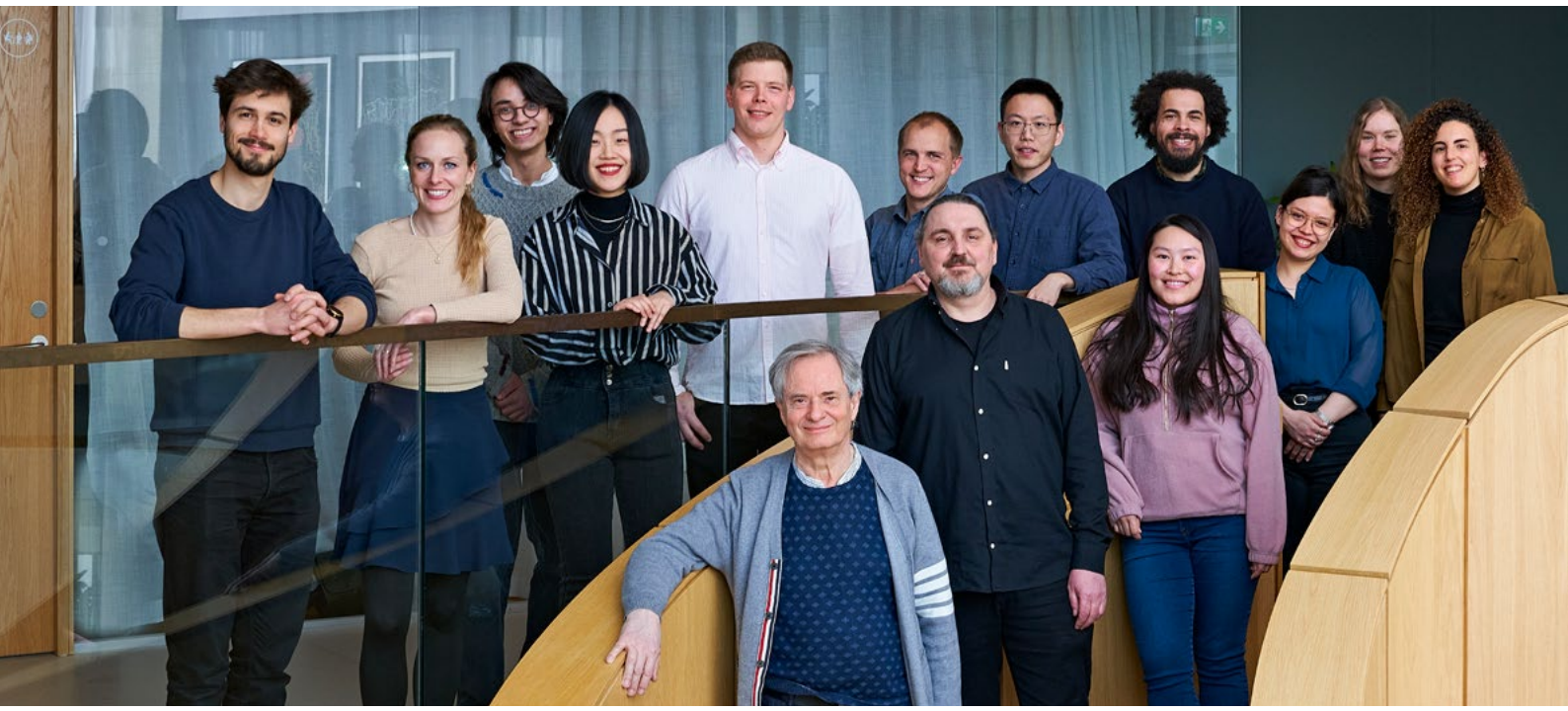
- Lisa Harth
- Maria Teresa Martin Monreal
- Marina Ramírez Galera
- Martin Rich Javadi Namini

Research Assistants
- Anders Lykkebo-Valløe
- Mariana Bronze
- Shayne Ford
- Ziao Zeng

Master's Student
- Lang Yan

Lab Managers, Technicians and Specialists
- August Ødum
- Heba Mahmoud
- Sana Ahmad



the blockage and largely restored the filaggrin skin barrier in experimental skin models and explanted lesional skin from CTCL patients. These beneficial effects were obtained with JAK inhibitors that are already in clinical use for chronic inflammatory diseases including chronic skin disorders. Thus, our findings indicate that JAK inhibitors can potentially reverse and improve a compromised skin barrier in CTCL patients (Gluud et al, Blood 2023). Accordingly, a clinical trial to address this is already underway.

In a complimentary line of research, we explored the damaging impact of Staphylococcus aureus on interferon gamma and other inflammatory effectors in skin and enhancement of malignant T cell proliferation. Moreover, we addressed how these effects can be broken by engineered recombinant endolysins derived from Staphylococcus aureus specific bacteriophages. Indeed, endolysin induced profound bacterial cell death and inhibition of the effect of staphylococcus aureus in ex vivo skin and models from healthy donors and CTCL patients (Pallersen et al JID 2023). A patent application on endolysins in CTCL has been filed at the European patent office.

Moreover, we have been engaged in a series of collaborative studies within SIC, ISIM, University of Copenhagen, and collaborates nationally and internationally resulting in a series of publications identifying mechanism involved in treatment failure using Omalizumab (a monoclonal anti-IgE-antibody) in patients with chronic spontaneous urticaria; the role of circularRNAs in myelodysplastic neoplasms; protein citrullination for autoimmune TH17 responses; novel cytokine networks in CTCL; vaccination against the regulatory cytokine TGFb; and studies on immune cell composition in unipolar depression.

Collectively, our studies have unravelled novel roles of "old" cytokines in immune regulation, chronic inflammation, and immunological and non-immunological diseases. In addition, we have discovered new disease mechanisms and identified putative novel targets and concepts for future therapy.

Finally, we are proud that group members successfully concluded their PhD studies, while other more senior group members have been headhunted by the pharmaceutical industry or awarded start-up grants for establishing their own research group. Simultaneously, new group members have been recruited.

T Cell Biology and Skin Inflammation

The T Cell Biology and Skin Inflammation Group investigates T cell activation, differentiation and effector functions as key factors in the development and treatment of in-flammatory skin disease. The group is headed by Professors Charlotte Menné Bonefeld and Carsten Geisler.

The focus of the group is to improve the understanding of the role of T cells in skin homeostasis and inflammatory skin diseases. The group aims to advance the knowledge of:

- immune responses against clinically relevant contact allergens, both against single allergens and allergen mixtures
- different subsets of epidermal T cells, including their developmental trajectories and function, in both healthy and inflamed skin
- the influence of diverse factors, including cytokines, vitamins, and hormones, on T cell activation and differentiation

In 2023, the group has investigated the local memory response induced by different clinically relevant contact allergens in mouse models of allergic contact dermatitis (ACD). In accordance to previous studies from our group using experimental contact allergens, we found a pivotal role played by $CD8^+$ epidermal-resident memory T (T_{RM}) cells in orchestrating local flare-up responses upon allergen re-exposure. Significantly, our study clearly demonstrated the allergen-dependent disparities in the formation of $CD4^+$ and $CD8^+$ epidermal T_{RM} cells, underscoring the nuanced nature of cutaneous immune responses.

We extended our study of the role of neutrophils in the flare-up response by investigating the flare-up response to nickel in patients allergic to nickel. In parallel to what we recently demonstrated in our well-established mouse model for ACD, we demonstrated a huge influx of neutrophils in both the epidermis and dermis of nickel allergic patients 24 hour after re-exposure to nickel.

We furthermore concluded our studies of the role of stress-molecules in the response to contact allergens. We have explored the involvement of JAML and CD100 and their respective ligands CXADR and Plexin B2 in the response to contact allergens. Our studies demonstrated $CD8^+$ epidermal T_{RM} cells express JAML and CD100 and that contact allergens induce the expression of their ligands on stressed keratinocytes. By studying JAML and CD100 knock-out mice, we demonstrated the important role of JAML and CD100 in the inflammatory responses to contact allergens offering potential targets for ACD interventions.

Keratinocytes play an important role in the initiation and facilitation of inflammatory responses in ACD. Immune responses are associated with major changes in metabolism. However, metabolic re-programming is not well studied in ACD; specifically, knowledge of metabolic alterations in structural cells is lacking. We studied metabolic re-programming in ACD in primary pooled keratinocytes and a keratinocyte cell line and by using publicly available transcriptome datasets. Stimulation of keratinocytes with contact allergens induced up-regulation of proteins representative for glucose uptake, fatty acid metabolism, oxidative phosphorylation and to some extent arginine biosynthesis).

Only few studies on contact allergy in African countries have been published. To provide an overview of the most common contact allergens identified by the use of patch tests in African countries, we performed a review of the existing literature. We found that nickel, cobalt, chromium, fragrance mix, and p-tert-butylphenol-formaldehyde resin were the dominating contact allergens responsible for 40% – 90% of the positive patch test reactions. This indicates that a targeted effort directed towards prevention, avoidance, and regulation of reliably identified contact allergens could reduce the disease burden of ACD considerable in some African countries.

In 2023, Anders Boutrup Funch and Veronika Mraz graduated as PhD and Emma Uttrup Ewing as Master in Molecular Biomedicine from our group. Furthermore, we had the great pleasure of having Mandy Menzel as a BRIDGE Postdoc and Alexandra Teresa Seibel and Sandra Suhner as guest researchers in our group.

Professors
- Charlotte Menné Bonefeld
- Carsten Geisler

Associate Professor
- Martin Kongsbak-Wismann

Assistant Professors and Postdocs
- Anders Boutrup Funch
- Helen Vaher
- Mandy Menzel
- Mia Hamilton Jee
- Veronika Mraz

Associate Professors (externally associated)
- Beatrice Dyring-Andersen
- Marianne Bengtson Løvendorf

PhD Students
- Julie Weber Friis
- Kelvin Yeung

Research Assistants
- Anne-Sofie Østergaard Gadsbøll
- Martine Dragsbæk-Friis
- Simone Stegenborg-Grathwohl

Master's Student
- Emma Uttrup Ewing

Lad Managers and Technicians
- Charlotte Bølling
- Rebecca Kitt Davidson Lohmann

Guest Reserachers
- Alexandra Seibel
- Sandra Suhner

Translational Skin Immunology

The Translational Skin Immunology Group studies study the composition of localised disease memories in psoriasis and vitiligo to identify new targetable mechanisms of skin pathology that would enable long-term clinical remission.

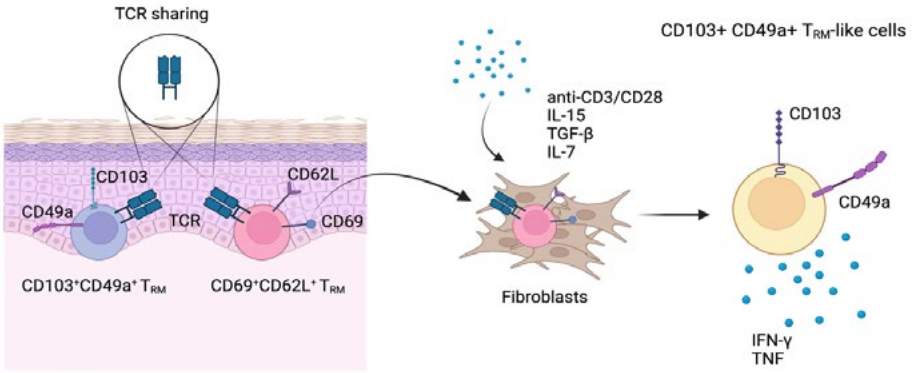
Skin health is maintained by constant cross talk between immune cells and stroma cells. In focal inflammatory skin diseases, homeostasis is broken in afflicted patches of the skin whereas the non-afflicted skin maintains macroscopic homeostasis. In resolved lesions, T cells and tissue derived cells retain inflammatory profiles and thereby creates localised disease memories where the thresh-hold for relapsing pathology is low. Immunomodulating therapies that target signalling molecules has revolutionised the treatment of severe psoriasis, but these treatments have not been efficient in eradicating disease memories. Importantly, T cells with the capacity to initiate relapsing disease persist resolved skin areas of lower threshold to inflammation.

Over the last few years, we have focused on basic mechanisms of formation of resident cytotoxic T cells in human skin to address how T cell-based disease memories are formed and maintained. In healthy skin, high resolution analysis highlights several specialised T cell-subsets in epidermis and dermis. Blood derived T cells can act as precursors to cytotoxic skin resident T cells (Zitti, Hoffer Immunity 2023) and cellular renewal by recruitment of T cells from the blood is one model of long-term persistence of T cells in the skin. Another possibility is local renewal from mature or precursor cells within the skin environment. By using single cell gene expression analysis, we found that healthy and diseased human skin harbour local precursors to resident T cells. During 2023, considerable effort was used to sort these rare precursors for functional experiments and to prove that these cells have high proliferative capacity and are wired to mature to bone fide resident T cells. In collaboration with Patrick Brunner

at Mount Sinai, USA, we had access to data from cutaneous T cell lymphomas and found that malignant T cell clones contained local precursors too. These data provide a framework for future therapies aimed at eradicating precursor cells instead of mature T_{RM} cells to normalise dysbalanced populations of resident T cells in diseased and resolved skin.

Signals from the local microenvironment are essential for the survival and functionality of local T cell populations, and the inflammatory state of the skin plays an important role in setting the threshold for disease development. To understand the milieu in different parts of resolved skin, we have established spatial transcriptomics using the VISIUM platform at SIC during 2023. This technology helps us identify environmental signals in the immediate vicinity of resident T cells and their precursors in resolved psoriasis to the complex architecture of the skin. Through combining data derived from spatial transcriptomics with mechanistic experiments, we are now starting to map niches of dysregulated stroma to anatomical structures in resolved skin. During 2023, the first collaboration with BIOSKIN was established and the material collected from this impressive biobank will allow us to compare changes in microenvironments within the skin during immunomodulatory treatments in resolved psoriasis.

To bring our work back to the patients, two BRIDGE fellows are following disease trajectories and triggering factors of cohorts of people living with psoriasis and hidradenitis suppurative. The combined effort of our fantastic team of medical doctors, bioinformaticians, biologists and students in the lab ensures that the patient remains in the focus of our studies.



The skin harbours a pool of resident T cells in disequilibrium with circulating T cells. By high resolution analysis using single cell sequencing, combined with ex-vivo experiment, we have characterised local precursors to mature effector T_{RM} cells. Spatial transcriptomics is used to identify tissue niches where these cells are found in healthy, diseased, and resolved skin.

Professor
- Liv Eidsmo

Lab Manager
- Maja Søberg Udsen

Lab Technicians
- Gustaf Olsson
- Marta Madacsi

Clinical Fellows (BRIDGE)
- Albert Duvetorp
- Rune Kjærsgaard Andersen

Postdocs
- Ekaterina Zhuraleva
- Wenning Zheng
- Rasmus Agerholm-Nielsen

PhD Students
- Elena Hoffer
- Trine Schønfeldt

Bachelors', Master's and MD Students
- Chenming Zhang
- Daniel Sortebech
- Mattia Dervasi

Guest Researchers
- Elisa Martini

Bioskin

In 2021, the Copenhagen Translational Skin Immunology Biobank and Research Program (BIOSKIN) was initiated through a grant provided by the LEO Foundation, in collaboration with SIC, and the Department of Dermatology and Allergy, Herlev-Gentofte Hospital. BIOSKIN is a prospective initiative encompassing a biobank and research study dedicated to gathering clinical data and biological samples from 3,000 patients with the most prevalent chronic inflammatory skin diseases: psoriasis, atopic dermatitis, and contact eczema. As of December 2023, around 825 participants have been enrolled in the study.

BIOSKIN is a prospective biobank and research study following patients with the most prevalent chronic inflammatory skin diseases; psoriasis, atopic dermatitis, and contact eczema. The project aims to enhance translational research in dermatology by following and collecting high-quality biological samples and clinical data from 3,000 patients for a minimum period of five years. The program's longitudinal open cohort design, featuring repeated sampling, allows participants to join and exit the study at various time points during monitoring. This approach facilitates a thorough characterization of the patient's disease trajectories, treatment response, and comorbidities risk. Ultimately, the outcomes of this research program are poised to enhance the quality of life for a substantial group of patients and bring us closer to finding a cure for debilitating inflammatory skin diseases.

Situated at Herlev-Gentofte Hospital, the biobank has in 2023 become an integrated part of the clinical practice and the research unit at the Department of Dermatology and Allergy. New members have been recruited and the BIOSKIN team now comprises 5 project nurses, a lab technician, and 4 PhD students among others. The ongoing PhD studies are anchored at the Department of Dermatology and Allergy,

Clinical Professors
- Jeanne Duus Johansen
- Lone Skov

Head of Research
- Marianne Bengtson Løvendorf

PhD Students
- Anna Schultz Vinge
- Anne Sophie Heinrichsen
- Marie Mila Broby Johansen
- Mie Sonne Goldeman

Associated Medical doctors/PhD Students
- Amanda Kvist-Hansen
- Charlotte Sigrid Erika Näslund Koch
- Mikkel Bak Jensen
- Morten Bahrt Haulrig

Project nurses
- Cecilie Marie Aarup Busch
- Ditte Viborg Petersen
- Helene Meyer Martin
- Ida Gebauer
- Maja Elmelund Wind

Lab Technician
- Signe Grønbek Petersen

Secretary
- Gitte Thoft Olsen

Student team
- Caroline Eismark
- Clara Sophie Bramsen Andersen
- Daniel Isufi
- Elvan E. Yilmaz
- Josephine Brandt
- Louise V. Rasmussen

The BIOSKIN program is anchored at the Department of Dermatology and Allergy, Herlev-Gentofte Hospital where it since its commencement of inclusion of patients in 2022, has been integrated into the daily clinical practice.

Herlev-Gentofte Hospital, but importantly, are linked to SIC researchers by the co-supervision of group leaders at SIC. This connection imbues the projects with a translational research dimension, bridging the gap between basic research and clinical practice. The PhD studies are dedicated to distinct objectives, such as differentiating between allergic and irritant contact eczema using single-cell sequencing, as well as immunological characterization of subtypes of psoriasis and atopic dermatitis, respectively.

In addition to internal collaborations, we have initiated new external partnerships, including efforts to explore extracellular matrix biomarkers for psoriasis. Furthermore, we are actively engaged in the establishment and optimization of methods for measuring skin biomarkers through non-invasive sampling approaches, such as tape strips.

Together, the BIOSKIN program encompasses an unprecedented level of biological sampling, clinical assessments, and the gathering of patient data. By the end of 2023 around 825 patients were enrolled in BIOSKIN. The initiative is set to enhance the collaborative synergy between basic and clinical science, and we expect that this resource will prove invaluable not only for SIC researchers but also serve as an asset for collaborators both nationally and internationally.


ISIM

Education and career development

PHD COURSE

In January 2023, Berthe Katrine Fiil and Mads Gyrd-Hansen orchestrated the annual PhD course on Mechanisms in Innate Immune Signalling, encompassing four full days of lectures and group work.

The course's primary objective was to furnish participants with knowledge of innate immune signalling, spanning from microbe detection to signal consequences, whether it led to successful pathogen clearance or, more detrimental, chronic inflammation.

Participating students brought diverse backgrounds, ranging from medical doctors pursuing a PhD to immunologists, protein chemists, and bioinformaticians. Some were already experts in innate immune signalling, while others, with no prior immunology knowledge, expressed a strong interest in learning, finding relevance to their PhD projects.

To establish a common foundation, the course contained a series of 'background talks' before delving into more specialised subjects.

Invited teachers from academic institutions in Copenhagen included Ieva Bagdonaite from the Center for Glycomics, Beatrice Dyring-Andersen from the Center for Protein Research and Herlev-Gentofte Hospital, Bill Agace – at that time a Professor at the Technical University of Denmark, and Mariena van der Plas from the LEO Foundation Center for Cutaneous Drug Delivery. These experts shared insights from their respective fields, enriching the academic depth of the course.

A journal club was integrated into the course, allowing students to present pre-selected papers, delve into relevant literature, engage in critical discussions, and connect with fellow participants.

To provide a more practical context, industry perspectives were incorporated in the course. Representatives from Christian Hansen discussed human milk oligosaccharides, and STiPe therapeutics providing insights into STING agonists, sharing career experiences and insights, bridging the gap between academic knowledge and industry practices.

Finally, invited speakers Julia Sanchez-Garrido, Imperial College and Søren Paludan, Aarhus University delivered a double seminar open to all and engaged in a meet-the-speaker session with students, offering detailed discussions and career advice.

In summary, the PhD course on "Mechanisms in Innate Immune Signalling" touched upon various aspects of innate immune signalling and host-microbe interactions. Student satisfaction was remarkably high, underscoring the course's effectiveness in delivering comprehensive and relevant knowledge.

INSPIRING TOMORROW'S SCIENTISTS

For the third consecutive year, SIC proudly hosted a two-day mini course in skin immunology for Gefion Gymnasium's biotech programme's final-year students. The event not only aimed to share knowledge about skin immunology but also provided a unique glimpse into the world of research and education at the University of Copenhagen.

The enthusiasm displayed by the high school students from 3.T. at Gefion Gymnasium was truly inspiring. It is rewarding to witness the passion these young minds bring to the study of skin immunology. Beyond being an educational platform, the mini course offered an opportunity for these students to experience a real research environment.

While the primary focus was on imparting knowledge about immunology, these two days also provided a valuable occasion to display the diverse educational offerings at the University of Copenhagen. It was a chance to open a dialogue about the myriad paths that students can embark upon after high school. The overarching message conveyed was that there is no singular trajectory; the key is to be driven by a desire to learn and fuelled by curiosity.

As we reflect on the success of this year's mini course, we remain committed to nurturing the next generation of scientists. SIC is proud to be a part of the journey these students undertake, and we look forward to continuing this tradition of education, inspiration, and collaboration in the years to come.

Teachers at the course: Anne-Sofie Gadsbøll, Martin Kongsbak-Wismann, Julie Weber, Veronika Mraz, Helen Vaher, Anders Funch, Kelvin Yeung, Karsten Pharao Hammelev and Charlotte Menné Bonefeld.

SIC PHD PROGRAMME

This new initiative funded by LEO Foundation Add-on Grant VI received and approved four PhD programmes. Recruitment of students started in late 2023:

The interplay between bacteria and cutaneous T cell lymphoma (CTCL).

- Student: Ziao Zeng
- Main supervisor: Professor Niels Ødum (SIC).
- Primary co-supervisor: Associate Professor Jonathan Coquet (SIC).
- International collaborator: Professor Tomas Mustelin (Div. Rheumatology, Dept Medicine, University of Washington, Seattle, USA).

Role of inflammatory mediators in the formation of local memory to contact allergens.

- Student: Simone Stegenborg-Grathwohl
- Main supervisor: Professor Charlotte Menné Bonefeld (SIC).
- Co-supervisors: Professor Carsten Geisler, (SIC), Professor Anders Woetmann, (SIC), Professor Jeanne Duus Johansen (BIOSKIN, National Allergy Research Centre, Department of Dermato- Allergology, Copenhagen University Hospital Herlev-Gentofte).
- International co-supervisor: Professor Cezmi Akdis (Swiss Institute of Allergy and Asthma Research (SIAF), Davos, CH).

Can allergic contact dermatitis be permanently cured?

- Student: Martine Dragsbæk-Friis
- Main supervisor: Professor Carsten Geisler (SIC)
- Co-supervisors: Professor Charlotte Menné Bonefeld (SIC), Professor Niels Ødum (SIC) and Professor Jeanne Duus Johansen (BIOSKIN, National Allergy Research Centre, Department of Dermato-Allergology, Copenhagen University Hospital Herlev-Gentofte).
- International collaborator: Professor Marc Vocanson (Centre International de Recherche en Infectiologie (CIRI), Lyon, France).

The role of the Met1-linked ubiquitin machinery in the immune biology of human keratinocytes and fibroblasts.

- Student: Under recruitment
- Main supervisor: Professor Mads Gyrd-Hansen (SIC)
- Co-supervisor: Professor Liv Eidsmo (SIC)
- International collaborator: Dr. Florian Schmidt (Inst. of Innate Immunity, University of Bonn).

SPRINGTIME SCHOOL

Bringing the international community together around the topic "Skin homeostasis and inflammation" at the SIC Springtime School

As spring arrived in Denmark, the SIC Springtime School 2023 gathered scholars, PhD students and postdocs from all over the world to share exciting contemporary science with relevance to our community. Invited speakers and scholars were invited based on their scientific excellence and to act as role models for the next generation of skin researchers.

During the three days, different aspects of skin renewal, molecular signalling and inflammation, tissue immunology and host-microbe interactions were discussed. Intense discussions were initiated during presentations and poster sessions and continued during meals and social gatherings. Participants were gathered from all over Europe as well as the US, Australia, and Asia and with time, strong networks and interactions between our alumni became evident on different social media platforms. It is always a delight to welcome new participants each year and it is great to meet up with our alumni in conferences around the world. The participants highlight that the atmosphere in Hornbæk is collegial and inspiring, facilitating deep scientific discussions and opportunities for collaboration and career progression for the younger audience.

In 2024 the topic of the Springtime School will be "Mechanisms of Inflammation in Skin and other barriers".

SPEAKERS AND TITLES OF TALKS AT SPRINGTIME SCHOOL 2023

- Shruti Naik, NYU Langone Health:
  Non-canonical functions of cutaneous immunity
- Yaron Fuchs, Augmanity Nano:
  Communication by dying cells within hair follicles
- Maria Kasper, Karolinska Institutet:
  The cellular atlas of the skin
- Neil Rajan, Newcastle University:
  Ubiquitination in CYLD syndrome
- Florian Schmidt, University of Bonn:
  The skin-specific NLRP1 inflammasome
- Jonathan Coquet, University of Copenhagen:
  All in the life of a Th2 cell
- Jessica Strid, Imperial College:
  Type 2 immunity in skin homeostasis and inflammation
- Maria Mittelbrunn, CMB Madrid:
  Immunometabolism and ageing in T cells and inflammation
- Patrick Brunner, Mount Sinai/ University of Vienna:
  Investigating benign and malignant skin inflammation using single-cell technology
- Stephan Rosshart, Friedrich-Alexander-University Erlangen-Nürnberg:
  The impact of natural microbiome on host physiology
- Lone Skov, BIOSKIN, Gentofte Hospital:
  Psoriasis and microbes
- John Common, Skin Research Institute of Singapore:
  Host-microbe interactions in skin diseases

Quotes from participants
– what did you enjoy most about Springtime School?

"Speaker's dinner" with the seating rotations with ability to have scientific and career path discussions in an informal way with senior researchers as well as peer young researchers from various fields.

The Springtime School has an exceptional atmosphere, that I have not seen replicated on other conferences/summer schools.

I really enjoyed the springtime school. The atmosphere was great, and the talks were of very high quality!

SUPERVISED PHD, MASTER, AND BACHELOR STUDENTS

PhD students

- Anders Boutrup Funch, PhD title, *Immune mechanisms behind local skin reactions to contact allergens.* Supervised by Charlotte Menné Bonefeld.
- Bin Yang, PhD title, *Investigation of the regulation of virtual memory T cells in response to interleukin 4 during helminth infection.* Supervised by Jonathan Coquet.
- Borislav Ignatov, PhD title, *Resident T cells steer tissue responses in human skin.* Karolinska Institutet. Supervised by Liv Eidsmo.
- Eileen Donohue Wedge, PhD title, *Circular RNA in Myelodysplastic Neoplasia.* Supervised by Niels Ødum.
- Elena Hoffer, PhD title, *Composition and maintenance of skin resident T-cells in health and disease.* Supervised by Liv Eidsmo.
- Jill Ziesmer, PhD title, *Hybrid antibacterial microneedle patches against skin infections.* Karolinska Institutet. Co-supervised by Liv Eidsmo
- Maria Gluud Grøndahl, PhD title, *The Interplay between Malignant T cells and Keratinocytes in Cutaneous T cell Lymphoma.* Supervised by Niels Ødum.
- Pia Aehnlich, PhD title, *Strategies to improve adoptive cell therapy with Vγ9Vδ2 T cells.* Supervised by Niels Ødum.
- Rasmus Erik Johansson Mortensen, PhD title, *Vaccination against TGF-ß - A novel way to modulate the tumor microenvironment.* Supervised by Niels Ødum.
- Shayne Lavondua Ford, PhD title, *Expression of Hepatocyte Growth Factor and Mesenchymal-epithelial Transition Factor by Human T cells.* Supervised by Anders Woetmann and Charlotte Menné Bonefeld.
- Tu Hu, PhD title, *Multi-omics Profiling of Atopic Dermatitis.* Supervised by Thomas Litman and Lone Skov.
- Veronika Mraz, PhD title, *Novel Insights in Pathophysiology of Allergic Contact Dermatitis – Studies on JAML-CAR and CD100-Plexin B2 interactions.* Supervised by Charlotte Menné Bonefeld.

Master students

- Daniel Reinholdt Sortebech, Master thesis, *Investigating T cell phenotypes and clonal relationships in different anatomical compartments of psoriatic arthritis patients.* Supervised by Liv Eidsmo.
- Emma Uttrup Ewing, Master thesis, *The effects of vitamin D on the human immune response.* Supervised by Carsten Geisler and Martin Kongsbak-Wismann.
- Hanna Kulvicki, Master thesis, *The role of SPATA2 in innate immune defense against Listeria monocytogenes.* Supervised by Berthe Katrine Fiil.
- Klara Nielsen, Master thesis, *Identification of ubiquitination substrates in AMPK signalling*. Supervised by Rune Busk Damgaard (DTU) and Mads Gyrd-Hansen.
- Valeria Magnusson, Master thesis, *The effect of inhibition of metabolic drugs during development of resident T cells.* Supervised by Liv Eidsmo.
- Ziao Zeng, master thesis, *Staphylococcus aureus mediated-crosstalk between malignant-, non-malignant T cell and keratinocyte in cutaneous T cell lymphoma.* Supervisor Niels Ødum.

Bachelor students

- Amanda Munk, Bachelor thesis, *Interaction between nociceptors and the immune system during allergic contact dermatitis*. Supervised by Veronika Mraz.
- Caroline Bjørn Hedegaard, Bachelor thesis, *The impact of vitamin D on the immune system. Lessons from the disease, Hereditary Vitamin D Resistant Rickets.* Supervised by Martin Kongsbak-Wismann.
- Laura Brun Søgaard Olesen, Bachelor thesis, *Vitamin D and its therapeutic effects in treatment of Mycobacterium tuberculosis.* Supervised by Martin Kongsbak-Wismann.
- Rebecca Kidd Petersen and Emma Sofia Vestergaard Knudsen, Bachelor thesis, *Vitamin D og infektion med Mycobacterium tuberculosis.* Supervised by Martin Kongsbak-Wismann.

YOUNG INVESTIGATOR NETWORK
INSPIRING EVENTS AND NEW COLLABORATIONS IN 2023

In 2023, the Young Investigator Network (YIN) not only continued its event series, addressing Imposter Syndrome and offering insights into the pharmaceutical industry, but fostered a meaningful collaboration between Associate Professor Martin Kongsbak-Wismann and dermatologist Caroline Meyer Olesen – a testament to the collaborative spirit at YIN's events.

"When will they figure out that I am not as good as they think I am?" "I am only in my current position because I was lucky being at the right place at the right time". The pervasive fear of being exposed as a fraud, despite evident success, is a common challenge in academia known as the "Imposter Syndrome."

In an effort to address these feelings, YIN invited the skilled facilitator Kathy Borys Siddiqui. Kathy created a safe environment that allowed participants to explore the complexities of this phenomenon through open dialogue and shared experiences. She outlined the various manifestations of Imposter Syndrome and provided strategies for recognizing and overcoming its detrimental effects.

The second event of 2023 took YIN members on a trip to the pharmaceutical company ALK-Abelló, providing a comprehensive programme that explored perspectives on collaborations between industry and academia.

Talks and discussions delved into the similarities and differences between the industry and academia, featuring insights from various employees at ALK-Abelló. Insights were shared by Maja-Lisa Clausen, representing Research and Development in Americas and International Markets, Kathrine Beck Sylvestersen, specialising in Mass Spectrometry and Proteomics, Simon

THE YOUNG INVESTIGATOR NETWORK

- Established in 2019 by early-career researchers from SIC and clinical dermatological departments in the Copenhagen area.
- Aims to establish collaborations between researchers and clinicians in the field of immunology and dermatology.
- Always looking for new members; if you are an early-career scientist or doctor working in the cross-field of immunology and dermatology, reach out at sic@sund.ku.dk.

Mayland Fredholm, from Corporate Intellectual Property, Helene Henmar from the Molecular Allergology team, Shashank Gupta and finally, Peter Sejer Andersen from translational research. This session facilitated a nuanced understanding of public-private partnerships and diverse career choices beyond traditional academic routes.
The original idea behind YIN was to naturally foster collaborations between SIC researchers and clinicians across Denmark. In the spirit of encouraging innovative partnerships, YIN has already now played a pivotal role in connecting young researchers at SIC with young dermatologists. One example of this collaborative spirit is the partnership between Associate Professor Martin Kongsbak-Wismann and dermatologist Caroline Meyer Olesen from Bispebjerg Hospital.

NEW COLLABORATION IN 2023

A few years ago, at a YIN event, Martin and Caroline found themselves seated next to each other, sparking a scientific discussion. Martin shared insights into his extensive laboratory experience analysing immune responses, while Caroline discussed her work involving tape-stripping for skin samples from patients with chronic hand eczema. This conversation unveiled collaborative potential, with Martin's laboratory expertise complementing Caroline's clinical insights and extensive patient samples. Throughout 2023, Martin and Caroline collaborated to optimize a protocol for protein and RNA extraction from tapes, a project that reached completion just before Caroline took maternity leave.

Resuming their collaboration in February 2024, Caroline and Martin are taking their research to the next level. Caroline will undertake protein and RNA purifications on all patient samples, and with assistance from other members of YIN, they plan to conduct SmartSeq on the purified RNA. This initiative aims to compare the skin of patients with chronic hand eczema to that of healthy individuals, providing unprecedented insights into this condition. Additionally, they have incorporated samples from patients treated with corticosteroids. By analysing skin samples before and after treatment, they aspire to reveal the molecular-level therapeutic impacts of the treatment on this patient group, potentially leading to groundbreaking findings in dermatological treatments.

Martin Kongsbak-Wismann and Caroline Meyer Olesen.

The collaboration initiated during an informal YIN event illustrates the importance of networking opportunities to catalyse meaningful scientific partnerships. This project not only spans the bridge between basic research and clinical practice but also carries the potential to make substantial advancements in translational medicine, especially within the realm of chronic hand eczema.

The YIN planning committee looks forward to many exciting meetings in 2024 and expresses gratitude to both members and funding institutions for their support throughout the year.

Planning committee, 2023
Martin Kongsbak-Wismann - Chair
Anne-Sofie Østergaard Gadsbøll
Berthe Katrine Fiil
Dorra Bouazzi
Farnam Barati Sedeh
Jennifer Astrup Sørensen
Martin Rich Javadi Namini
Pernille Lindsø Andersen
Sofia Botvid
Stine Rønholt

PROTEOMICS SYMPOSIUM

The Proteomics Symposium, organised by Associate Research Professor Beatrice Dyring-Andersen and Professor Mads Gyrd-Hansen, took place on September 22nd, 2023, at the Mærsk Tower where SIC is also situated.

This hybrid event brought together experts in proteomics to share their insights. The symposium featured informative talks and a networking session aiming to promote collaboration and knowledge sharing in the dynamic field of proteomics.

The symposium commenced with a warm welcome from Beatrice Dyring-Andersen, who introduced proteomics and how it is advancing our understanding of biological systems. The welcome address was followed by an introduction to posttranslational modifications and how to study these using proteomics by Mads Gyrd-Hansen. Subsequently, Marcel Teunissen from the Amsterdam Institute for Infection and Immunity shared recently published research findings on the proteome of skin-resident innate lymphoid cells.

After a coffee break and networking where the attendees had a chance to refresh, Postdoctoral Researcher Julie Sølberg from the Department of Dermatology and Allergy, Gentofte hospital presented her research on hand eczema and the use of tape stripping combined with proteomics. The last speaker at the symposium was Assistant Professor Attila Gábor Szöllősi from University of Debrecen who provided valuable insights on Langerhans cells' significance.

The symposium had an engaging atmosphere and the attendees asked questions and offered comments, leading to an interactive and successful event.

DRUG DELIVERY OVER THE EPITHELIAL BARRIER TO MODULATE IMMUNITY AND INFLAMMATION · 22 NOV. · MÆRSK TOWER · ORGANISED BY LIV EIDSMO

The vast majority of persons living with inflammatory skin diseases experience a limited disease burden and that excludes access to the modern and systemic drugs that are becoming available for people living with severe disease. To discuss ways to tailor drugs to the site of pathology, local and international experts were gathered in a workshop titled:" Drug delivery over the epithelial barrier to modulate immunity and inflammation". Sixty participants from SIC and SUND engaged in lively discussions. Andrea Heinz, our colleague from the LEO Foundation Center for Drug Delivery, introduced ways to overcome the skin barrier on local drug delivery. Thomas Bjarnsholt from the Department of Immunology and Microbiology, SUND, and Keira Melican, Karolinska Institutet, discussed ways to address the microbes that cover the skin. Liv Eidsmo, from SIC, introduced the complexity in eradicating disease driving T cells residing in the skin and Florian Schmidt, from the University of Bonn in Germany, and Georgios Sotiriou, Karolinska Institutet, introduced nanobodies and microneedle patches as potential ways to directly place active drugs in diseased skin. The discussions continued over coffee and has initiated projects that we hope will benefit patients in the years to come.

Mie Sonne Goldeman - PhD Student

Immunological Differences in Allergic and Irritant Contact Dermatitis

Contact dermatitis (CD) is a common inflammatory skin disease influenced by a complex interplay of environmental and immunological factors. It has a negative impact on individuals' quality of life and places a substantial burden on individuals and society. The two primary subtypes, Allergic Contact Dermatitis (ACD) and Irritant Contact Dermatitis (ICD), exhibit similar clinical and histopathological characteristics, despite having distinct triggers. These similarities make it difficult to distinguish between them.

Today we differentiate between ICD and ACD through a combination of clinical assessment, exposure history, and allergy test outcomes. However, the accuracy of these assessments depends on the knowledge and resources available to healthcare professionals, which can lead to misclassifications. Misclassification can have negative consequences for the disease prognosis, as it is important to understand that CD, which is not adequately treated from the beginning can progress to a chronic condition that does not improve even when the triggering exposures are removed.

Attempts to distinguish between ACD and ICD through experimental studies have been made, but no reliable biomarkers have yet been identified. A clear distinction is necessary to effectively provide guidance and information on trigger avoidance, prevention, and treatment strategies.

In this project we aim to investigate the immunological differences between ACD and ICD, to enhance our understanding of the underlying mechanisms and examine whether the immune profiles of the two disease entities differ. To explore this, we will investigate the impact of time and clinical severity including the influence of the eliciting allergen on the immune profile (Fig. 1). Additionally, we will investigate the local memory T cell response to the eliciting allergen or an irritant (Fig. 2). Finally, we will make a T cell assessment in chronic hand dermatitis to further expand our understanding of CD (Fig. 3).

Data will be collected through a series of experimental and clinical studies involving punch biopsies for RNA sequencing or single-cell RNA sequencing. The experimental studies will include patch testing with allergens and/ or an irritant. Patients with chronic hand dermatitis will be included through the BIOSKIN program.

This will allow us to compare the experimental findings with the clinical disease as well as validate how the experimental models fit the chronic disease (Fig. 3). Finally, it will help expand our knowledge of how chronic CD are sustained and may lead to the discovery of new potential treatment targets.

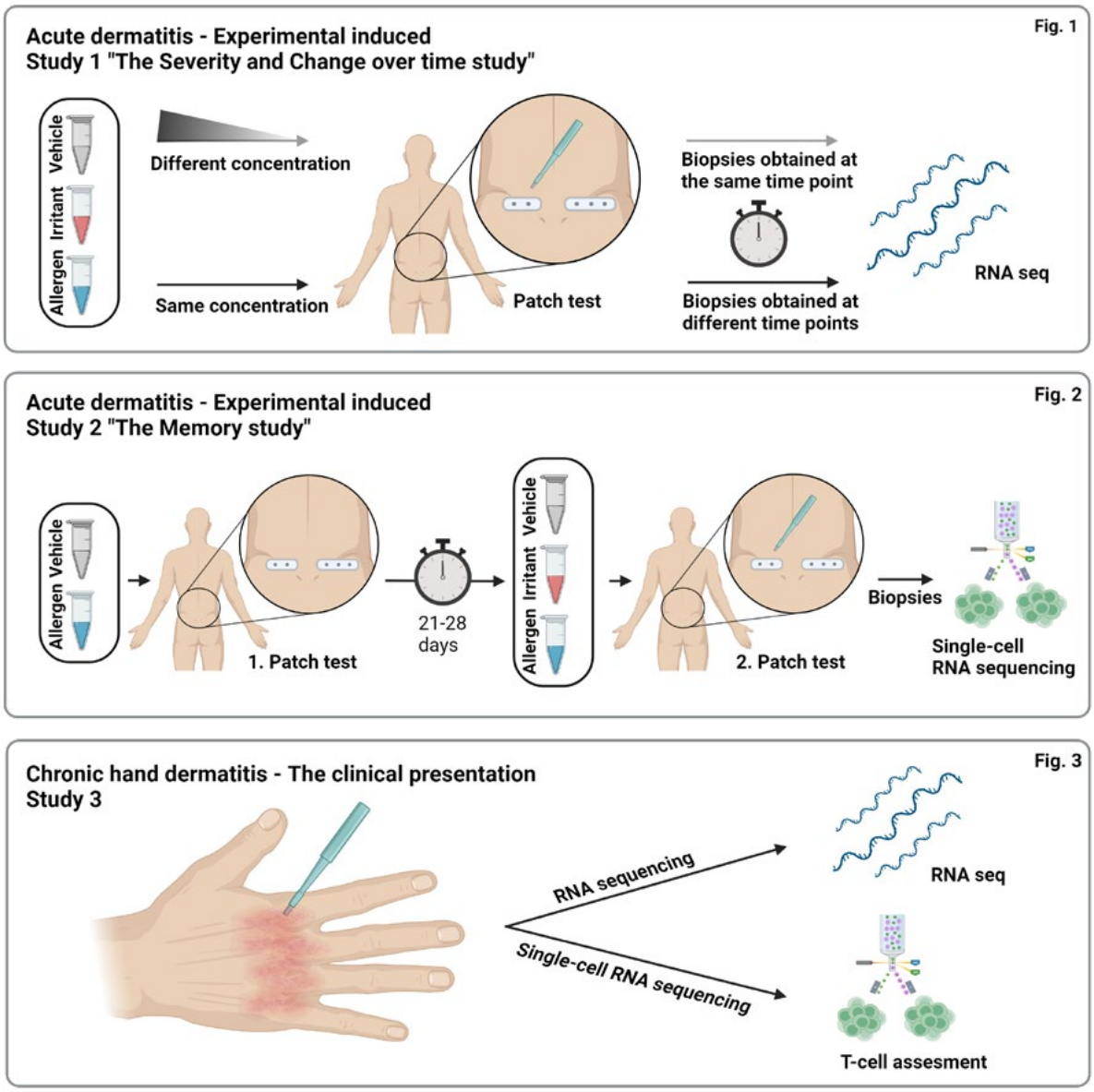


Fig. 1: In the experimental studies dermatitis is induced with patch test on the lower back. Study 1 is evaluating dermatitis severity by using varying concentrations of an irritant or an allergen, alongside a vehicle control site. These biopsies are collected after 48 hours for transcriptomic analysis. To evaluate the time aspect a single concentration is used, and the biopsies are collected at different time points from 0 to 120 hours post-exposure for transcriptomic analysis.

Fig. 2: Study 2 consists of a two-phase patch testing process to evaluate the memory T cell responses in allergic contact dermatitis with an irritant component. Phase one includes allergen exposure and a vehicle control site, followed by a recovery period. Phase two includes both allergen, vehicle and irritant exposure followed by biopsies for single-cell RNA sequencing. In collaboration with PhD student Julie Friis Weber.

Fig. 3: In study 3, patients with chronic hand dermatitis will be enrolled through the BIOSKIN program. Punch biopsies will be collected for RNA sequencing to compare clinical outcomes with experimental findings from Study 1 or for single-cell RNA sequencing for a T-cell assessment. Fig 1-3 Created with BioRender.com

Venla Väänänen - PhD Student

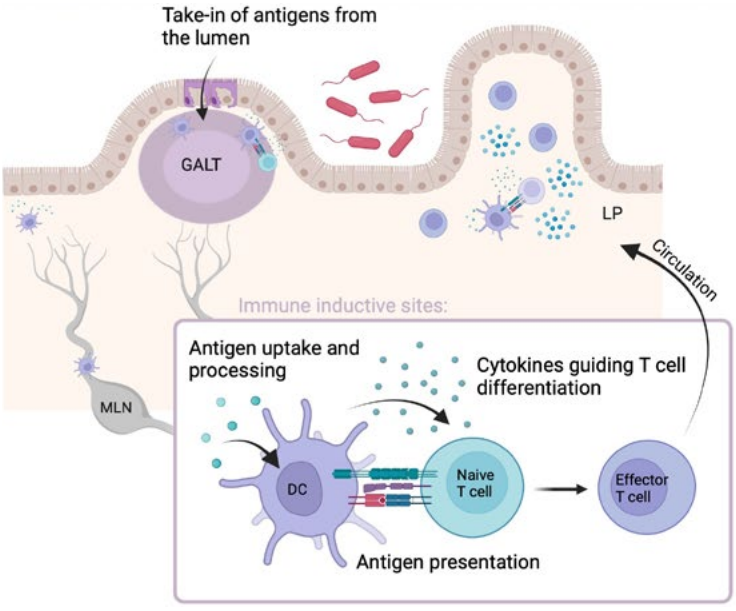
Deciphering the complexity of intestinal antigen presenting cells in health and inflammatory bowel disease

The intestinal immune system must tolerate food antigens and commensal microbiota but also be able to generate protective immune responses towards potential pathogens. Our intestinal immune system is highly complex and a disbalance in the cross talk between our immune system and the intestinal environment is thought to contribute to the initiation and maintenance of inflammatory bowel diseases (IBD) such as Crohn's disease and ulcerative colitis. Currently, the prevalence of Crohn's disease is increasing but our understanding of the major cellular players that contribute to disease remains incomplete.

Conventional dendritic cells (cDC) are the major professional antigen presenting cells (APC) in the body and as such are essential in the priming and differentiation of adaptive immune responses (Figure 1). While numerous studies, including those from our own laboratory, have shown that distinct cDC subsets play non-redundant roles in the regulation of intestinal immune responses in mice, APC diversity and function in distinct immune compartment of the human intestine, and how these are altered in Crohn's disease, remains unknown.

Previously, our group has developed a technique to isolate gut-associated lymphoid tissues (GALT) and GALT-free lamina propria from human intestinal samples, opening up the possibility to study these distinct immune niches independently of one another. In my project, I use a range of state-of-the-art techniques including single cell RNA sequencing, bioinformatics, cell sorting and in vitro cultures, immunohistochemistry, and flow cytometry to study APC diversity within immune niches of the human intestine and the changes that occur within this compartment in the setting of Crohn's disease.

With this project, I hope to increase our understanding of the role of different cDC subtypes play in the maintenance of intestinal immune homeostasis and in contributing to Crohn's disease pathology.



Dendritic cells take up antigens and process them for antigen presentation at immune inductive sites of the intestine, such as gut-associated lymphoid tissues (GALT) and mesenteric lymph nodes (MLN), where dendritic cells prime naïve T cells and guide T cell differentiation by secreting cytokines. Effector T cells leave the inductive sites to the circulation from where they locate to the lamina propria (LP) to perform their effector functions. DC = dendritic cell, GALT = gut-associated lymphoid tissue, LP = lamina propria, MLN = mesenteric lymph node

Deciphering the role of intestinal fibroblasts during health and inflammatory bowel disease

Urs Michael Mörbe - Postdoc

The intestinal barrier is exposed to trillions of microorganisms that make up the intestinal microbiota. While the host immune system must be able to mount functional immune responses against pathogens, most microbial species are beneficial for human health and hence should be tolerated. Failure of this intricate balancing act can have grave consequences for the host, such as the development of inflammatory bowel disease (IBD), caused by chronic immune responses against the intestinal microbiota.

Most immune cells responsible for intestinal immune responses during health and disease are located in a connective tissue layer called the lamina propria, where for example plasma cells produce antibodies and T cells effector cytokines. Additionally to the lamina propria as key effector site, the intestinal wall harbors specialized immune priming niches, collectively termed gut-associated lymphoid tissues (GALT), where naïve and memory-type lymphocytes can survive long term and screen for their cognate antigen. Moreover, such GALT do not only contain immune cells, but also a network of fibroblasts, phenotypically different from their counterparts in the lamina propria.

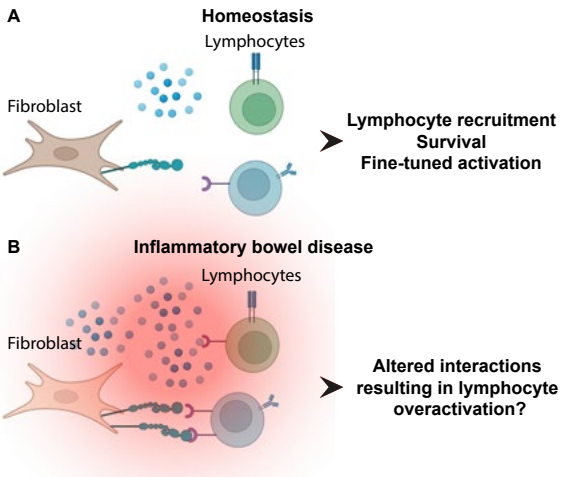


Figure: Fibroblasts in GALT steer intestinal immune responses. (A) During homeostasis, fibroblasts in GALT can interact with naïve and memory-type lymphocytes via surface-bound or secreted molecules, impacting on lymphocyte migration, activation status and survival. (B) While it yet remains unclear where and how lymphocytes become overactivated during active IBD, we hypothesize that dysregulated fibroblasts in human GALT could contribute to pathogenic local immune responses. (Figure generated with Biorender)

Studies in mice have previously shown that fibroblasts in lymphoid tissues such as GALT do not only have structural functions, but can closely interact with immune cells by an array of secreted and surface molecules, impacting on the survival, activation status and migration of immune cells (Figure 1). However, the functions and diversity of lymphoid tissue fibroblasts in humans remains understudied, despite of the notion that the sizes and cellular compositions of GALT differ drastically between species and that IBD in associated with profound phenotypical changes within the intestinal immune cell and fibroblast landscape.

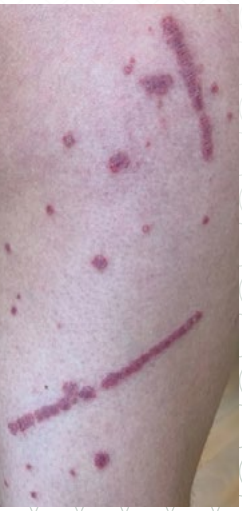
In my project, I would like to shed some light on fibroblasts as suspected key organizers of intestinal immunity during health and IBD. By applying confocal laser microscopy, flow cytometry and single cell RNA-sequencing, I have established an in depth cellular atlas of these cells during health, and showed that there is a remarkable functional diversity. My ongoing efforts aim to extent our knowledge around intestinal fibroblasts in the setting of IBD. A key focus will be to study these cells in GALT as putative priming sites for excessively activated immune cells in IBD-associated inflammatory lesions. Ultimately, I hope to identify yet unappreciated cellular and molecular interactions that contribute to IBD and could potentially be used as targets for future treatment modalities.

BRIDGE FELLOW PRESENTATION

Nils Albert Duvetorp - BRIDGE Fellowship

PSODEEP 1 and PSODEEP2 - Using Koebner to study Psoriasis Dynamics.

The clinical manifestation of psoriasis often changes over time and patients typically experience periods of flare-ups with high disease activity followed by periods of remission with low or no disease activity. Focal patches of psoriasis are initiated and maintained by the immune system and systemic immunomodulatory treatments targeting signalling molecules such as TNF, IL-23 and IL-17 have revolutionised the treatment of severe psoriasis. However, the disease relapses in a majority of patients if the treatment is stopped. The inherent dynamic natural course of psoriasis disease activity makes treatment decisions difficult and results in both over- and under-treatment. My BRIDGE project is designed to meet the need for both better tools to evaluate and track disease-activity over time and to investigate the how individuals with psoriasis experience fluctuation of their disease. Mapping patient´s experience of their disease variability and disease triggers could provide important understanding of disease initiation, maintenance, resolution, and relapse. Such insights offer opportunities to design translational studies focusing on the mechanisms of disease.



Koebner triggered linear psoriasis lesions.

I study the potential of the Koebner phenomenon as a clinical biomarker. In patients affected by Koebner, new psoriasis lesions develop at sites of physical trauma. The Koebner phenomenon can be induced experimentally, thereby providing an elegant model to study development of psoriasis. Since Koebner induction response can vary over time and between individuals it can potentially serve as a model that can be used to discover clinical biomarkers with relevance for disease activity and progression.

In the PSODEEP1 study, patients with psoriasis and/or psoriatic arthritis from four different countries (Denmark, Chile, Sweden, and the Netherlands) will be distributed a digital questionnaire to answer questions on Koebner phenomenon, disease variability, disease severity, symptoms of arthritis and other self-experienced disease triggers. This project's main focus is to investigate the prevalence of self-reported Koebner and if this phenomenon is associated with psoriatic arthritis but will also explore other disease triggers.

Individuals who have reported the experience of Koebner in PSODEEP1 will be recruited to the PSODEEP2 study in which new psoriasis plaques will be induced by the means of skin injury (tape-stripping and microneedling). This model will allow in-depth analysis of changes in stratum corneum proteomics, local skin T-cell reactivity, skin epigenetics and skin bulk gene sequencing during early phases of psoriasis development. As such, this project has the potential to provide an increased understanding of local mechanisms of disease development. If biomarkers of disease "reactivity" are identified, then these can be tested in further translational psoriasis studies focusing on disease dynamics, thereby linking back to the clinical questions addressed in PSODEEP1.

The translational potential of this BRIDGE project is to provide improved disease monitoring strategies and new tools to support better treatment decisions. This project also has the potential to identify new pharmacological targets aiming to stop disease development rather than treating already established disease.

Outreach and communication

All members of SIC are instrumental in our outreach and communication programme. 2023 kicked off with an article in SUND news featuring Martin Kongsbak-Wismann's insights into Vitamin D's effectiveness in combating tuberculosis. This was swiftly followed by "Talks på Toppen," a popular public seminar series at the University of Copenhagen (UCPH). Martin's presentation on Vitamin D and its impact on the immune response captured the interest of an engaged audience of 75 attendees at this open event.

BLOOM FESTIVAL

SIC has participated in the "BLOOM Festival" – a three-day family nature and science festival - since 2020 and this year, Liv Eidsmo and zoologist, Bengt Holst, engaged in a panel debate on shedding of skin in humans and animals. This conversation was later transformed into a podcast available on-line on BLOOM festival's website.

Liv Eidsmo at BLOOM Festival

ECZEMA ON SOCIAL MEDIA

As winter arrived in Copenhagen, Liv also shared insights on how to handle hand eczema in a video on SUNDs social media.

PROJEKT FORSKERSPIRER

Ambitious high school students interested in science were invited to participate in a two-day workshop called "Projekt forskerspirer" at UCPH to expose the students to the life of a researcher, and the career paths that can lead to becoming a researcher. Martin Kongsbak-Wismann presented and is now the official mentor of the high school students participating in the programme.

MINI COURSE WITH GEFION GYMNASIUM STUDENTS

Charlotte Menné Bonefeld's group at SIC hosted its annual two-day mini course in skin immunology for Gefion Gymnasium's biotech programme's final-year students, offering a unique opportunity to delve into the world of research and education at UCPH. Read more on page 27.

DIS STUDY ABROAD PROGRAMME

Global perspectives were incorporated as 30 college students from 18 US universities, part of the DIS – International students – study abroad programme, visited SIC. Hosted by Niels Ødum, the day included research lectures, presentations, networking, and insights into studying at UCPH.

CONNECTING WITH AN BROADER AUDIENCE

Niels Ødum's contribution to The Danish Cancer Society newsletter broadened the center's outreach, connecting with a more extensive audience. Additionally, Niels participated in an interview with ndtv, a follow-up to the SUND news titled "Killing Multidrug-Resistant Bacteria Without Antibiotics" – an article about the discovery of an enzyme which kills both resistant and non-resistant staphylococcus bacteria, which not only eradicates staphylococcus aureus; but also inhibits their ability to promote cancer growth.

Gefion Gymnasium students in the labratory.

MEMORY T CELLS ON SOCIAL MEDIA

Liv Eidsmo was also in SUND news with an article about a discovery of memory killer T cells contributing to the development of more efficient immunotherapy for diseases like melanoma.

IMMUNOLOGY HUBS

In the "Immunology Hubs" series in "Immunology and Cell Biology," Jonathan Coquet interviewed Liv Eidsmo and shed light on her experience of the scientific environment at SIC and move to University of Copenhagen. The Immunology Hubs series aims to bring attention to great immunology research environments around the globe.

SIC ON LINKEDIN

SIC's LinkedIn profile is actively used to share articles authored by scientists from SIC's research groups, demonstrating our commitment to sharing valuable research insights across our diverse scientific community, which is becoming more and more popular among SIC's ~2,500 followers.

SIC SEMINARS

Finally, the SIC Seminars, organised by SIC's own young researchers at the Mærsk Tower, served as a forum attracting researchers not only from the Department of Immunology and Microbiology (ISIM), but also other departments at SUND and various Danish universities and clinics.
In 2023, SIC hosted an impressive lineup of 11 speakers globally (see box), including seminars which were held in connection with PhD defences and visits by professors to other SIC members. The momentum continues with exciting speakers already lined up for 2024.

Niels Ødum and the international students who are part of the DIS study abroad programme.

TESTING THE HYGIENE HYPOTHESIS IN THE LABORATORY SETTING

This year, Egon Urgard, Javiera Alvarez and Jonathan Coquet at SIC, published their long-awaited results delving into the hygiene hypothesis in the journal Science Immunology. The hygiene hypothesis is the notion that more sterile living conditions may lead us to develop allergies. It is thought that some microorganisms that may be lacking in humans today may help to train our bodies and make them less likely to respond to allergens in our environment.

In their study, SIC researchers compared the allergic immune response of specially-bred and highly-exposed 'wildling' mice to those of standard clean laboratory mice. Importantly, the genetics of both clean and wildling mice was identical! Contrary to what might have been expected, the researchers found that the allergic immune responses in these highly exposed mice was not entirely different to those of the clean mice. When looking specifically at T and B cells in mice, and at the inflammatory signs of allergic disease, the scientists could observe no obvious difference in the quality of inflammation and concluded that these highly-exposed mice showed no signs of being protected from developing allergic immune responses.

The study has triggered great interest in the public realm, having been covered by more than 40 news outlets including SVT in Sweden, and featured on blogs, podcasts and radio shows including Sunday morning with Jim Mora in New Zealand. Given that the hygiene hypothesis has been at the forefront of the public imagination for close to 40 years, more work has to be done to understand how our environment can impact on the development of allergy. Work is underway at SIC and at the University of Copenhagen to make experiments in such mouse model systems available to more researchers.

SEMINARS ORGANISED BY SIC RESEARCHERS AND HOSTED AT THE MÆRSK TOWER

Professor Ulrich auf dem Keller, Technical University of Denmark
Proteases pivotal roles in diseases.

Professor Bill Agace, previously Technical University of Denmark, now SIC
Exploring intestinal dendritic cell heterogeneity *and function.*

Professor Søren Riis Paludan, University of Aarhus, Denmark
Novel mechanisms in innate immune defence against virus infection.

Postdoc Julia Sanchez Garrido, Imperial College London, UK
Bacterial effectors during infection: an intersection of pathogenic and cellular networks.

Professor Marc Vocanson, Centre International de Recherche en Infectiologie (CIRI), France
Tissue Resident Memory T-cells in Allergic Contact Dermatitis.

Professor Julie Jameson, California State University San Marcos, USA
The complex roles of epidermal T cells: from wound repair to psoriasis to alopecia areata.

PhD Nanna Fyhrquist, Karolinska Institutet, Sweden
Environmental exposure and skin inflammation – discovery of severity associated signatures and biomarkers for novel diagnostics.

Professor Jenny Mjösberg, Karolinska Institutet, Sweden
The role of human innate and adaptive lymphocytes in gut and lung inflammation.

Associate Professor Daniel Pellicci, The University of Melbourne, Australia
Unconventional T cell development in the human postnatal thymus

Professor Federica Marelli-Berg, Queen Mary University of London, UK
Regulation of $CD8^+$ T cell responses by the Glucose Transporter 2

Professor Dr. Richard Moriggl, University of Veterinary Medicine, Austria
Too little or too much JAK-STAT3/5 pathway activity is like YIN/YANG for immunity or cancer

Organising committee of the SIC seminars

- Mia Hamilton Jee
- Rasmus Agerholm-Nielsen
- Chris Kedong Wang
- Ekaterina Zhuravleva
- PI: Jonathan Coquet

Funding

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 29.2 million, and the turnover from the add-on grants totalled DKK 13.3 million in 2023. Also, SIC obtained a total of DKK 29.8 million in new funding from 13 external research grants.

External research grants awarded in 2023

Funder	Recipient	Title	Amount in DKK
Stiftelsen Psoriasisfonden	Albert Duvetorp	The study of Koebner in patients with psoriasis and psoriatic arthritis	SEK 100,000
Carlsberg Foundation	Anders Boutrup Funch	Role of B cells in allergic contact dermatitis and in tolerance to contact allergens.	1,220,000
Sofus Friis Legat	Carsten Geisler	Can allergic contact eczema be treated by shifting the composition of epidermal T cells?	600,000
Danmarks Frie Forskningsfond	Charlotte Menné Bonefeld	Can contact eczema be treated by altering the composition of epidermal T cells?	2,770,560
The Danish Cancer Society	Chella Krishna Vadivel	Spatial transcriptomics analysis at UC Irvine, USA to investigate how Staphylococcal enterotoxins induce drug resistance in cutaneous T cell lymphoma	93,865
Carlsberg Semper Ardens Accelerate Grant	Jonathan Coquet	Allergies: Why me and why now?	5,000,000
BRIDGE, UCPH and Novo Nordisk Foundation	Liv Eidsmo	BRIDGE fellowship for Albert Duvetorp	1,500,000
The Danish Cancer Society	Niels Ødum	Staphylococcus aureus drives disease progression in cutaneous T cell lymphoma	2,985,000
Danmarks Frie Forskningsfond	Niels Ødum	JAK-inhibition as a novel multilevel treatment of cutaneous T cell lymphoma	3,153,600
Aase og Ejnar Danielsens Fond	Rune Kjærsgaard Andersen	Personal and early detection of the progression of the skin disease hidradenitis suppurativa	100,000
LEO Foundation	Terkild Brink Buus	Staphylococcus aureus drives inflammation and disease activity in atopic dermatitis – novel approaches to old problems	12,000,000
Psoriasis Forskningsfonden	Wenning Zheng	Investigating pathogenic T cell clones in skin and joints of psoriatic patients – exploring functional differences and tissue-specific chemokine/cytokine expression	100,000
Novo Nordisk Foundation	William Winston Agace	Sponsorship International Conference of Mucosal Immunology	250,000

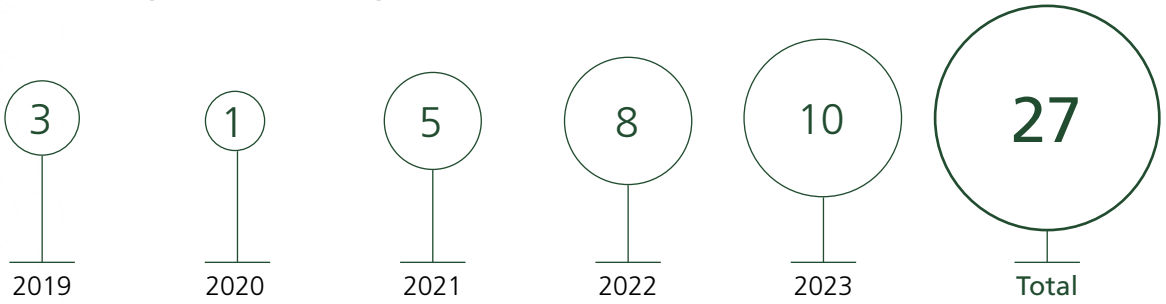
Scientific output

SIC and Bioskin researchers authored 42 publications in peer-reviewed journals in 2023.

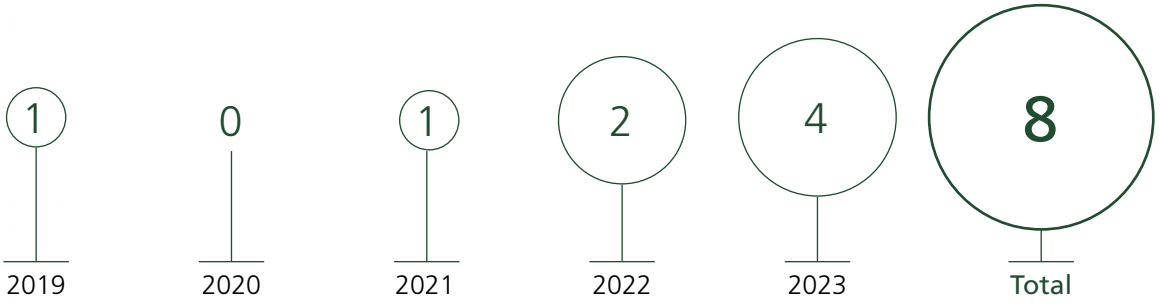
SIC publications 2019-2023

2019	2020	2021	2022	2023
25	19	34	22	34

Number of publications · impact factor >10



Number of publications · impact factor >20



Publications

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

A conversation on allergy: recognizing the past and looking to the future.
Melén E, Lambrecht BN, Lloyd CM, Rothenberg ME, Kabashima K, Luciani F, Coquet JM, Ober C, Nawijn MC, Platts-Mills T, von Mutius E.
Immunol Cell Biol. 2023 Nov-Dec;101(10):936-946. doi: 10.1111/imcb.12688. Epub 2023 Sep 9. PMID: 37688499. **JIF 5.85**

Bridging the gap between scientific discoveries and clinical application at the Utrecht Science Park.
Peperzak V, Coquet JM.
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CD100 boosts the inflammatory response in the challenge phase of allergic contact dermatitis in mice.
Mraz V, Funch AB, Jee MH, Gadsbøll AØ, Weber JF, Yeung K, Lohmann RKD, Hawkes A, Ødum N, Woetmann A, McKay D, Witherden D, Geisler C, Bonefeld CM.
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CD4⁺ T cells inhibit the generation of CD8⁺ epidermal-resident memory T cells directed against clinically relevant contact allergens.
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Zwijnenburg AJ, Pokharel J, Varnaitė R, Zheng W, Hoffer E, Shryki I, Comet NR, Ehrström M,

Gredmark-Russ S, Eidsmo L, Gerlach C.
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Human skin-resident CD8⁺ T cells require RUNX2 and RUNX3 for induction of cytotoxicity and expression of the integrin CD49a.
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*shared senior and corresponding authorship
Immunity. 2023 Jun 13;56(6):1285-1302.e7. doi: 10.1016/j.immuni.2023.05.003. Epub 2023 Jun 2. PMID: 37269830. **JIF 43.5**

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Safety and Efficacy of Topical Calcineurin Inhibitors in the Treatment of Facial and Genital Psoriasis: A Systematic Review. Amiri D, Schwarz CW, Gether L, Skov L.
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In-depth proteomic map of innate lymphoid cells from healthy human skin and blood.
Teunissen MBM*, Pilgaard Møller LB*, Løvendorf MB, Skov L, Bonefeld CM, Bekkenk MW, Clark RA, Mann M, Dyring-Andersen B. *shared first authorship
J Invest Dermatol. 2023 Aug 4:S0022-202X(23)02492-2. doi: 10.1016/j.jid.2023.07.011. Online ahead of print. PMID: 37544588. JIF: **7.59**

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Sølberg JBK, Quaade AS, Drici L, Sulek K, Ulrich NH, Løvendorf MB, Thyssen JP, Mann M, Dyring-Andersen B, Johansen JD.
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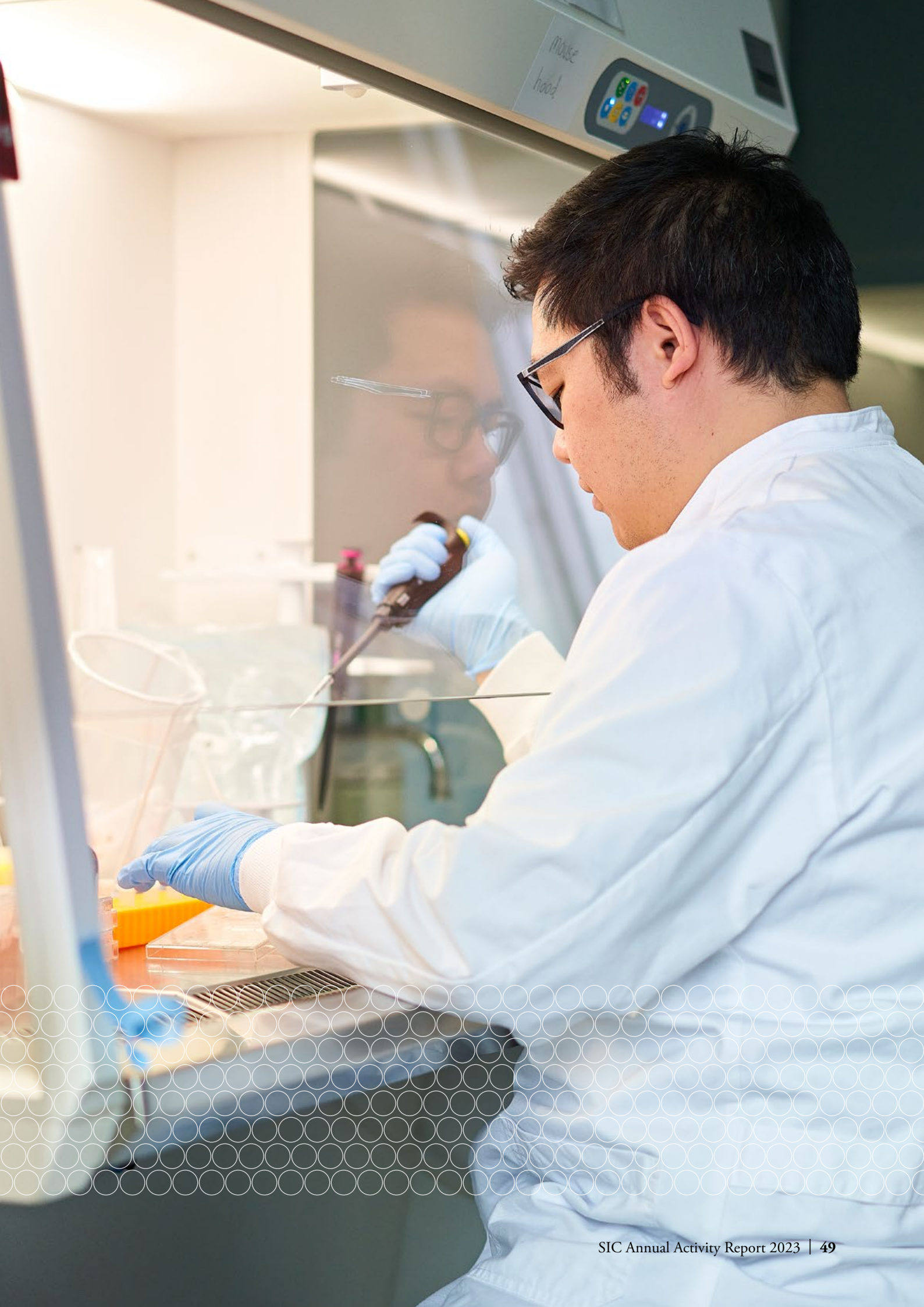

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