Annual Activity Report 2025

LEO Foundation
Skin Immunology
Research Center

Content

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Introduction

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

The skin is our largest barrier to the external environment and over 3,000 different skin diseases are known to affect the human population. Some are extremely common. For instance, up to 20% of school children in Denmark suffer from atopic dermatitis, the most common form of eczema. Meanwhile, over 100 million people are known to suffer from psoriasis around the world. Other skin conditions may be exceedingly rare and driven by mutations in genes, which are not well understood. Our understanding of inflammatory skin diseases has accelerated over the past decade and discoveries particularly within the field of immunology have paved the way for new treatments. Despite this progress, inflammatory skin diseases still have a large impact on our quality of life as curative treatments continue to prove elusive. Patients with skin diseases frequently present with co-morbidities such as asthma, arthritis and inflammatory bowel disease, making it increasingly clear that promoting a healthy skin barrier can impact positively on the health of the whole body.

Through the LEO Foundation's generous DKK 400 million donation in 2019, the LEO Foundation Skin Immunology Research Center (SIC) was established at the University of Copenhagen to advance research and education in inflammatory skin diseases. SIC aims to bridge and integrate basic and clinical analysis of the skin to advance our understanding and treatment of skin diseases. Over the course of the grant, SIC has made important investments that include the establishment of a large biobank for patients afflicted by skin diseases, and in the recruitment of researchers at the forefront in their fields of skin, lung, and intestinal barrier research. Through recruitment and internal capacity building, SIC has also strengthened its computational biology competence, an essential ingredient in modern-day research.

Today, SIC is a thriving research Center providing a new understanding of what healthy skin immunity is and unravelling the immune failures that occur in people living with skin diseases. SIC scientists educate the next generation of leaders in skin immunology research, while concurrently increasing the knowledge and awareness of skin diseases among medical professionals, patients, and the public.

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

Director's Corner

Executive Director of SIC, Professor Jonathan Coquet.

Reaching new frontiers in skin immunology research

To begin, it was an absolute honour to step into the role of Executive Director of our Skin Immunology Research Center (SIC) on the 1st of October 2025. I thank Professor Niels Ødum for his dedicated service as SIC's Executive Director until the end of September 2025 and it is with Niels' considerable influence in mind that I outline some of SIC's achievements over the past year.

Thanks to a generous donation from the LEO Foundation in 2019, SIC has established itself as a leading centre in skin immunology. Now comprising seven research groups and over 70 dedicated full-time staff, 2025 was a year of scientific breakthroughs, new partnerships and tremendous investment in SIC's future. Researchers at SIC published important work on many fronts. In the setting of cancer, researchers identified genetically distinct subclones of cutaneous T-cell lymphoma, which had different abilities to respond to standard therapies, providing important insights with clinical implications for the treatment of patients with this disease.

SIC made important contributions into our understanding of how T cells respond to stimuli and are maintained in the skin over the long term. T cells were found to require the presence of contact allergens directly in the skin for their persistence and studies revealed that the allergen nickel induced very different immune features between individuals, which was surprising.

Technologically, researchers developed a new scalable technique for the preparation of skin samples that leads to markedly better protein recovery, which should vastly improve our ability to analyse skin protein biomarkers. Meanwhile, methods that specifically detect T cell clones directly in tissue were developed, opening up the possibility of being able to identify disease-causing T cells in various disorders in barrier tissues like the skin and intestines.

In conditions of inflammation, mesenchymal stromal cells were also shown to be affected on various parameters affecting their potential clinical utility, while in two separate studies from SIC researchers, stromal cells and phagocytic cells were found to be altered in patients suffering from intestinal bowel disease.

In addition to our research output, 2025 was a year of considerable investment. Firstly, we were pleased to welcome Prof. Lars Rønn Olsen and his *Immunological Bioinformatics* group to SIC. Lars' group greatly strengthens the computational competence of SIC at a time when analysing 'big data' and using artificial intelligence in the workplace is of critical importance. Lars' group leverages current and newly generated datasets in new forms of analysis, providing insights into human genetics that are often deemed too difficult using standard analytical pipelines. Lars' integration into SIC is already facilitating meaningful data interpretation in several collaborative projects.

SIC also made several important strategic investments that set up the centre and our collaborators for years to come. An intravital imaging facility was launched at the University of Copenhagen that will facilitate live cell imaging in the skin and other barriers on the back of a considerable investment from SIC. This allows not only SIC researchers but others at the university to track the responses of cells, nerves and tissues in real time. Our researchers also began imaging skin and gut samples in various disease settings using the Xenium Spatial Transcriptomics Platform, part of a strong collaboration with the Center for Basic Metabolic Research (CBMR) at the University of Copenhagen. Xenium allows for detection of over 5,000 genes at once in diseased tissue samples and a flexibility to change gene panels based on the disease of interest.

3-Dimensional skin models were established at the centre to allow for streamlined analysis of the impacts of inflammation on multi-layered skin. 3-D skin models are amenable to genetic manipulation allowing SIC researchers to target any gene of interest in a complex skin system and analyse the downstream consequences. A wildling mouse facility was established, one of only a handful in the world, to investigate the impact of microbes on barrier health and barrier immunity.

A major development this year was the strengthening of our research and education pathways in Sub-Saharan Africa. We launched several projects with partners in South Africa and Tanzania that will assess the dermatological challenges facing the region. The projects will document the burden of skin diseases in these countries, analyse the immunological aspects of several skin and allergic diseases and through a robust exchange programme, facilitate training of junior researchers at SIC and at our partner universities.

We continued a thoroughly enriching collaboration with Profs. Lone Skov and Jeanne Duus Johansen at BIOSKIN, Herlev-Gentofte hospital. Together, we are able to delve into the complexity of the skin and diseases affecting the skin at a level we may not otherwise be able to achieve. Understanding the immunological basis for *how* patients respond to therapies and *why* certain therapies are not equally effective across all individuals remains a key area of focus across all SIC research groups. A new collaboration with Mikkel Herly, Copenhagen University Hospital – Rigshospitalet, has also driven considerable work into healthy skin and aims to provide a healthy reference point for the disease settings in which we often work.

SIC team leaders and staff were recipients of several grants and awards, including Luiza Moraes Holst, recipient of a BRIDGE fellowship and Erik van Tilburg Bernardes, who was awarded a Marie Curie award, both from the *Barrier Immunology* group. SIC staff attended many scientific conferences to share knowledge and dedicated considerable time to education at various levels, including the university undergraduate and post-graduate Biomedicine and Medicine programmes. Outreach to educate high-school students was again a major achievement, while our 5th Skin Immunology Summer School brought young trainees and renowned scientists together from around the world.

In all, 2025 was a year filled with achievements but also filled with promise for the future. In 2026, we look forward already to our 6th Skin Immunology Summer School which had a record number of applications this year. The upcoming European Society of Contact Dermatitis (ESCD) Congress hosted at Mærsk Tower will follow shortly after and the SIC community will continue to share our ideas and research results through research articles, seminars, podcasts and through different media outlets.

Finally, I cannot emphasise enough what a privilege it is to come to work every day. I would like to thank all my colleagues at SIC for making our workplace exciting and fun and extend my sincerest thanks to the LEO Foundation for their continued support, which makes our work possible.

Reflections from the Dean

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

It has been another productive year for the LEO Foundation Skin Immunology Research Center (SIC), consolidating the progress achieved in 2024 and translating strategic ambitions into tangible results.

I would like to extend my sincere thanks to Professor Niels Ødum for his leadership of SIC during his period as Executive Director. From May 2024 to October 2025, he ensured continuity, stability, and steady progress across the Center's strategic priorities. His commitment has been important in maintaining momentum during a period of transition.

In October, Professor Jonathan Coquet assumed the role of Executive Director. Under his leadership, SIC continues to strengthen its scientific direction, reinforce international partnerships, and advance initiatives aligned with the priorities of both the Center and the University of Copenhagen.

Over the past year, research coming from SIC has not only enhanced our understanding of the skin and diseases affecting the skin, but also promoted our faculty's ambitions in other ways. Through large investments in the Intravital Imaging Facility and the Wildling Mouse Facility in particular, SIC initiatives are bringing great benefit to researchers across our university.

SIC's engagement in Africa has developed further over the past year. Projects are now moving from planning to implementation, reflecting a sustained institutional commitment to long-term collaboration with African partners. This development contributes meaningfully to the Faculty's broader internationalisation strategy and positions SIC as an active participant in shaping equitable and research-driven partnerships.

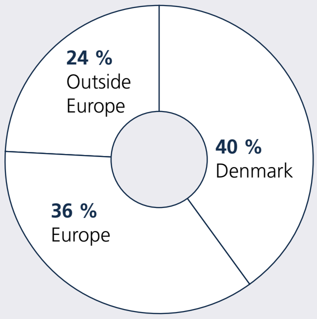
The integration of Professor Lars Rønn Olsen and the Immunological Bioinformatics group is already contributing to SIC's research environment. The strengthening of bioinformatics capacity supports data-driven discovery across research themes and enhances opportunities for interdisciplinary collaboration within the whole Department.

Early-career researchers at SIC continue to demonstrate high scientific quality and engagement. Their success in attracting competitive research funding and active contributions to teaching underline the Center's role in developing research talent and supporting the Faculty of Health and Medical Science's educational mission.

SIC remains characterised by a focused and collaborative research culture, where strategic direction and scientific ambition are closely aligned. On behalf of the Faculty, I thank all staff for their continued commitment and contributions over the past year and look forward to following SIC's tremendous progress.

Organisation and governance

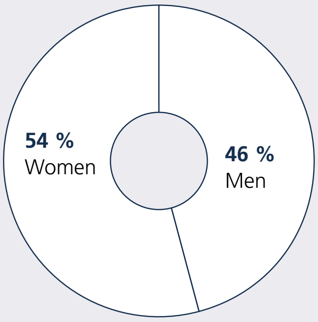
SIC operates as a center within the Department of Immunology and Microbiology (ISIM) at the Faculty of Health and Medical Sciences (SUND) at the University of Copenhagen. Situated at the Mærsk Tower in Copenhagen, SIC's research groups engage in scientific collaborations across the Faculty, national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



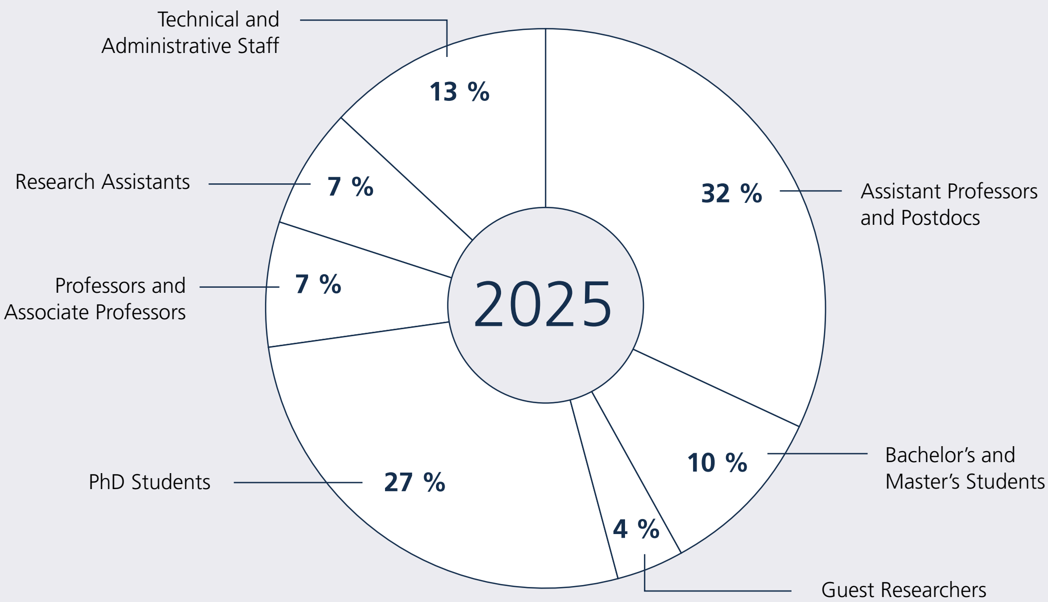
Nationalities of scientific staff and students

Staff composition

During 2025, the SIC community consisted of 121 members, representing 29 nationalities. The SIC community includes members of core research groups at SIC, visiting researchers, bachelor's and master's students conducting their thesis work or participating in exchange programmes.



Gender distribution of scientific staff and students



Distribution of staff and students by position

The core members

SIC hosts seven core research groups and affiliated Clinical Professors at Herlev/Gentofte Hospital, Lone Skov and Jeanne Duus Johansen lead The BIOSKIN Biobank Program. The core members form SIC's Steering Committee, spearheading strategic scientific initiatives.

Management

SIC's Daily Leadership Team, consisting of Executive Director Jonathan Coquet, ISIM Head of Department Charlotte Menné Bonefeld, Head of Administration Nils Erik Samdal, and Center Coordinator Hannah Paludan, oversees day-to-day operations.

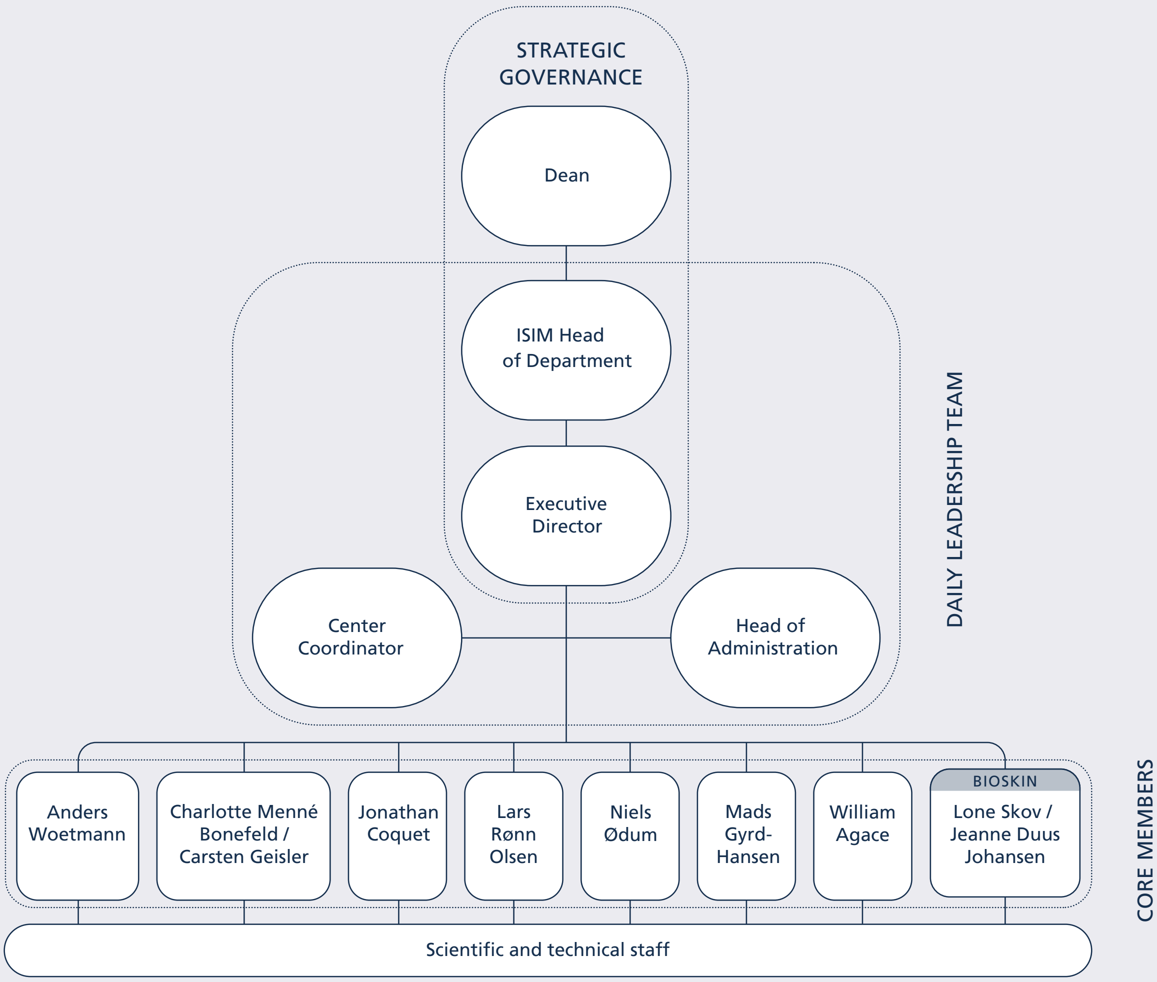
Regular consultations with Dean Bente Merete Stallknecht guide strategic decisions. Annually, Rector David Dreyer Lassen aligns with Center Management and the LEO Foundation to review strategic progress and development. The Center Management also meets annually with the LEO Foundation to present the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

Scientific advisory board 2025

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

THE SCIENTIFIC ADVISORY BOARD CONSISTS OF

- Tomas Mustelin, University of Washington, USA (Chair)
- Emmanuella Guenova, Johannes Kepler University Linz, Austria
- Johann Gudjonsson, University of Michigan, USA
- Kenji Kabashima, Kyoto University, Japan
- Mübeccel Akdis, University of Zurich, Switzerland
- Riitta Lahesmaa, University of Turku, Finland



Organisation and governance chart

Allergic Inflammation

In our third year at SIC, the Allergic Inflammation Research Group took significant strides on several fronts in 2025. Members of the group actively participated in many meetings around the world, including the ENII Sardinia Summer school, the ESDR meeting in Antwerpen, the ESDR Future Leader Academy, the Centre for Allergy Research Network and the Scandinavian Immunology Meetings in Sweden. In the first half of 2026, Mattia Dervasi begins his PhD, Joaquín Rodríguez Rayego will commence his PhD with Assistant Prof. Wenning Zheng and postdoctoral scientist Dr. Abigail Grootveld joins our team.

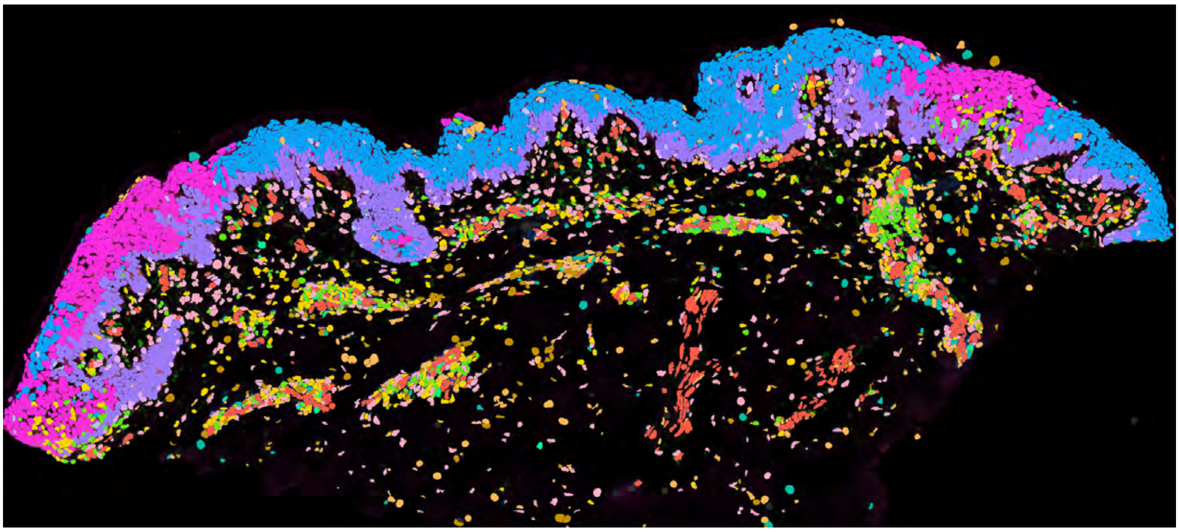
On the research front, the group is working hard to understand the tissue niches that T cells inhabit in inflamed skin, the genetic requirements of T cell antigen recognition and the impact of microbes on allergic barrier responses. In 2025, postdoctoral scientists Egon Urgard and Isabel Ulmert took the lead in establishing a functioning wildling mouse facility, which is now up and running. This has been a tremendous undertaking that stands to benefit SIC research groups and the greater University of Copenhagen environment. Work is underway to thoroughly characterise the skin, lung and intestines of these microbially enriched mice, which will help us to understand how microbes influence barrier immunity and our susceptibility to disease. This work is being conducted in collaboration with all SIC research groups.

Javiera Alvarez has uncovered interesting cellular niches in the sinuses of patients with sinonasal cancers. Javiera’s work is at the technological forefront, since by combining single cell RNA-Sequencing and Spatial-Sequencing technologies, she has been able to develop a pipeline that accurately tracks T cell clones in space. This has meant that we can precisely map the interaction between $CD8^+$ T cell and $CD4^+$ T cell clones in the sinus and confidently determine the cellular interactions that are made by these cells, which includes contacts with macrophages, dendritic cells and stromal cells. This pioneering work will be adapted to analysing T cell clones in many disease conditions. To that end, Assistant Prof. Wenning Zheng and Maja Søberg Udsen have been profiling T cells from matched skin and blood of patients with psoriasis and atopic dermatitis (AD), and in the setting of psoriatic arthritis, examining the relationship of T cell clones between the skin, blood and the arthritic joint.

Alma Lindell has analysed the immune composition of the skin of patients with AD and those effectively treated with biologics. She has pinpointed striking enhancements in cytokine-producing T cell populations in AD skin, which are now being mapped in space using the Xenium spatial transcriptomics platform. Taking on such a challenging project means that Alma has been supported by team members Egon Urgard and Jebunnahar Mishu, experts in immunohistochemistry and computational analysis respectively.

Lastly, Kilian Maire and Mattia Dervasi have uncovered striking patterns in T cell responses that are genetically encoded in response to allergens. Kilian and Mattia are working in both mouse and human systems to effectively characterise our genetic predisposition to allergens, which is likely to have important implications for patients that suffer from AD and asthma.

In 2025, our group co-published articles with the groups of Charlotte Menné Bonefeld and Niels Ødum and currently, a number of manuscripts are submitted for publication and under preparation. With the progress made over the last year, our team-first ethos and the support of our clinical and experimental collaborators within SIC and at BIOSKIN, the *Allergic Inflammation* group is poised for an exciting and productive 2026.



A section of skin from a patient with atopic dermatitis, imaged on the 10x Genomics Xenium platform.

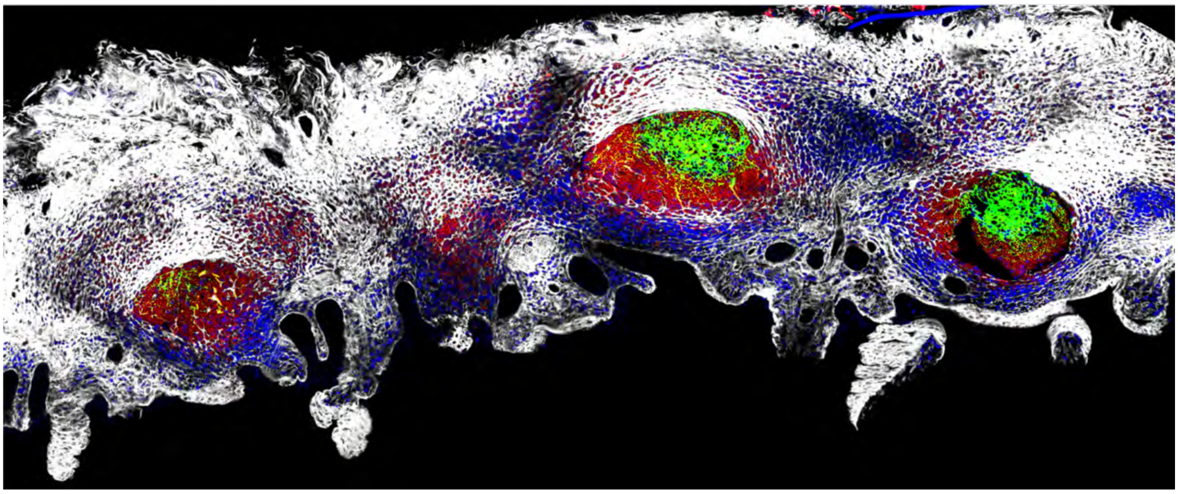
Barrier Immunology

The Barrier Immunology Research Group at SIC focuses on understanding immune responses at our barrier surfaces and how such responses are altered in disease and contribute to chronic inflammation. We are particularly interested in characterising and understanding (1) the function of the various immune niches within and along the length of the human intestine, (2) the complex dialogue between the environment, immune cells and tissue resident fibroblasts that help maintain intestinal homeostasis, (3) the alterations in this cross-talk that contribute to the initiation and maintenance of inflammatory bowel disease (IBD) including Crohn's disease and ulcerative colitis and (4) how immune responses in the intestine may influence diseases of other barrier surfaces such as the skin. The group is headed by William Agace.

Since joining in 2023, the team, which consists of 12 members, has become well embedded within SIC and plays an active role in contributing to the center's scientific and social activities. During the year, several more-or-less formal collaborations have been established with our SIC research colleagues, and we look forward to seeing the rewards of these activities and extending such collaborations in the years to come. The group has published two primary papers in the year; the first, led by Ass. Prof. Urs Mörbe (*J. Exp. Med,* 2025) describing fibroblast diversity and function in human gut associated lymphoid tissues; the second, co-led by PhD student Venla Väänänen (*Science Immunology,* 2025) assessing mononuclear phagocyte diversity within the human intestine and its alteration in Crohn's disease. PhD student Christian Ashworth also contributed towards a successful collaboration with the Bellodi group, BRIC, KU (*Cell Reports,* 2025). The laboratory was also represented at several conferences, including EMBO barrier immunology conference, Basel (Mörbe), European Mucosal Immunology Group (EMIG) meeting, Aachen (Agace, Kabbert), Immox conference, Oxford (Agace), the European Macrophage Dendritic Cell Society (EMDS) meeting, Edinburgh (Agace) and the Irish Society of Immunology Annual meeting, Galway (Agace).

Dr Johanna Kabbert, spent one month in the laboratory of Prof Oliver Pabst, Aachen University as part of an ongoing research collaboration, while Ass. Prof. Urs Mörbe visited the laboratory of Prof Mark Coles, Oxford University and Dr Andrew Brown the laboratory of Prof Oliver Pabst for technique exchange. Our long-term collaborator Prof Allan Mowat, Glasgow University, visited the laboratory 4 times during the year, including at our NNF challenge grant yearly retreat which took place in Blekinge, Sweden with over 20 researchers from 3 of the 4 participating groups. As well as providing valuable feedback to our ongoing projects Allan gave tutorials to interested SIC participants during each of these visits.

A big congratulations to Dr Fredrik Junghus, who successfully defended his PhD thesis within the group with Prof. K. Maloy, Glasgow as the external international examiner. Also congratulations to Dr Luiza Holst for obtaining a prestigious BRIDGE grant in collaboration with Prof. Jakob Seidelin (Herlev Hospital), for her project that will focus on dissecting the cellular and molecular mechanisms underlying mucosal healing and how this is impacted in patients with inflammatory bowel disease. We look forward to continued science and fun in 2026!



Peyer's patches are immune structures in the intestine containing large numbers of T cells (blue) and B cells (red) that are waiting to become activated. Inside these structures, specialized supporting fibroblasts help organize the immune cells. These include follicular dendritic cells (green), which guide the arrangement of B cells, while T-zone reticular cells (white) organize the T cells.

Immune Regulation

The Immune Regulation Research Group at SIC investigates the mechanisms that control immune responses in barrier tissues, including the skin, gut, and lungs. Our research focuses on how immune homeostasis is maintained and how immune dysregulation in inflammatory skin diseases is triggered. Additionally, we work on understanding how the microbiota and their metabolites shape immune function, and how adipose-derived mesenchymal cells exert immunomodulatory effects, with the long-term goal of informing new therapeutic approaches. The group is led by Professor Anders Woetmann and currently includes one Postdoc, one PhD student and two lab assistants.

In 2025, our group published two papers on the therapeutic potential of adipose-derived mesenchymal stem cells (AD-MSCs) for cutaneous inflammatory diseases and submitted additional two manuscripts.

AD-MSCs possess strong immunomodulatory and regenerative properties, but clinical translation is limited by suboptimal efficacy. Therefore, the first published paper systematically compared 2D and 3D culture formats and bioreactor systems to optimise AD-MSC expansion, revealing marked platform-dependent differences in gene and protein expression and underscoring the importance of culture conditions for preserving AD-MSC functionality. The second published paper examined continuous interferon-gamma (IFNγ) exposure across serial passages, showing that sustained IFNγ drives extensive transcriptomic remodelling, shifts metabolism towards oxidative phosphorylation, reduces proliferation and induces senescence-like features, while preserving immunosuppressive activity. These findings clarify how chronic inflammatory milieus constrain AD-MSC expansion while maintaining immunosuppressive competence, informing optimisation of AD-MSC-based therapies. Building on this work, the group is finalising a collaborative study with

Tapio Lönnberg's group (University of Turku, Finland) investigating how psoriasis-like cytokine milieus alter AD-MSC differentiation capacity, transcriptional profiles and T cell suppressive activity, and the resulting manuscript is currently in preparation for submission.

In the third manuscript, Lisa Harth has been exploring how influenza A virus infections unfold at the single-cell level in primary human alveolar macrophages. In close collaboration with Professor Rune Hartmann's group at Aarhus University, we used single-cell RNA sequencing to reveal striking heterogeneity in viral replication and antiviral responses, with only a small fraction of exposed cells producing interferon and others showing high viral loads but weak immune activation. The study also uncovers species-specific features of type III interferon signalling in human alveolar macrophages, underscoring the value of combining primary human models with experimental systems to understand antiviral, and interferon-driven immunity. The manuscript is currently being finalised for submission in early 2026.

In the fourth manuscript, PhD student Mariana Bronze, working in collaboration with Professor Jakob Sedelin (Herlev Hospital), has completed a study characterising innate lymphoid cell (ILC) populations in ulcerative colitis (UC), a chronic inflammatory bowel disease characterised by regionally restricted relapses. By analysing blood and colonic biopsies from UC patients in long-term remission, the study identified a selective enrichment and altered composition of mucosal ILC subsets – most notably ILC2s and ILC3s – in previously affected regions, while T and NK cell numbers remained unchanged. These findings support a model in which tissue-resident ILCs function as local "trigger cells" that shape the anatomical pattern and recurrence of UC inflammation, and a manuscript describing our findings has been submitted.

In 2025, PhD students Marina Ramírez Galera and Lisa Harth successfully defended their theses and were awarded their PhD degrees. Lisa's work, "Regulators of Interferons in Macrophages: Drivers and Inhibitors", provided in-depth insight into interferon control in macrophages, while Marina's thesis, "Immunosuppressive Role of Adipose-Derived Mesenchymal Stromal Cells for Skin Inflammatory Diseases", underscored the therapeutic potential of mesenchymal stromal cells in cutaneous inflammation.

We are excited to continue driving our research forward in 2026, deepening our national and international collaborations, and pursuing new treatment strategies for inflammatory and immune-mediated diseases.

Immunological Bioinformatics

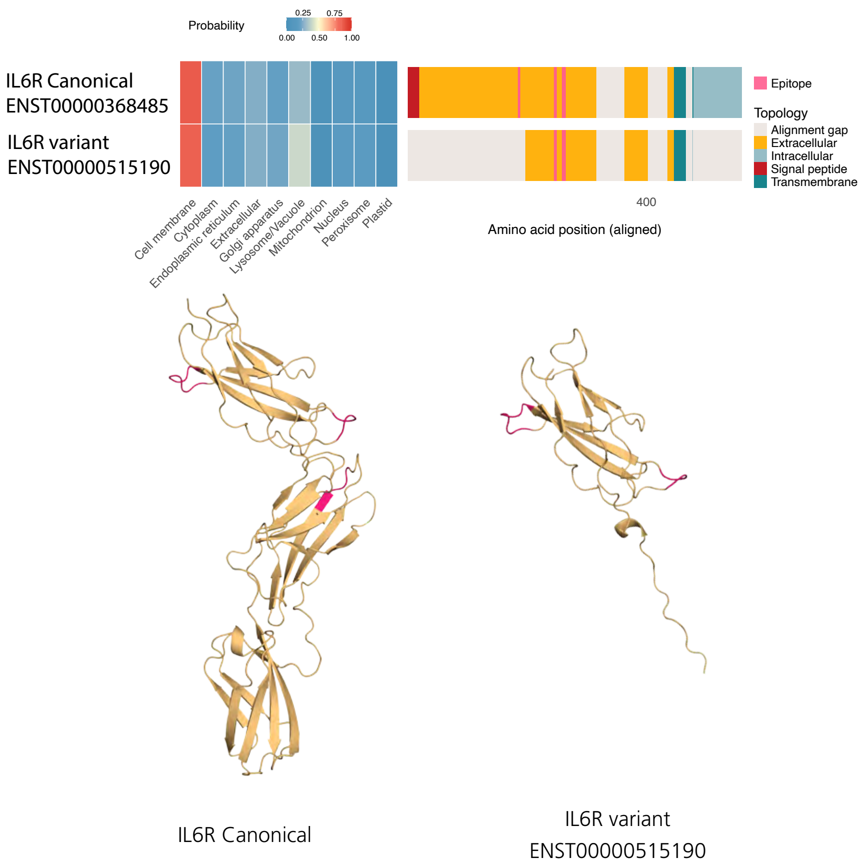
The Immunological Bioinformatics Research Group develops and applies computational methods to study immune regulation, disease mechanisms, and therapeutic response. The group combines close collaboration with experimental researchers at SIC with independent, hypothesis-driven research in computational immunology.

The group joined SIC in January 2025, relocating seven members and recruiting two new PhD students. Now consisting of three postdoctoral researchers and four PhD students, the group had a productive first year, supervising ten Master's level projects and securing an industrial PhD fellowship for 2026. Over the year, we established extensive collaborations with nearly all research groups at SIC, becoming fully integrated into the center's research environment.

Output-wise, 2025 began with the publication of two studies in *Nature and Science Immunology* resulting from collaborations predating the move to SIC. These works utilised single-cell transcriptomic analyses to characterise immune responses to cancer immunotherapies, exemplifying analytical approaches directly relevant to ongoing SIC research. Later in the year, we published two collaborative studies with the Barrier Immunology Group in *Science Immunology* and the *Journal of Experimental Medicine*, applying computational methods to investigate immune organisation in barrier tissues.

Our integration into SIC's experimental community has also driven the group's independent research. Working with primary human samples has led us to focus on modeling immune function as an emergent, context-dependent property shaped by cellular interactions and biological history. This motivates analytical efforts that go beyond simple cell-population cataloging, including transcript-resolved analyses and integrative modeling of immune states across tissues. To support the growing emphasis on spatially resolved immunology at SIC, we worked closely with the Skin Inflammation and Cancer, Allergic Inflammation, and Barrier Immunology groups on spatial transcriptomics data. This effort will be bolstered in 2026 with the onboarding of a dedicated spatial transcriptomics specialist. Education and capacity building were also central activities. We designed and co-taught a PhD-level course on bioinformatics algorithm benchmarking with experts from the University of Zürich and organised a center-wide seminar on AI in science. Additionally, Lars Rønn Olsen gave invited talks in Basel and at meetings of the Danish Society for Clinical Biochemistry and the Nordic Societies for Flow Cytometry. Notably, postdoc Giorgia Moranzoni received the Best Poster Award at the 2025 ELIXIR Bioinformatics Conference. Together, these activities establish a strong foundation for continued analytical support and methodological innovation across the center.

IL6R Isoforms



Tocilizumab is a humanized monoclonal antibody targeting the interleukin-6 receptor (IL6R), widely used to inhibit IL-6–mediated signaling in inflammatory diseases. To assess potential isoform-specific differences in antibody binding, we developed an analysis framework to annotate transcript variants for subcellular localization and membrane topology, and mapped the reported tocilizumab epitope onto the encoded protein sequences. Comparative structural modeling of the canonical isoform and ENST00000515190 revealed that while the epitope is fully exposed in the canonical receptor, it is partially truncated and structurally buried in ENST00000515190. These findings suggest that this isoform may reduce or abrogate tocilizumab binding, representing a potential mechanism of isoform-dependent escape from IL6R-targeted therapy.

Molecular Immunology and Inflammation

The Molecular Immunology and Inflammation Research 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.

A central focus of the group is to understand the molecular mechanisms that regulate signal transduction by immune receptors and how they impinge on immune responses and inflammation *in vivo*, with a particular focus on Met1-linked ubiquitin chains generated by LUBAC (Linear ubiquitin chain assembly complex). For this, we employ genetic engineering of cell culture systems and we have generated novel genetically-modified mouse models that are being extensively characterised in different experimental inflammation and infection models. Complementing our murine in vivo models, we are also implementing state-of-the-art 3D human epidermal skin models, which are being established through a Leo Foundation grant for SIC. Our long-term goal is to uncover novel molecular mechanisms underlying human inflammatory diseases of the skin and other barrier tissues.

2025 was characterised by transitions in the Molecular Immunology group; Three PhD students – Frederik Timmermann, Wenxin Lyu, and Malin Jessen – successfully defended their PhD theses describing new insights into the cellular mechanisms regulating LUBAC in inflammatory signalling and the role of these in in vivo models. Collectively, the studies reveal that LUBAC's function in immune receptor signalling is tightly regulated through interactions with other proteins via a conserved PUB domain in the subunit HOIP. Using mouse models, the studies reveal that these interactions have important implications for the systemic and skin-specific sensitivity to TNF-mediated toxicity. Manuscripts describing our findings have been submitted for publication.

Through an excellent collaboration with dermatologists in Denmark, including at

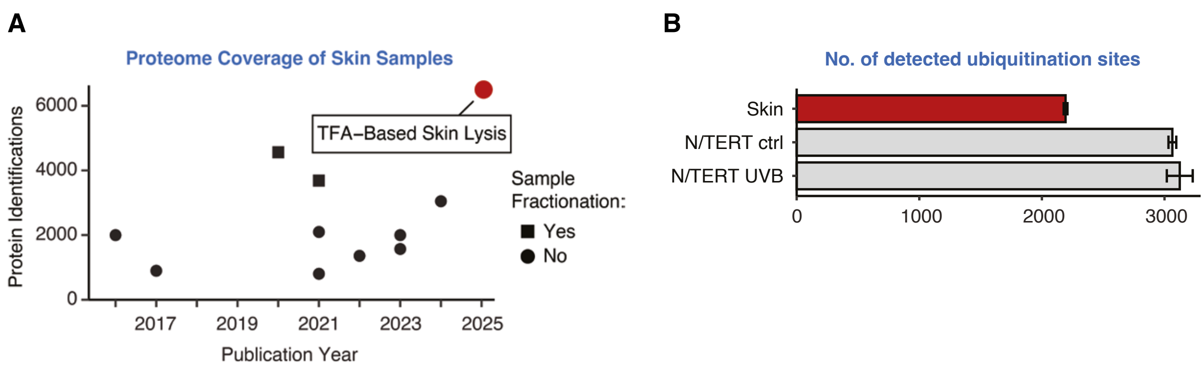
BIOSKIN, and Switzerland, we published a skin proteomics study entitled "Scalable Acid-Aided Lysis of Skin Samples Improves Proteome Coverage". Link: https://www.jidonline.org/article/S0022-202X(25)02410-8/abstract. In this study, led by postdoctoral fellow Max Sauerland, we describe a simple, fast, and scalable method for preparing skin samples for mass spectrometry-based proteomics analysis. The method achieves better proteome coverage than other reported methods and can be used both with punch biopsies and tape strips. Using this method, we also identified more than 2000 ubiquitination sites in human skin and human keratinocytes, showing that the method is compatible with analysis of posttranslational modifications for the study of dynamic signalling processes in the skin (Fig. 1). We believe the method will help promote the use of proteomic analyses in skin disease research. Based on his work, Max Sauerland was in 2025 awarded a 2-year LEO Foundation Visiting Researcher grant to continue his proteomics and machine learning research at the University Medical Center Freiburg, leveraging their expertise in clinical proteomics and strengthening ties between Denmark and Germany in translational skin research.

The group has been engaged in several education and research dissemination activities. I and other members of the group have presented our research at scientific meetings and research institutions in Denmark and internationally, including at the University of Freiburg, University of Zurich, Danish Immunology Society Annual Meeting 2025 in Aarhus, and the CAG – The Zealand Inflammation Research Initiative (ZIRI) Workshop in Roskilde. At the Scandinavian Society of Immunology (SSI) conference in Stockholm Assistant Professor John Rizk presented his work on LUBAC and was also presented with the SSI "Young Investigator of 2025" award.

Our education activities include running the MSc course "Chronic Inflammation and Autoimmunity - From Basic Research to Therapy" and the PhD course "Mechanisms in Innate Immune Signalling", along with lectures on several other courses run by the department.

Building on our recent findings, our focus in 2026 and beyond will be to further explore how altered sensitivity to TNF in the skin and at other barrier tissues affects local immune cell niches and inflammatory responses within the tissue.

Acid-based lysis improves proteome coverage of human skin



(A) comparison of proteome coverage by mass spectrometry in our study versus previous studies (B) Ubiquitin-modified sites identified in human skin biopsy and in N/TERT-1 human keratinocytes before and after UVB exposure.

Skin Inflammation and Cancer

The Skin Inflammation and Cancer Research Group at SIC investigates the mechanisms underlying chronic skin inflammation and the role of bacteria in disease progression and treatment resistance in cutaneous T-cell lymphoma (CTCL) and atopic dermatitis (AD). Although driven by malignant and non-malignant CD4$^+$ T cells, respectively, these diseases share numerous clinical and histopathological features, including susceptibility to disease exacerbation by *Staphylococcus aureus.*

Our current research primarily focuses on CTCL and AD as skin barrier diseases:

- How the interplay between pathogenic CD4$^+$ T cells and the lesional microenvironment impact skin barrier homeostasis
- The role of *S. aureus* in driving inflammation, skin barrier deterioration and treatment-resistance
- The identity and functional properties of pathogenic CD4$^+$ T cells

Key Findings in 2025

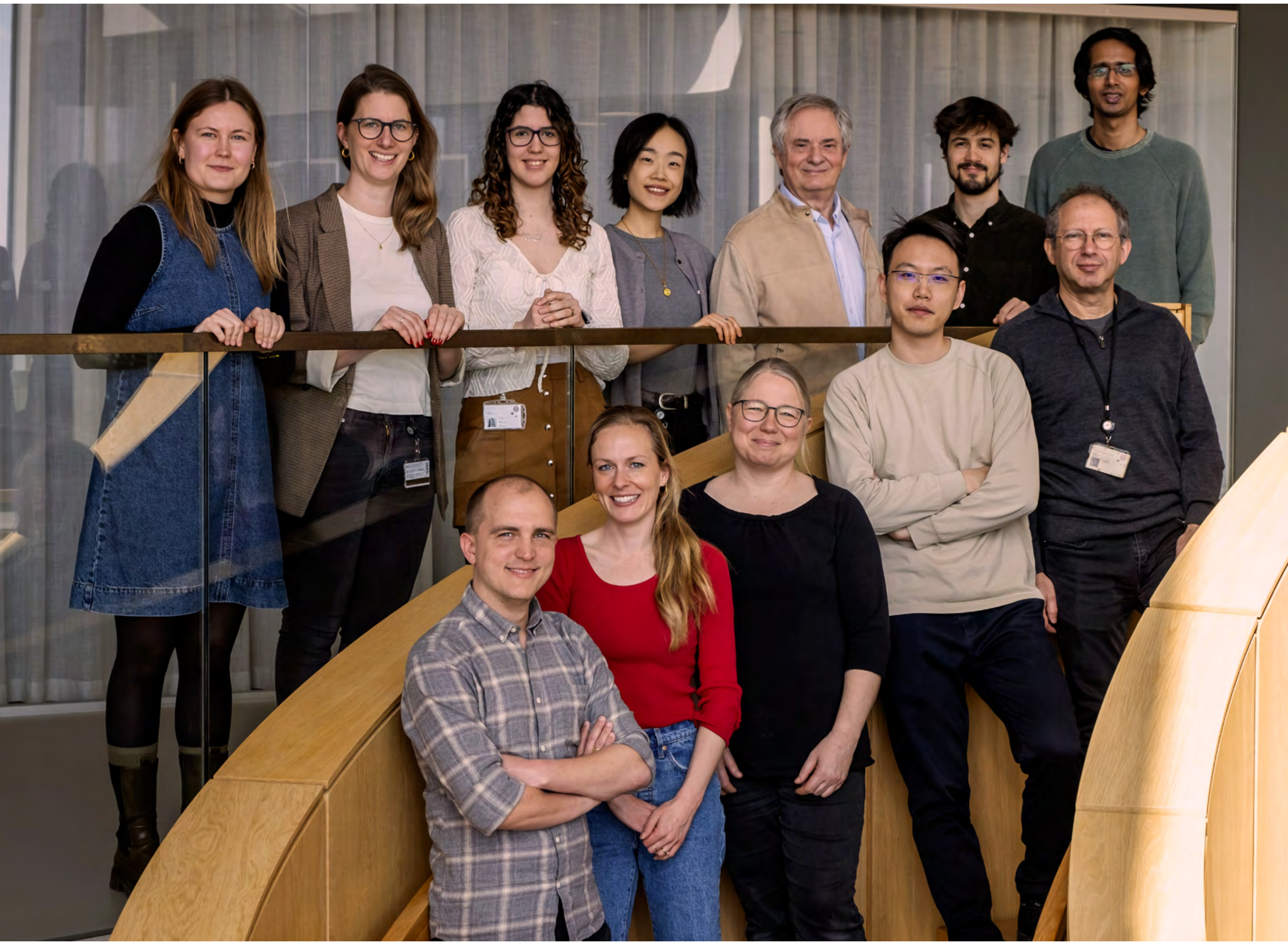
Building on our discovery (Blood 2023) that malignant T cells induce repression of filaggrins – key skin barrier proteins associated with a compromised skin barrier and increased susceptibility to *S. aureus*, we have now discovered a vicious circle whereby *S. aureus* through the secretion of enterotoxins activate T cells (including malignant T cells) to produce cytokines that in turn aggravate skin barrier deterioration. Of note, antibiotics and *S. aureus* targeting endolysins blocks the process. Importantly, this effect could be replicated in an animal model of microbial driven T cell lymphoma and in CTCL patients with severe disease and skin colonisation by enterotoxin-producing *S. aureus*. Thus, these patients displayed profound repression of skin barrier proteins like filaggrins and loricrin, both of which were partly normalised following bacterial eradication by aggressive antibiotic treatment (Gluud et al, Allergy, in press).

In parallel, we have discovered that pathogenic CD4$^+$ T cells operate at the edge of redox tolerance and propagate oxidative stress in cutaneous T-cell lymphoma. Interestingly, CTCL harbors a rare, targetable SOD2-high/PRDX2-low redox imbalance that renders malignant T cells vulnerable to ROS induction while simultaneously propagating oxidative stress to keratinocytes in the tumor microenvironment. Moreover, they impose keratinocyte stress visualised as upregulation of stress keratins and alarmins in the sorrounding keratinocytes which like plays a key role in the deregulated skin barrier homeostasis and progressive barrier deficiency. Again, bacteria aggravate skin barrier homeostasis by stimulation of malignant T cells to produce factors that enhance keratinocytic stress which is inhibited *in vivo* following antibiotic treatment of CTCL patients (Namini et al., submitted, Yan et al, in preparation).

Collectively, our findings emphasize a novel role of malignant T cells in synergy with *S. aureus* to disrupt the skin barrier homeostasis in CTCL. Furthermore, we have filed another patent on the use of endolysin-based therapies for *S. aureus* in skin diseases.

A Novel Perspective on Cancer Sub-clones and Treatment Resistance

Our most recent breakthrough concerns our discovery of multiple genetically distinct cancer subclones in most patients with cutaneous lymphomas. Importantly, cancer subclones within a single patient express identical T cell receptors (TCRs) yet exhibit distinct responses to external stimuli, including cancer-drugs and *S. aureus*. This suggests that tumor heterogeneity enables cancer cell populations to adapt and evolve within the tumour microenvironment. This also provide an explanation of how treatment resistance emerges, as certain



subclones may be preferentially selected under therapeutic pressure (Buus et al., Cancer Discovery, 2025).

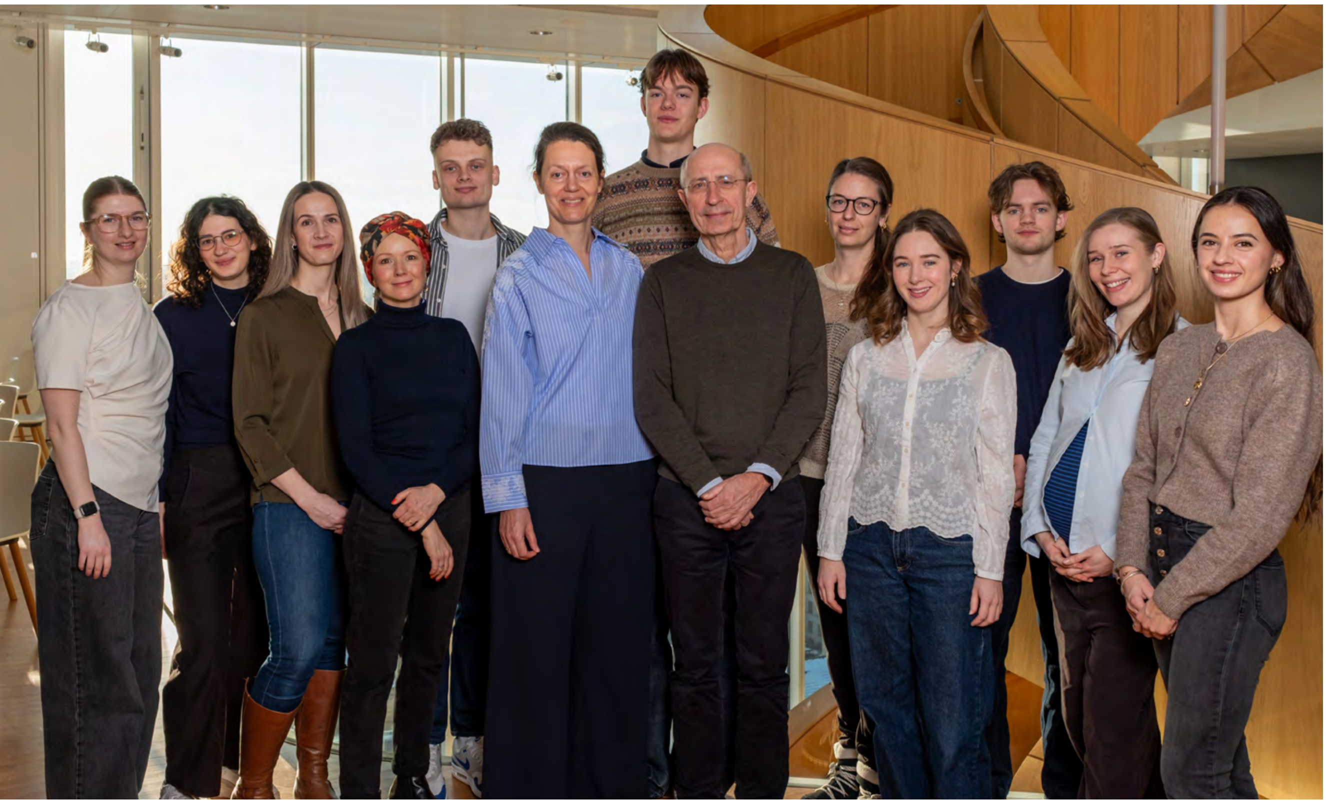
New Research Initiatives in 2025

In addition to our ongoing work, we have initiated several new lines of research, including:

- Development of a novel cancer cell-targeted treatment model
- Investigation of bacterial regulators of virulence factors and toxins (e.g., SEs), with the aim of identifying novel small-molecule inhibitors
- Implementing new technologies (such as Xenium spatial transcriptomics)
- Setting up collaboration with researchers in Moshi, Tanzania

T Cell Biology and Skin Inflammation

The T Cell Biology and Skin Inflammation Research Group, led by Professors Charlotte Menné Bonefeld and Carsten Geisler, investigates how T cells shape skin health and drive inflammatory skin diseases. Our aim is to understand the T cell biology of the epidermis, how T cells respond to everyday allergens like metals, preservatives and fragrances, and how factors like prior inflammation alter those responses, so patients can receive more precise prevention and treatment.



In 2025 our work centered on tissue-resident memory T (T_{RM}) cells, T cells that are generated in previously affected skin and react quickly when the same skin area is re-exposed to an allergen. Two complementary studies framed the year: a human study of nickel allergy (Yeung et al., 2026) and a mechanistic mouse study clarifying what keeps these memory cells in the skin (Funch et al., 2026).

Many people with nickel allergy encounter the metal repeatedly at the same skin sites (e.g., belts, buttons, jewelry). In our study, 12 adults allergic to nickel were patch-tested three times at the same site with 21 days between each test. The skin reactions became stronger with each exposure, highlighting how experienced skin is primed to flare. We found a steady build-up of T cells in the epidermis. Most of these were T_{RM} cells (marked by CD69), T cells that stay in the skin and respond rapidly. Both helper T cells ($CD4^+$) and killer T cells ($CD8^+$) expanded, but the balance between them differed from person to person. Some individuals showed a pattern dominated by Th2-like helper cells; others leaned toward Th17-like helpers or cytotoxic

CD8$^+$ T cells. We also saw regulatory T cells and T cells with an exhausted-like phenotype (Yeung et al., 2026).

The personalised mix of resident T cells we observed suggests that severe or persistent cases of contact allergy may benefit from tailored immunomodulation rather than one-size-fits-all treatment.

A key question is why T_{RM} cells persist in the epidermis. Using mouse models and a reporter of T cell receptor (TCR) signaling (Nur77), we showed that long-term persistence of CD8$^+$ epidermal T_{RM} cells requires ongoing recognition of cognate antigen in the skin. Inflammation alone can induce the formation of T_{RM} cells in the skin, but to keep them there month after month, the specific allergen must still be present locally. We tracked this in several ways. After exposure to an experimental allergen (DNFB), DNFB-modified protein adducts were detectable in the epidermis for up to a year, and a fraction of the CD8$^+$ T_{RM} cells continued to show Nur77 signaling over the same period, strongly supporting that ongoing antigen engagement took place. TCR sequencing revealed expansion of T cell clones over time, consistent with local stimulation shaping the resident population. We then compared clinically relevant allergens. All three, cinnamaldehyde, para-phenyelenediamine (PPD) (a hair-dye component), and methylisothiazolinone (MI), could generate CD8$^+$ T_{RM} cells at 30 days. But by 180 days, only MI maintained Nur77$^+$ CD8$^+$ T_{RM} cells, suggesting that MI, like DNFB, leaves longer-lived antigen footprints in the skin, whereas cinnamaldehyde and PPD do not. Finally, adoptive-transfer "prime-and-pull" experiments showed the split between generation and persistence. Induced skin inflammation without allergen could recruit and form CD8$^+$ T_{RM} cells that were Nur77$^-$ and short-lived. However, adding a tiny dose of DNFB restored Nur77 signaling and kept those cells around for months (Funch et al., 2026).

Our human nickel study shows how repeated exposure sculpts a complex, individual-specific immune ecosystem in the epidermis. Our mechanistic work explains how and why T_{RM} cells persist, namely because specific allergen signals linger and keep those cells fit and engaged.

To further study the cellular interactions between immune cells and skin resident cells during and after skin inflammation, we have initiated a collaboration with Professor Kenji Kabashima, Kyoto University, Faculty of Medicine, Japan.

In 2025, William Steiner Olsen graduated as Master in Immunology and Inflammation from our group. Alexandra Teresa Seibel started as PhD student in our group. Furthermore, we had the great pleasure of having Janeth Mwasse from Regional Dermatology Training Centre (RDTC), Kilimanjaro Christian Medical Centre (KCMC), Moshi, Tanzania and Jacob Sons from University of KwaZulu-Natal, South Africa as guest researchers in our group.

BIOSKIN

The Copenhagen Translational Skin Immunology Biobank and Research Program (BIOSKIN) is a prospective cohort study of patients with inflammatory skin diseases, initiated in 2022. The overall aim of BIOSKIN is to improve understanding of disease phenotypes to support precision diagnostics, risk prediction, and targeted treatment strategies. This is achieved by integrating clinical practice at the Department of Dermatology and Allergy, Herlev and Gentofte Hospital, with fundamental research at the LEO Foundation Skin Immunology Research Center (SIC).

Clinical data and biological samples are systematically collected from patients with inflammatory skin diseases, including psoriasis, atopic dermatitis, and contact allergy. BIOSKIN is among the first large-scale longitudinal biobanks worldwide dedicated to inflammatory skin diseases. To date, 1,525 patients have been included, accounting for nearly 6,000 patient visits.

Research Outcomes and Communication in 2025

In 2025, BIOSKIN generated important new insights into inflammatory skin diseases. Within psoriasis research, a clinical study demonstrated that fatty liver disease is associated with increased cardiovascular risk, primarily driven by obesity and diabetes, highlighting the importance of managing metabolic risk factors in this patient group. A large questionnaire study showed that patients with psoriasis generally follow official dietary recommendations and do not differ significantly from healthy individuals.

A comprehensive review addressed key clinical considerations in the management of women of childbearing potential with psoriasis and concluded that most patients can be safely treated during pregnancy using topical therapies or UVB phototherapy, while selected systemic treatments may be considered when necessary.

Inspired by the promising use of blood biomarkers to predict disease severity and treatment response in psoriatic arthritis, analyses from the BIOSKIN cohort showed that biomarkers of extracellular matrix fragments are not currently suitable for diagnosing or monitoring psoriasis.

In atopic dermatitis, a population-based study demonstrated an increased risk of both hand eczema and contact allergy, as well as more severe disease. These findings highlight the need for earlier intervention and more targeted treatment strategies for patients with concurrent conditions. Furthermore, a randomised controlled study examining skin microbiome and lipid composition identified differences between atopic dermatitis and healthy skin. Moisturiser use showed a trend toward a healthier lipid profile, while the microbiome remained stable despite treatment with moisturisers and antimicrobial fragrance, indicating that longer or more targeted interventions may be required.

In addition, BIOSKIN published a review and metaanalysis on the prevalence of vitiligo, a review on the association between piercings and nickel allergy, explored sex differences in quality of life in psoriasis, and reported a case series on treatment-resistant psoriasis. The project also contributed to the development of advanced methods for skin protein analysis and identified alterations in salivary microbiota in patients with psoriasis.

BIOSKIN maintained strong international visibility in 2025 through presentations at major international conferences, including the Skin Inflammation & Psoriasis International Network (SPIN) Meeting Paris 2025, the European Society for Dermatological Research (ESDR) Meeting Antwerp 2025 and the European

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.

Academy of Dermatology and Venereology (EADV) Meeting Paris, where the project's structure, methodological advances, and clinical findings were shared with the global research community.

In 2025, a new website (www.bioskin.dk) was launched, providing updates on study progress, news, and research findings.

Future Directions

BIOSKIN will continue to expand the biobank with a primary focus on the three most prevalent chronic inflammatory skin diseases – psoriasis, atopic dermatitis, and contact dermatitis – while also including conditions such as hidradenitis suppurativa, alopecia areata, and vitiligo. Multiple studies are ongoing, and new projects are continuously being initiated.

Education and Career Development

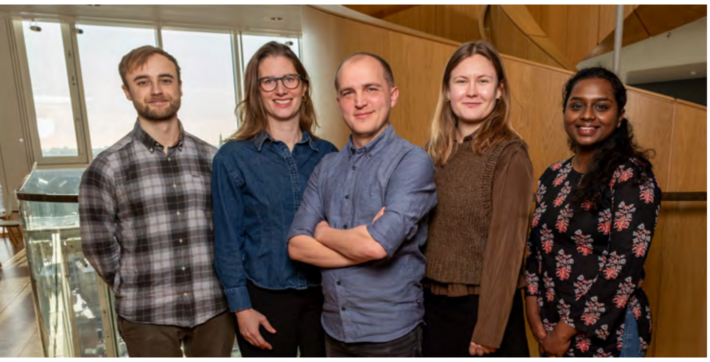
Education and career development are core to SIC's mission to improve the understanding, prevention, and treatment of skin diseases, and to its vision of educating the next generation of research leaders in barrier tissue immunology. A strong educational foundation is essential to this effort, and SIC researchers contribute extensively to teaching across undergraduate, graduate, and postgraduate levels, as well as through specialised courses and training activities.

In 2025, SIC continued to strengthen its training environment across career stages through targeted initiatives and scientific exchange. Activities included PhD courses, symposiums, the SIC Summer School, platforms for PhD and postdoctoral researchers to present their projects as well as support for early-career researchers and clinicians through initiatives such as the Young Investigator Network.

The following section outlines selected education and career development activities carried out in 2025.


Nimolab Service

Decoding how Staphylococcal toxins worsen Atopic Dermatitis



Atopic dermatitis (AD) is a common inflammatory skin disease, often beginning in childhood. For many patients, the disease comes in waves: the skin can be relatively calm for a period and then suddenly flare with intense itch, redness, and oozing lesions. One striking clinical pattern is that flares frequently coincide with an overgrowth of the bacterium *Staphylococcus aureus* (*S. aureus*) on the skin. This is not just a passive passenger. Staphylococci can release toxins that amplify inflammation and destabilise the already fragile skin barrier.

With support from a LEO Foundation Dr. Abildgaard Fellowship awarded in 2023, Assistant Professor Terkild B. Buus established his research team in summer 2024 at SIC including postdoctoral Lab Manager, Edda P. Blümel, PhD Student, Emma E. Uttrup, MSc student Gowri P. Sajeev as well as Research Assistant William Hagedorn-Rasmussen and Postdoc Daniel Vera starting in April and May 2026, respectively. The team's mission is to understand how bacterial toxins interact with the immune system in AD, and to use that knowledge to guide new, more precise treatment strategies.

When bacteria hijack our immune system: the superantigen concept

The immune system usually responds to threats with high specificity: a T cell is activated when its receptor recognises a particular threat (antigen), presented by other cells. *S. aureus* can short-circuit this path. Some *S. aureus* strains produce superantigens – toxins that can forcefully connect immune cells and T cells in a way that triggers broad, rapid activation of many T cells at once irrespective of the antigens they would normally respond to.

This matters because a wide, non-specific activation can generate large amounts of inflammatory signalling molecules that drive immune dysregulation, damage the skin barrier and amplify itch. Evidence across the field suggests *S. aureus* toxins can shape inflammation in AD lesions, but it has been difficult to directly identify the role of superantigens and determine which T cells are responding to these toxins inside patient skin.

> *"If we can spot the toxin-responsive T cells in the tissue – and see who they talk to – we can separate the drivers of inflammation from the bystanders."*

Identifying toxin-responsive T cells in patient skin samples

In the skin of patients with AD, the inflammatory environment can leave many T cells in a generally activated state – regardless of whether they are driving disease or are simply bystanders. To identify and distinguish the T cells that truly engage *S. aureus* superantigens (and may therefore contribute directly to pathology), Buus' team has developed new superantigen "probe" reagents that can directly tag toxin-responsive T cells at single-cell resolution.

A central challenge in AD research is that the most informative patient material is also the scarcest: typically small skin biopsies. Classical approaches often average signals across thousands or millions of cells, which can obscure rare but important pathogenic populations and blur the distinction between drivers and bystanders. Buus' team therefore uses modern single-cell technologies to generate detailed maps of individual immune cells. For each T cell, these methods capture its unique T cell receptor sequence (its molecular fingerprint), the genes it has turned on, and the proteins it displays on its surface – together with readouts that report whether the cell can respond to *S. aureus* superantigens.

Equally important is where these cells are located. In a skin lesion, immune cells are organised into neighbourhoods: some sit close to the epidermis, others cluster around hair follicles or blood vessels, and many interact directly with keratinocytes and antigen-presenting cells. By combining single-cell profiling with spatial methods, the team can map toxin-responsive T cells in their native tissue context and pinpoint the cell–cell interactions most likely to fuel flares.

From mechanism to treatment: the role of superantigens and moving beyond antibiotics

It is widely accepted that *S. aureus* contributes to disease activity and flares in AD. What remains much less clear is which bacterial factors matter most *in vivo*, and in particular whether superantigens are key amplifiers of skin inflammation in relevant AD settings. Buus' team is therefore establishing pre-clinical models in which superantigen exposure can be controlled. By working with defined *S. aureus* strains (including strains that differ in toxin production) and by applying purified superantigens in experimental mouse systems and human skin models, the team can test focused mechanistic questions: Do superantigens expand and activate specific toxin-responsive T cell populations in skin? Do they amplify hallmark AD inflammatory circuits beyond what is seen with colonisation alone? And which antigen-presenting cells and tissue compartments are required for these effects?

These models are also designed as a treatment-testing platform. Because long-term antibiotic strategies are not an attractive solution – given resistance concerns and potential disruption of the broader microbiome – the team is evaluating alternative approaches that target *S. aureus* and its toxins. By reading out toxin-responsive T cells, local cytokine programmes, and spatial cell-cell interactions, the team can quantify whether candidate interventions specifically dampen superantigen-driven immune activation and thereby reduce the inflammatory "boost" that potentially worsens AD lesions.

Finding the right patients: 'TCR fingerprints' and precision stratification

AD is heterogeneous – patients differ in triggers, immune pathways, and response to therapy. A key translational question is therefore not only whether toxin-directed strategies can work, but also who they are most likely to help. Buus' team is developing a framework to detect patterns in T cell receptor repertoires that indicate toxin responsiveness. These TCR 'fingerprints' can be combined with clinical features and other molecular readouts to define patient subtypes (endotypes) that are more strongly influenced by Staphylococcus toxins. To scale this approach across cohorts and data types, the team leverages advanced computational analysis and machine learning methods tailored to immune-repertoire data. The long-term ambition is to provide practical biomarker logic for future clinical trials: select patients based on measurable immune signatures, test toxin-neutralising strategies in those most likely to benefit, and thereby increase the chance of meaningful clinical impact.

Outlook

In the coming period, the team will refine its ability to identify toxin-responsive T cells in patient skin, map their spatial 'interaction networks', and set up pre-clinical models to determine the role of *S. aureus* superantigens in AD. In parallel, the repertoire-fingerprinting pipeline will be expanded to support larger cohorts and enable robust patient stratification. By integrating skin immunology, bacterial pathogenesis, and computational biology, the Buus team aims to turn a common clinical observation – Staphylococcus-linked flares – into a mechanistic understanding and a translational route toward more precise, durable control of AD.

Each year SIC welcomes early-career researchers from around the world to its annual Summer School. The 2025 edition, held in the quaint seaside town of Hornbæk on the scenic northern coast of Zealand, focused on *"The innate immune system in barrier health"*.

Supported by an add-on grant from the LEO Foundation, the conference offers an inspiring scientific programme and an intimate setting for exchange and collaboration. Now an established event in the skin immunology calendar, the Summer School is increasingly recognised as a leading conference for young researchers, attracting a high number of applications and drawing scientific talent from across Europe, North America, Asia, and Australia.
The programme featured a wide range of talks delivered by 12 invited speakers, and themes included neuro-immune interactions, antigen sensing in the skin, barrier cross-talk, and T cells in barrier tissue. The programme also included short talks by early-career researchers and poster sessions, encouraging knowledge sharing and dialogue across career stages.

The unique coastal setting created an ideal backdrop for scientific discussion, informal networking, and new collaborations. Time spent together over shared meals, walks, and social activities contributed to a vibrant and collegial atmosphere that extended beyond the formal sessions.

Summer School continues to be a cornerstone of SIC's commitment to supporting the next generation of researchers and advancing our

understanding of skin immunology and barrier-related disease mechanisms.

Organisers
Scientific committee: Anders Woetmann, William Agace, Charlotte Menné Bonefeld and Jonathan Coquet.

Coordinator and administration: Hannah Paludan.

The next Summer School will take place from 18th – 20th of May 2026. We are pleased to announce that the 2027 Summer School will be held from 24th – 26th of May 2027.

SPEAKERS AND TITLES OF TALKS AT SUMMER SCHOOL 2025

- Ben Marsland, Monash University, Australia: *Exploring host-microbe and their impact on barrier tissue integrity*
- Caroline Sokol, Harvard Medical School, USA: *Scratching the Surface: Neuroimmune control of allergic immunity*
- Claire Higgins, King's College London, UK: *Skin derived neuropeptides and their impact on skin health*
- Fabio Luciani, University of New South Wales, Australia: *Immunogenomics analysis to unravel pathogenic rogue T cell clones*
- Franca Ronchese, Malaghan Institute, New Zealand: *Induction of allergic immune responses by skin dendritic cells*
- Itziar Martinez Gonzalez, Karolinska Institutet, Sweden: *Cross-Tissue immunity mediated by memory ILC2s*
- Jesper Elberling, Herlev and Gentofte Hospital and UCPH, Denmark: *Skin Immunology: What's sensory got to do with it?*
- Lilian Basso, INSERM, France: *Distinct nociceptor roles in inflammation and itch revealed by subset-specific transcriptomic adaptation*
- Melanie Conrad, Charité Medical University, Germany: *Antibiotic use during pregnancy: the influence of maternal gut microbial dysbiosis on offspring barrier function and immune system development*
- Paola Di Meglio, King's College London, UK: *The Aryl Hydrocarbon Receptor (AHR): Peacekeeper of the skin*
- Terkild Brink Buus, University of Copenhagen, Denmark: *Malignant Persistence in Cutaneous T-cell Lymphoma: Divergent Evolution and Bacterial Interactions*
- Vasileios Bekiaris, Technical University of Denmark, Denmark: *Neonatal development and homeostasis of IL-17- producing gd T cells in the gut*

In 2025, the Young Investigator Network (YIN) hosted three events that were designed around the needs voiced by early career colleagues: wellbeing and sustainability, access to funding knowledge, and visibility of diverse career pathways.

Wellbeing and sustainable performance

A visit to the Stress Reduction Clinic at Bispebjerg Hospital addressed maintaining performance and motivation under sustained pressure. Attendees gained practical strategies for stress recognition and management, anchored in a clinical and evidence-based setting. Importantly, the format created space for participants to reflect on work habits and expectations, and to exchange experiences with peers. For many, the value lay not only in learning techniques, but in reframing wellbeing as a professional competence rather than a personal afterthought. Participants left with tools they could apply immediately – both individually and within their work groups – and with a strengthened sense that sustainable careers are built intentionally.

Funding insight and strategic planning

The second event addressed funding opportunities, an area where early career researchers often feel they are learning "too late" or without a roadmap. This session offered structured insight into the funding landscape relevant to early-stage researchers. Coupled to

About YIN

YIN, established in 2019 and hosted by SIC, supports PhD students, postdocs, and early career clinicians and scientists working at the interface of immunology and dermatology. Participants are primarily affiliated with SIC, the LEO Foundation Center for Cutaneous Drug Delivery (LFCCDD), and regional hospital departments.

YIN provides a structured platform for connection, collaboration, and career development. It complements formal academic training by addressing competencies often acquired informally: resilience, strategic positioning, funding navigation, and long-term career planning. Through recurring, low-threshold meetings, the network strengthens professional ties, facilitates knowledge exchange, and reduces isolation in a highly specialised research landscape.

knowledge on the operations of a foundation, attendees benefited from clarity: how to identify appropriate calls, how to interpret eligibility and expectations, and how to align proposals with realistic timelines and career stages. Just as importantly, participants gained language and confidence to discuss funding goals with supervisors and mentors, turning abstract ambitions into actionable plans.

Career pathways beyond academia

The third event explored career opportunities beyond academia, responding to a growing need for transparent discussion of career diversity. Early career researchers often encounter a narrow narrative of success, even though many valuable roles exist across industry, clinical development, regulatory work, health technology, science communication, and the public sector. By explicitly engaging with non-academic trajectories, YIN gave attendees permission to explore options without stigma. Participants gained an expanded understanding of how their skills translate beyond academic roles – critical thinking, data interpretation, project management, and domain expertise in dermatology – and what additional competencies may be useful to develop. For some, the session provided reassurance and direction; for others, it sharpened their commitment to academia by clarifying alternatives and values. In both cases, the outcome was increased agency in career decision-making.

The 2025 programme illustrates what YIN does best: it meets early career colleagues where they are, with activities that are both relevant and immediately useful. Attendees do not simply receive information; they gain perspective, confidence, and a community that lowers barriers to collaboration and growth. YIN's impact is therefore twofold. At an individual level, participants leave better equipped to manage wellbeing, pursue funding strategically, and plan careers proactively. At a community level, the network strengthens connections across SIC, LEO Foundation Center for Cutaneous Drug Delivery (LFCCDD), and hospital departments – supporting a more integrated dermatology research environment in Greater Copenhagen.

By continuing to focus on what early career researchers need most – peer connection, practical insight, and honest career conversation – YIN remains a valuable investment in both people and scientific progress.

YIN is 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 to us at sic@sund.ku.dk.

Planning committee, 2025
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Berthe Katrine Fiil, SIC
Christian Thomas Ashworth, SIC
Erik van Tilburg Bernardes, SIC
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BENCHMARKING OF BIOINFORMATICS TOOLS 2025

In November–December 2025, Lars Rønn Olsen ran the first edition of the PhD course *Benchmarking of Bioinformatics Tools* at the Department of Immunology and Microbiology, University of Copenhagen. The course combined two intensive lecture days with three weeks of structured asynchronous group work, concluding with final presentations and manuscript submission.

The course was designed to address a growing need within computational biology: the rigorous, transparent, and reproducible evaluation of bioinformatics methods. As new tools continue to emerge at high pace, the ability to benchmark algorithmic performance in a principled and statistically sound manner has become essential for both developers and applied researchers.

21 bioinformatics PhD students from 4 different universities, hospitals and companies participated. Participants ranged from method developers to applied researchers seeking to critically evaluate tools relevant to their own projects.

Conceptual foundations and hands-on frameworks

The course began with foundational lectures covering the principles of benchmarking, evaluation metrics and task-specific performance assessment, sources of bias and common pitfalls in benchmarking studies, and last, but not least extendability and reproducibility.
For the latter part, participants were introduced to the OmniBenchmark community benchmarking framework, developed by the team of Professor Mark Robinson from University of Zürich. Professor Robinson joined the course for two days along with two of the key developers, giving lectures and guiding the participants.

Project-based learning and scientific output

Following the introductory module, students worked in groups for three weeks to design and execute a small-scale benchmarking study. Projects were either aligned with the participants' own research questions or based on curated case studies. The course concluded with group presentations and structured peer feedback. Three of the five groups produced manuscripts that have been submitted for peer review, demonstrating that the course format not only strengthened methodological competence but also generated tangible research outputs with publication potential.

Collaboration and expertise

The course was co-taught with Frederik Otzen Bagger (Center for Genomic Medicine, Rigshospitalet), Mark Robinson, Izaskun Mallona Gonzales, and Benjamin Carillo Chica (University of Zürich). Their expertise in statistical genomics, reproducible workflows, and methodological evaluation provided an international and cross-institutional perspective on benchmarking practices.

GRADUATED PHD, MASTER, AND BACHELOR STUDENTS

PhD students

- Bjørn Kroman Hansen. *Proteomics and Immunopeptidomics in Psoriasis*. Supervised by Beatrice Dyring-Andersen, Lone Skov and Marianne Bengtson Løvendorf.
- Christoffer Kursawe Larsen. *Contact allergy to rubber accelerators: Clinical, Epidemiological, and Experimental Studies*. Supervised by Jeanne Duus Johansen and Jakob Schwensen.
- Christopher Schwarz. *Effect and Safety of New Biologic Treatments for Psoriasis*. Supervised by Lone Skov.
- Fredrik Junghus. *The transcriptomic and clonal diversity of $CD4^+$ T Cells in Crohn's disease.* Supervised by William Agace.
- Frederik Timmermann. *The LUBAC PUB domain as a protein-interaction interface regulating Met1-linked ubiquitin and inflammation.* Supervised by Mads Gyrd-Hansen.
- Kristina Munke. *Host-pathogen interactions in mycobacterial infection*. Supervised by William Agace.
- Leon Cyranka. *Targeting complement pathways and the C5a receptor to modulate inflammatory responses: exploring complement interaction with Escherichia coli and Aspergillus fumigatus*. Supervised by Lone Skov.
- Lisa Harth. *Regulators of interferons in macrophages: drivers and inhibitors.* Supervised by Anders Woetmann.
- Malin Jessen. *SPATA2 and CYLD: shaping inflammation, cell death, and immune homeostasis*. Supervised by Mads Gyrd-Hansen.
- Marina Ramírez Galera. *Immunosuppressive role of adipose-derived mesenchymal stromal cells for skin inflammatory diseases.* Supervised by Anders Woetmann.
- Søren Helweg Dam. *Algorithms for integrative analysis of genes, transcripts, and proteins in cellular systems.* Supervised by Lars Rønn Olsen.
- Wenxin Lyu. *Inflammation as a Double-Edged Sword: Physiological Role of the LUBAC-OTULIN Complex in Immune Regulation*. Supervised by Mads Gyrd-Hansen.

Master students

- Benedikte von Spreckelsen. *Nickel allergy and piercings, a systematic review and meta-analysis.* Supervised by Jeanne Duus Johansen and Malin Ahlström.
- Faidra Papalamprou. *Dendritic Cells in the Intestinal Immune Landscape: Diversity, Development and Roles in Inflammation.* Supervised by Andrew Brown and William Agace.
- Lara Perucho Sorrosal. *Effect of Honokiol DCA in Cutaneous T cell lymphoma*. Supervised by Niels Ødum.
- Olivia Jensen. *The Cellular Landscape of Tertiary Lymphoid Organs in Crohn's Disease.* Supervised by Urs Mörbe and William Agace.
- Martin Murmann Voldby. *Investigating SIGLEC15 as a potential target for peptide cancer vaccination*. Supervised by Aimilia Schina.
- Patrick Hilt Bartholin. *Investigating the Role of SPATA2, RIPK2, and IRAK1 in Listeria monocytogenes Infection.* Supervised by Berthe Katrine Fiil.
- William Steiner Olsen. *Interactions Between Allergen-Specific Epidermal T_{RM} Cells during Sensitization to Secondary Contact Allergens*. Supervised by Charlotte Menné Bonefeld.

Bachelor students

- Lou Vandour-Marty. *Method optimization for identification of LL37 specific T Cell clones in Peripheral Blood Mononuclear Cells of healthy controls and psoriatic patients. (Hosted intern from Université de Bordeaux, France)*. Supervised by Wenning Zheng.

PHD COURSE
MECHANISMS IN INNATE IMMUNE SIGNALING 2025

In January 2025, Berthe Katrine Fiil and Mads Gyrd-Hansen organised and taught the annual PhD course Mechanisms in Innate Immune Signaling. The course spanned four intensive days and combined lectures with interactive group work. Its overall objective was to provide participants with a solid understanding of innate immune signaling, covering processes from microbial recognition to downstream signaling outcomes, including effective pathogen elimination as well as maladaptive responses such as chronic inflammation.

Participants and Scientific Programme
The course welcomed nine PhD students with diverse academic backgrounds, ranging from medical doctors enrolled in PhD programmes to immunologists, microbiologists, and bioinformaticians. While some participants already had substantial experience in innate immunity, others entered the course with limited prior exposure but a strong motivation to learn. To establish a common foundation, the programme included a series of introductory background lectures before progressing to more specialised topics.

A number of invited lecturers contributed to the course, including Troels Scheel (ISIM), Bjørn Kromann Hansen (Center for Protein Research and Herlev-Gentofte Hospital), Anne Rosbjerg (Region H), Mariena van der Plas (LEO Foundation Center for Cutaneous Drug Delivery), and William Agace (SIC). Each speaker introduced background material pertinent to the course aim and brought perspectives from their own research areas, enriching the scientific breadth and depth of the course.
An integral component of the programme was a journal club, where students presented and discussed pre-selected research papers. This format encouraged in-depth engagement with the literature, critical thinking, and active scientific discussion among participants.

Industry Perspectives and Invited Seminars
To further broaden perspectives, the course also included an industry session. Nick Stub Laursen, co-founder of Commit Biologics, shared his career path and the scientific ideas underpinning the startup, offering valuable insight into how academic research can translate into industry applications.

In addition, two open seminars were held as part of the course. Frederick Sheedy (Trinity College Dublin) presented Train to Win: *Immunometabolic changes in β-glucan-induced trained immunity*, and Professor Rune Hartmann (Aarhus University) lectured on *Recognition of viral infection by innate immunity and initiation of antiviral immunity*. Both seminars attracted a large audience. Following the lectures, the speakers met with the course participants in smaller meet-the-speaker sessions, allowing for detailed scientific discussion and career guidance.

Overall, the PhD course *Mechanisms in Innate Immune Signaling* covered a broad range of topics related to innate immune pathways and host–microbe interactions. Student feedback was very positive, highlighting the course's success in delivering relevant, high-quality, and comprehensive training

SIC-VIB SYMPOSIUM
UNDERSTANDING THE MOLECULAR MECHANISMS OF INFLAMMATION

This year, SIC hosted researchers from the Center for Inflammation Research (IRC), a branch of the Flemish Institute of Biotechnology (VIB). The VIB is the premier research initiative of Belgium, and researchers at IRC are focused on understanding the molecular mechanisms of inflammation in innate and adaptive immune cells of the skin, lung and gut.

We were treated to cutting-edge talks from IRC director Bart Lambrecht on adaptations of lung macrophages, from Lars Vereecke on genotoxic gut bacteria and from Esther Hoste on the skin epithelial repair response. Complementary talks from William Agace on intestinal phagocytes in intestinal bowel disease, Charlotte Menné Bonefeld on skin tissue-resident memory T cells and Mads Gyrd-Hansen on genetic regulation of TNF-driven inflammation rounded out a highly rewarding day of science.

The day highlighted the incredible cellular and molecular diversity of our barrier organs, how inflammation drives cellular adaptations and how immune cells can contribute both to maintaining barrier health and causing barrier destruction.

The highly complementary scientific visions of our two centres provided for stimulating scientific discussions and highlighted obvious points for collaborations and student exchange in the future. We look forward to following the IRC's progress in the coming years and maintaining our partnership through shared ideas.

The Scientific Programme:

Bart Lambrecht, IRC, VIB. *Transcriptional regulation of mononuclear phagocyte function.*

Charlotte Menné Bonefeld, SIC. *The role of T cells in allergic contact dermatitis.*

Esther Hoste, IRC, VIB. *The role of linear deubiquitination in skin biology.*

Lars Vereecke, IRC, VIB. *How sticky bacteria drive colon cancer.*

Mads Gyrd-Hansen, SIC. *Molecular determinants of TNF-driven pathology.*

William Agace, SIC. *Intestinal cDC heterogeneity in health and Crohn's disease.*

Organiser: Jonathan Coquet


X-tra™

Profiling the immunological landscape in atopic dermatitis

Alma Lindell - PhD Student, *Allergic Inflammation*

Atopic dermatitis (AD) is a chronic inflammatory skin condition characterised by itchy, painful, and red skin. It is most common in children but can persist into adulthood, with over 200 million people affected globally. Over the past few decades, the underlying immune response in AD has been unravelled, shedding light on the important role of T cells in the inflammatory cascade. T helper (Th) 2 cells, which secrete the cytokines interleukin- (IL-) 4, IL-5 and IL-13 have been implicated in driving the inflammation and an antibody targeting the IL-4 and IL-13 cytokine pathways can successfully reduce disease in patients with severe AD. One issue is withdrawal of antibody treatment (known as dupilumab) leads to relapse of disease. A deeper understanding of the cells in AD lesions and how dupilumab affects cell composition and/or function is needed.

My PhD project aims to explore the function of lymphocytes in the skin of people with AD and understand the impact that dupilumab has on these cells. In collaboration with our collaborators at BIOSKIN, we have been analysing the skin and blood from AD patients. We receive skin biopsies from areas with active lesions, non-lesional skin, and previously lesional skin which now has been successfully treated by dupilumab. As a starting point we used multiparameter flow cytometry to analyse different immune cell subsets in the blood and skin on a single cell level, and in accordance with existing literature we found an overall increase of Th2 and Th22 cells in active AD lesions, which appeared to persist in successfully treated patients. Thus, while treatment is successful in reducing disease, it does not appear to be having an impact on these inflammatory T cells.

To understand more about the disease and how dupilumab functions, we are now analysing skin lesions using spatial transcriptomics, a sensitive technique which can help us investigate where different cells reside in the skin and understand the cell-cell contacts that are occurring. Preliminary work with spatial transcriptomics has revealed niches of antigen-presenting cells and fibroblasts where Th2 cells may reside, and this remains an area of active investigation.

We will complement these observations with studies in mice, where we can perturb specific molecules and cell-cell interactions more easily to try to fully understand the underlying immunology of AD.

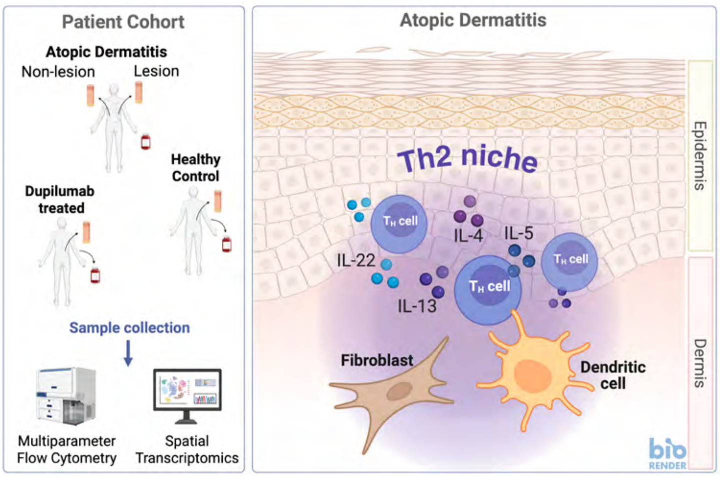


Figure: Overview of experimental setup and a schematic representation of the skin microenvironment in atopic dermatitis

Andrea Michaela Sonnenholzner - PhD Student,
Immunological Bioinformatics

Computational dissection of coordinated immune responses in inflamed barrier tissues

Single-cell technologies have transformed how we study disease by enabling the measurement of gene expression in thousands of individual cells simultaneously. This resolution has advanced our understanding of conditions like inflammatory diseases by revealing which cells change and which biological pathways are engaged during inflammation. Yet a narrow focus on individual cells can obscure the coordinated behaviour that ultimately drives tissue damage and repair.

Inflammatory bowel disease (IBD) is a chronic condition in which the immune system mistakenly attacks the gut lining, causing recurring cycles of inflammation, tissue damage, and incomplete repair. It is also a highly heterogeneous disease: different patients, and even different regions of the intestine within the same patient, can involve distinct combinations of cell behaviours. This makes IBD an ideal setting to determine how we can reliably capture disease-relevant changes at the level of cellular systems, with the long-term goal of better matching patients to therapies that work for them.

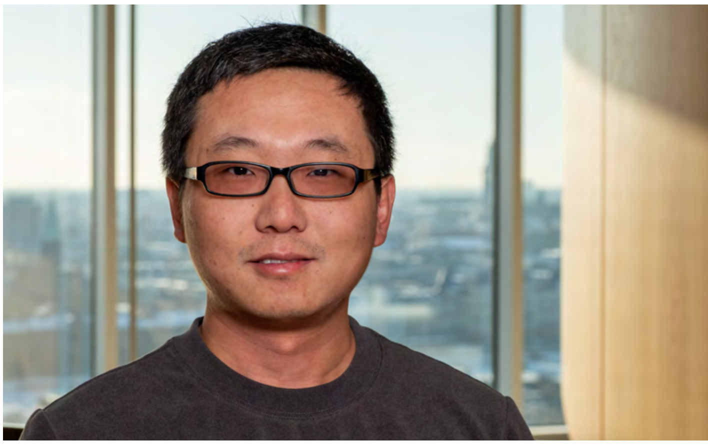
A central challenge is that cell identity in single-cell data is not directly observed; it is computationally inferred. What we call a cell type or cell state depends on what we choose to measure, how we bioinformatically define similarity between cells, how we correct for technical noise, and the biological context a cell sits in. When these choices are poorly calibrated, we risk mistaking technical artefacts for real biology or missing subtle disease programmes that only become visible when cells are considered in relation to one another. To address this, in collaboration with the barrier immunology group at SIC, I will implement a computational approach that makes cell-state inference more robust and interpretable. Rather than assigning cells to discrete categories, I use data-driven gene activity programmes to capture gradual transitions cells undergo, for example, from resting to activated, or from repair-promoting to inflammatory states in a way that is easier to compare across patients and disease contexts.

Building on this, a major focus of my project is coordinated cell behaviour and cell–cell communication. Many current approaches infer communication by assessing whether one cell expresses a signalling molecule and another expresses a matching receptor, thereby estimating only interaction potential. However, co-expression alone does not establish that signalling occurred or that it influenced cell behaviour. I am therefore developing a framework that prioritises evidence of downstream pathway activation in the cells potentially receiving the signal. By identifying coordinated gene-expression response programmes consistent with signal reception, this approach aims to construct more biologically grounded maps of the cellular networks that drive inflammation and healing.

Overall, the project aims to move from lists of cell populations to system-level maps of immune states and interactions in IBD, supporting improved disease stratification and more targeted therapeutic hypotheses.

POSTDOC PRESENTATION

Investigating tissue tolerance and immune regulation through translational control of TNFR1



Biao Ma - Postdoc, *Molecular Immunology and Inflammation*

Inflammation is an essential part of the body's defence system. When we are injured or infected, immune signals help eliminate threats. However, if inflammation becomes too strong or lasts too long, it can damage the tissues. This raises an important question: how do tissues stay functional during inflammation? One important part of the answer lies in tissue tolerance, the ability of tissues to limit damage and maintain function during immune responses.

My research explores how tissue tolerance is controlled at the molecular level, focusing on how cells regulate their sensitivity to inflammatory signals. Inflammatory responses are regulated through transcription of large sets of genes, leading to a rapid increase in mRNAs encoding inflammatory mediators such as cytokines. However, even when an mRNA is present, cells can still regulate how much protein is actually made. My work examines this often overlooked level of control during inflammation: translation, the process by which cells turn mRNA into protein.

Tumour necrosis factor (TNF), a key molecule that orchestrates inflammatory responses. Cells detect TNF through a receptor called TNFR1. The amount of TNFR1 present on the cell surface strongly influences how the cells respond. I identified a small regulatory element within the TNFR1 mRNA known as an upstream open reading frame (uORF). This short sequence acts like a molecular brake on protein production. Under normal conditions, it limits how much TNFR1 is made, preventing cells from becoming overly sensitive to inflammatory signals. In this way, the uORF helps maintain balance, allowing immune responses to occur while protecting tissues from excessive damage. Using mouse models, my work shows that disruption of this control mechanism leads to rapid cell death and tissue damage in response to TNF levels that normally are well-tolerated.

Importantly, this control system is not fixed. Cells can adjust TNFR1 production depending on their environment. Stress conditions such as low oxygen levels, ultraviolet radiation, or inflammatory signals can change how proteins are translated. When this happens, the uORF can alter how strongly it restricts TNFR1 production. This allows cells to fine-tune their inflammatory sensitivity based on their condition, linking environmental stress directly to immune responsiveness.

Overall, this work highlights translational regulation as an essential player of immune control. Understanding this mechanism may eventually help guide new strategies to manage inflammatory diseases, not by blocking immunity entirely, but by helping tissues better withstand it.

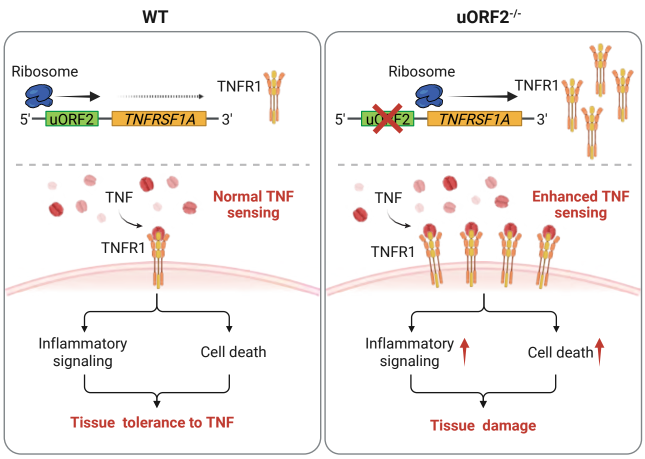


Figure: Schematic model of translational regulation of TNFR1 abundance via uORF2. uORF2 restricts TNFR1 abundance through translational control, thereby limiting TNF-induced proinflammatory signalling and cell death. Disruption of uORF2 increases TNFR1 translation and consequently enhances cellular TNF sensing, which amplifies pro-inflammatory signalling and cell death, ultimately leading to tissue damage.

Helen Vaher - Marie Curie Fellow, *T Cell Biology and Skin Inflammation*

Epigenetic and cytokine regulation of keratinocyte–immune cell crosstalk in inflammatory skin disease

The skin is a highly active immunological organ in which keratinocytes and immune cells continuously communicate to maintain tissue homeostasis and protect against environmental insults such as allergens, pathogens, and chemical irritants. In inflammatory skin diseases, including allergic contact dermatitis (ACD), this communication becomes dysregulated, leading to chronic inflammation and disease recurrence. A central feature of ACD is the persistence of activated immune cells in the epidermis, particularly tissue-resident memory T (T_{RM}) cells, which drive rapid and exaggerated responses upon allergen re-exposure. At the same time, keratinocytes actively shape local immune responses by producing cytokines and regulatory factors that influence immune cell activation, survival, and function. The molecular pathways mediating the dynamic crosstalk between keratinocytes and immune cells during inflammation remain only partially understood.

My research aims to define how epigenetic regulation by microRNAs (miRNAs) and cytokine-mediated signaling coordinate keratinocyte–immune cell interactions in inflammatory skin disease, with a primary focus on ACD. miRNAs are post-transcriptional regulators that fine-tune gene expression programmes in both epithelial and immune cells, while cytokines act as key mediators of intercellular communication within the skin. I hypothesize that dysregulated miRNA expression and altered cytokine networks reinforce each other to drive pathological immune–epithelial cell crosstalk during allergic skin inflammation.

To dissect the dynamic regulation of epidermal T_{RM} cells during allergic skin inflammation, I will use a clinically relevant mouse model of allergic contact dermatitis with defined sensitization and challenge phases. By analysing epidermal T_{RM} cells at multiple time points following allergen exposure, this approach enables a temporal and cellular-resolution assessment of miRNA expression, capturing molecular heterogeneity within the T_{RM} cell compartment over the course of disease initiation, exacerbation, and resolution. Integrating miRNA and mRNA profiling allows identification of regulatory networks that control T_{RM} cell proliferation, long-term maintenance, and functional activity in the inflamed epidermis, as well as the upstream signals regulating these epigenetic programmes.

In parallel, the project investigates keratinocyte-derived cytokine signals that regulate immune cell behavior in inflamed skin, with a particular focus on interleukin-34 (IL-34). IL-34 is a keratinocyte-expressed cytokine implicated in skin immune homeostasis and is consistently downregulated in lesional skin from patients with ACD and other inflammatory skin diseases. Using skin samples, I will assess whether IL-34 expression correlates with disease activity and treatment response. Mechanistic studies in primary human keratinocytes, 3D skin models, and skin explants will be used to determine how inflammatory signals and epigenetic mechanisms regulate IL-34 expression.

Together, this project aims to provide a mechanistic understanding of how epigenetic and cytokine-driven communication between keratinocytes and immune cells drives the pathogenesis of ACD. By identifying key regulatory molecules at the interface between epithelial and immune compartments, this work has the potential to uncover novel biomarkers and therapeutic targets for inflammatory skin diseases.

Unlocking the Secrets of Mucosal Healing: The REPAIR-IBD Study

Luiza Moraes Holst - BRIDGE Fellow, *Barrier Immunology*

Wound healing is a complex process involving the tight spatiotemporal tuning of consecutive events that are essential for restoring homeostasis. In a healthy body, tissue repair is a perfectly timed three-act play: an initial inflammatory phase to clear debris, a proliferative phase to build new tissue, and a remodeling phase to restore tissue function. However, in chronic inflammatory conditions, cycles of injury followed by dysfunctional resolution, ultimately lead to lifelong complications with permanent organ damage.

During my BRIDGE fellowship, I will delve into healing processes that occur in the intestinal mucosa and how this is potentially altered in inflammatory bowel disease (IBD), a chronic immune-mediated disorder of the gastrointestinal tract, where Crohn's disease and ulcerative colitis (UC) are the major subtypes. IBD is a life-long condition that presents as alternating phases of disease activity and remission, resulting in progressive intestinal damage. In the clinical management of IBD, achieving "mucosal healing" – the complete structural and functional restoration of the intestinal lining – is the ideal outcome. Yet, for many patients, this remains an elusive goal. Despite the advancement of pharmacotherapies, up to 30% of patients fail to respond to treatment, and nearly half of those who do respond never achieve full mucosal recovery.

Previous research conducted by our clinical collaborator, Prof. Jakob Seidelin, has laid the groundwork for understanding the impairment of the wound healing process in IBD. Utilizing an innovative in vivo injury model, earlier studies identified a significant delay in epithelial reconstitution in patients with UC compared to healthy controls. His research also revealed that 48 hours post-injury, UC patients exhibited an overexpression of genes associated with adaptive immune responses, alongside the engagement of "inflammatory fibroblasts", involved in propagating inflammation and promoting scarring. These findings suggest that the complex choreography of wound healing is disrupted in IBD.

To gain a deeper understanding of the mechanisms underlying mucosal healing and how this is altered in IBD, the REPAIR-IBD (Regeneration and Epithelial rePAIR in Inflammatory Bowel Disease) study, seeks to provide a comprehensive map of the cellular and molecular paths underlying repair of the human intestine in vivo. Here, we hypothesize that alterations in immune cell recruitment and stromal cell plasticity disrupt the orchestrated transition between healing phases, contributing to the chronic inflammation and fibrosis observed in IBD.

In our in vivo experimental model, we create superficial wounds in the colon of healthy volunteers and IBD patients in remission, observe the healing process in real-time and collect biologic material for further molecular and cellular analysis. Our approach integrates several state-of-the-art technologies, including single-cell RNA sequencing and spatial transcriptomics providing a deep mRNA "fingerprint" of individual cells to assess activity, differentiation, and their spatial context within the tissue architecture.

By understanding the subtle transitions between healing phases, we hope to identify potential "pro-resolution" strategies that promote successful barrier restoration. Ultimately, this research aims to identify disease-modifying targets and non-invasive biomarkers, paving the way for permanent mucosal recovery and a surgery-free future for IBD patients.

Maria Gluud Grøndahl - Postdoc, *Skin Inflammation and Cancer*

The interplay between malignant T cells and keratinocytes in Cutaneous T cell lymphoma

Cutaneous T-cell lymphoma (CTCL) is a lymphoid malignancy, with poor curative therapeutic options. CTCL is characterised by malignant T cells residing in chronically inflamed skin lesions as well as the presence of malignant cells in the blood in some CTCL variants. The skin lesions of CTCL patients cause serious symptoms that hamper quality of life for patients and are entry sites for bacterial infections, a major cause of morbidity and mortality in advanced disease. One pathogen frequently colonising the skin of patients is *Staphylococcus aureus (S. aureus)* which has been consistently linked to increased disease activity and increased risk of progression. The mechanisms driving the pathological changes in the skin lesions remains to be fully characterised to help uncover novel therapeutic targets for patients with CTCL. Thus, we seek to explore how skin lesions develop and evolve, by studying the crosstalk of cells in the tumour microenvironment (TME) of CTCL. A major focus of our project is to investigate how malignant T cells affect surrounding keratinocytes and play a role in destroying the skin barrier.

Our ongoing research show that CTCL lesions have a deficient skin barrier as judged by reduced expression of important skin barrier related proteins including filaggrin and disturbed barrier function. The cytokine environment in CTCL is highly complex and a range of cells contribute to the pathogenesis. Of note, epidermotrophic malignant T cells play an important role in hampering the skin barrier structure by orchestrating a TH2-dominated inflammatory environment - secreting IL-13, IL-22 and OSM that induce JAK/STAT3-driven changes in keratinocytes. Thus, highlighting the interest of future studies evaluating the potential of inhibiting JAK/STAT signalling to improve skin symptoms in CTCL.

In parallel, we seek to uncover the mechanisms by which the presence of *S. aureus* affects CTCL skin lesions. *S. aureus* can produce toxins that activate T cells, then affecting the TME. Importantly, *Staphylococcal* enterotoxins (SEs) induce cytokine production in CTCL cells that suppresses key skin-barrier proteins including filaggrin indicating that eradication of *S. aureus* can improve the skin barrier. In support, antibiotic treatment partially normalises expression of skin barrier proteins in an EL4 murine lymphoma model of bacteria-driven tumour progression, and in CTCL patients colonised with SE-producing *S. aureus*.

In summary, we explore how the crosstalk of malignant T cells and interactions with *S. aureus* in the TME fuel inflammation, barrier damage and bacterial overgrowth affecting CTCL pathogenesis. A better understanding of the vicious cycle in CTCL can hopefully help uncover new therapeutic targets.

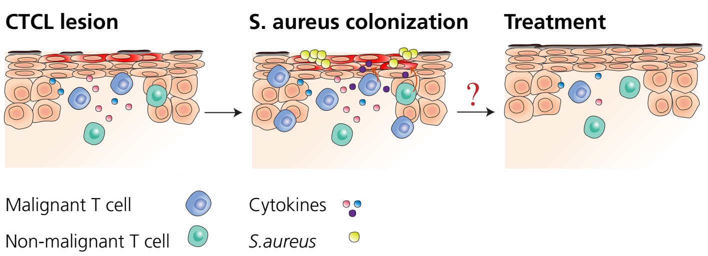


Figure overview: Cutaneous T cell lymphoma skin lesions.
CTCL lesions have a disturbed skin barrier. 1) Malignant T cells produce cytokines that repress important skin barrier related proteins.
2) *Staphylococcus aureus*-derived enterotoxins stimulate malignant and non-malignant cells to induce cytokines that can aggravate skin barrier deterioration in CTCL. 3) Exploring the underlying mechanisms can help uncover therapeutic targets to improve the skin barrier.

Deciphering the Gut-Skin Axis: Shared Immune Pathways in Psoriasis and Inflammatory bowel disease

Psoriasis (PS) and Inflammatory bowel disease (IBD) – comprising Crohn's disease and Ulcerative colitis – are chronic, relapsing immune-mediated inflammatory diseases that, despite affecting different organs (the skin and gut, respectively), share a striking clinical and genetic connection. Epidemiological studies have established a strong bidirectional link between the two, and recent genetic research suggests shared susceptibility factors. Patients with IBD are significantly more likely to develop PS, and vice-versa. However, the underlying mechanisms driving this "gut-skin axis" remain poorly understood. Interestingly, while certain biological therapies benefit both conditions, others that are highly effective for PS can trigger or worsen IBD. Our research seeks to resolve this paradox.

This project, in collaboration with Professor Jakob Seidelin (at Herlev Hospital), aims to determine whether PS patients develop pathological immune cell populations in the colon, contributing to an interplay between skin inflammation and (subclinical) intestinal inflammation. To address this, we are employing multiparameter flow cytometry, proteomics, and single-cell RNA sequencing (scRNA seq) to profile key inflammatory markers and immune cell populations in both skin and colon samples.

Mariana Bronze - PhD Student, *Immune Regulation*

A central focus of the project is to investigate whether T cells mediate inflammation by migrating between the gut and the skin, by assessing shared T cell clonality using scRNA seq. One of our key objectives is to compare immune signatures between PS, IBD, and PS/IBD overlap patients to identify common inflammatory pathways.

Ultimately, this research seeks to determine if PS patients – even those without gastrointestinal symptoms – exhibit subclinical intestinal immune engagement that could drive skin disease activity. By uncovering these shared cellular platforms and migratory pathways, we hope to provide mechanistic insights with potential therapeutic relevance, helping to define more integrated therapeutical strategies for patients living with these conditions.

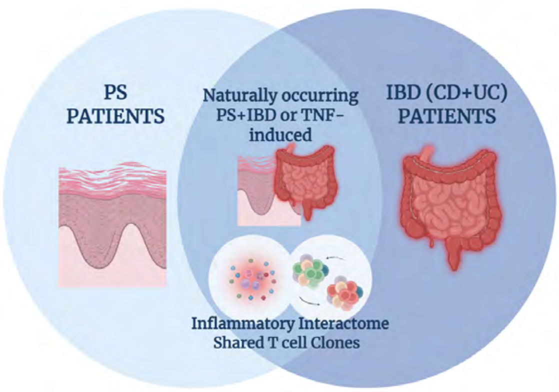


Figure: Project overview. This study explores the immune overlap between Psoriasis (PS) and Inflammatory bowel disease (IBD), including Crohn's disease (CD) and Ulcerative colitis (UC). We intend to compare immune signatures between PS, IBD, and PS/IBD overlap patients to identify common inflammatory pathways. A key objective is to determine if pathogenic T cells migrate between organs by analysing T cell clones within the skin and colon. Figure made with Biorender.

Outreach and communication

SIC researchers actively engage in outreach and communication to ensure that research findings reach clinicians, researchers, students, and the wider public.

In 2025, outreach activities included contributions to professional healthcare media, university press releases, podcasts, invited international lectures, student visits, and our open SIC Seminar series. The following section outlines selected outreach and communication activities carried out in 2025.

MEDIA AND INTERVIEWS

DAGENS MEDICIN

Lene Bay was featured in an article titled *'Atopisk eksem udligner gavnlige forskelle i hudens mikrobiom'*. The piece provided an overview of data published in mSphere on unique dermal bacterial signatures in atopic dermatitis skin. The publication reaches healthcare professionals and researchers. The publication reaches a broad audience, including specialists, hospital staff, and primary healthcare providers.

UNIVERSITY OF COPENHAGEN PRESS RELEASE

Niels Ødum and Terkild B. Buus were featured in a press release by the University of Copenhagen which discussed how cancer subclones can open the door to more personalised treatment. This was based on a study and journal article published in *Cancer Discovery.*

FILM AND PODCAST CONTRIBUTIONS

DERMA-DERMA PODCAST

DERMA-DERMA is an eight-part podcast series focused on skin biology, diseases, and treatment. Distributed via social media, the series aims to raise awareness of skin health among younger audiences (15–22 years old).

The podcast, hosted by Karen Marie Groth from BeautyHero, serves as a platform for knowledge sharing on skin health and skin diseases, with regular contributions from SIC and ISIM researchers.

In 2025, SIC researchers and colleagues from BIOSKIN, including Anders Boutrup Funch, Anders Woetmann, Carsten Geisler, Charlotte Menné Bonefeld, Jeanne Duus Johansen, Lene Bay, Lone Skov, Niels Ødum, shared their research on the podcast.

DIS STUDY ABROAD PROGRAMME

Niels Ødum welcomed three groups of international students from the DIS Study Abroad Programme to the center. The students were represented from more than 10 US Universities, and many of them experienced Scandinavia for the first time. Each visit featured a guided tour of the Mærsk Tower, an introduction to SIC and the field of immunology, and insights into studying in Copenhagen.

TALKS IN TANZANIA

Charlotte Menné Bonefeld was invited to speak at the Regional Dermatology Training Centre at Kilimanjaro Christian Medical University College, Tanzania on 'Allergic Contact Dermatitis from an Immunological Perspective'

HANDS-ON COURSE FOR FUTURE SCIENTISTS FROM GEFION GYMNASIUM

SIC welcomed biotech students from Gefion Gymnasium for the fifth edition of its two-day introductory course in skin immunology, organised by Professor Charlotte Menné Bonefeld, her research group and Anders Woetmann. The programme combined focused scientific sessions with hands-on laboratory training, enabling students to work directly with selected methods and technologies used in SIC's research.

Through practical exercises in an active research setting at the Mærsk Tower, the students gained first-hand insight into experimental immunology and everyday laboratory workflows. The course is part of SIC's continued commitment to stimulating early interest in biomedical research and providing qualified exposure to academic science in practice.

SIC SEMINARS

The SIC Seminar Series, organised by SIC's own young researchers at the Mærsk Tower, continue to serve as a vibrant forum attracting researchers not only from the Department of Immunology and Microbiology (ISIM), but also from other departments at SUND, as well as universities and clinics across Denmark. In 2025, a total of 15 speakers presented, and the series remains a valuable platform for scientific exchange, with more engaging speakers already planned for the coming year.

Upcoming seminars and the full programme can be found on the SIC website: sic.ku.dk/sic-calendar

SEMINARS ORGANISED BY SIC RESEARCHERS AND HOSTED AT THE MÆRSK TOWER

Dr. Frederick Sheedy, Trinity College Dublin, Ireland
Train to Win; Immunometabolic changes in β-Glucan induced Trained Immunity.

Professor Rune Hartmann, Aarhus University, Denmark
Recognition of viral infection by innate immunity and initiation of antiviral immunity

Dr. Katharina Lahl, University of Calgary, Canada
Immune responses to Rotavirus at the maternal-neonatal interface

Dr. Joshua Koenig, McMaster University, Canada
Lineage-ambiguous Memory T cells Drive Early Allergic Sensitization Through De Novo IgE Generation

Dr. Tyler Burns, Burns Life Sciences Consulting, Germany
Best practices for analysing complex single-cell sequencing data

Professor Daniel Krappmann, Helmholtz Munich, Germany
Maintenance of immune homeostasis by balancing MALT1 scaffolding and protease functions

Professor Annika Meinander, Åbo Akademi University, Finland
Ubiquitin, caspases, and flies – Molecular mechanisms of inflammation

Professor Geert van Loo, Ghent University & VIB (VIB-UGent), Belgium
Pyrin inflammasome-driven arthritis caused by defects in the regulation of mevalonate signalling

Dr. Niamh O'Boyle, Trinity College Dublin, Ireland
Lipids in Skin Allergy – Central Contributors or Collateral Damage?

Professor Shalin Naik, WEHI (Walter and Eliza Hall Institute of Medical Research), Melbourne, Australia
Clonal Biology

Professor Oliver Pabst, University of Aachen, Germany
Gut IgA responses: Everything – Everywhere – All at Once

Professor Daudi Mavura, Regional Dermatology Training Centre in Tanzania
An overview of Training at the Regional Dermatology Training Centre in Tanzania

Professor Neil Rajan, University of Birmingham, UK
CYLD and the Matrix: Does ubiquitin shape tissue architecture?

Professor Christoph Schlapbach, Bern University Hospital, Switzerland
Th2 cell subsets – splitting hairs or separating wheat from chaff?

Professor Thomas Decker, University of Vienna, Austria
A new look at interferon signaling

Organising committee of the SIC seminars

Alexandra Seibel
Chella Krishna Vadivel
Egon Urgard
Helene Scheel Wegener
Malin Jessen
Mia Hamilton Jee
Peter Tougaard
Tiana Ida Stanisic
Urs Michael Mörbe

With support from William Agace and Hannah Paludan

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 31.6 million, and the turnover from the add-on grants totalled DKK 16.6 million in 2025. Also, SIC obtained a total of DKK 46 million in new funding from 13 external research grants.

External research grants awarded in 2025

Funder	Recipient	Title	Amount in DKK
Psoriasis Forskningsfonden	Amanda Kvist-Hansen	Systemic inflammation in psoriasis – platelets, neutrophils and their interaction	109,400
LEO Foundation	Charlotte Menné Bonefeld	Increased scientific collaboration and networking on skin immunology and allergies in skin of colour	394,170
Ministry of Foreign Affairs, Denmark	Anders Woetmann/ Charlotte Menné Bonefeld/ Christian Wang/Lea Barfod/ Michael Alifrangis	UPIVAC Africa – University Partnership for Immunology and Vaccinology Capacity in Africa	33,992,400
Horizon MSCA Postdoctoral Fellowship	Erik van Tilburg Bernardes	Deciphering the role of microbiome-fibroblast crosstalk in intestinal immune development, homeostasis and inflammation	1,846,825
BRIDGE Translational Excellence Programme	Luiza Moraes Holst	REPAIR IBD: an In vivo characterization of wound healing in IBD	1,692,740
A.P. Møller Fonden	Martin Kongsbak-Wismann	Kan bakterier undvige vores immunforsvar ved at manipulere med vitamin D receptoren i makrofager	50,000
LEO Foundation	Max Sauerland	From Minimal Biopsies to Maximal Insights: A Deep Proteomic and Machine Learning Platform for Targeting Fibrosis in Hidradenitis Suppurativa	1,687,500
Fonden til Lægevidenskabens Fremme	Mia Hamilton Jee	Påvirker kontaktallergener udviklingen af T-celler i thymus?	50,000
Alfred Benzons Fond	Niels Ødum	Topical JAK inhibitor and Chlormethin gel as treatment for cutaneous T-cell lymphoma	1,000,000
The Danish Cancer Society (Kræftens Bekæmpelse)	Niels Ødum	Unraveling the factors that drive malignant proliferation and using this to find a cure for T cell cancer in the skin	3,300,000
LEO Foundation	Terkild Brink Buus	LEO Foundation Fellows Leadership Coaching Program	39,000
LEO Foundation	Terkild Brink Buus	'Visiting Researcher' Grant. Dissecting the Immune Microenvironment of Chronic Viral Dermatoses	2,000,000
Psoriasis Forskningsfonden	Wenning Zheng	Investigating autoreactive T cell clones in psoriatic diseases	231,696

Scientific output

SIC and BIOSKIN researchers authored 40 publications in peer-reviewed journals in 2025.

SIC publications 2019-2025

2019	2020	2021	2022	2023	2024	**2025**
25	19	34	22	34	45	**33**

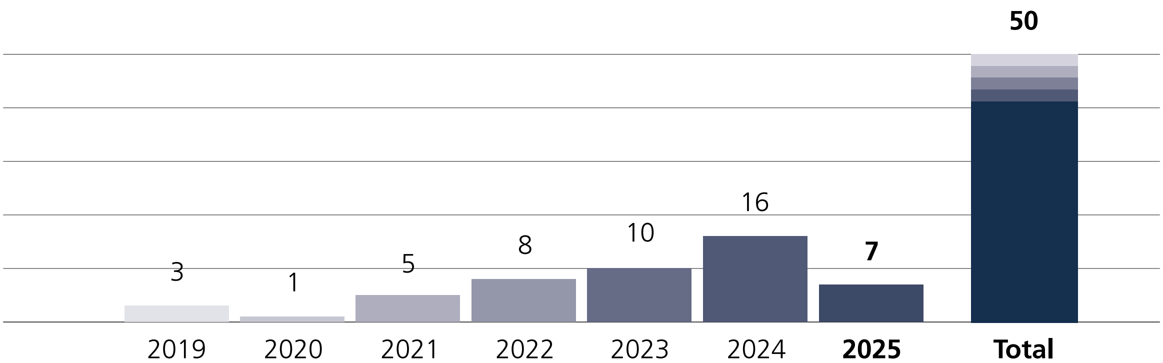
3,968

Total citations from SIC Group Leaders in 2025

212

Total SIC publications

Number of publications · impact factor >10



Publications

Publications are listed in alphabetical order by article name. Journals are in bold and SIC affiliated authors are underlined.

Allergic Contact Dermatitis: Immunopathology and Potential Therapeutic Strategies.
Funch AB, Geisler C, Bonefeld CM.
J Clin Med. 2025 Oct 11;14(20):7175. doi: 10.3390/jcm14207175. PMID: 41156043; PMCID: PMC12564274.

CD8$^+$ Skin-Resident Memory T Cells Require TCR Signaling for their Persistence in a Mouse Model of Allergic Contact Dermatitis.
Funch AB, Weber JF, Mraz V, Kongsbak-Wismann M, Lohmann RKD, Jee MH, Vaher H, Yeung K, Gadsbøll AØ, Ødum N, Woetmann A, Johansen JD, Geisler C, Bonefeld CM.
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