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

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

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

SIC’s focus is to integrate and advance basic and clinical scientific approaches to skin disease and develop future leaders in the field, at the same time increasing knowledge and awareness of skin and skin diseases among medical professionals, patients and the public. Our aim is to grow into a beacon for skin research in Denmark with a worldwide impact.

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

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

SIC focuses on inflammatory skin diseases including psoriasis, atopic and contact dermatitis, and cutaneous T cell lymphoma (the latter as a model disease). These skin diseases are all characterized by a strong immunological component.
The establishment of SIC is a tale of common interests, high ambitions and the joining of forces to explore as of yet unreleased potential. I first had the chance to discuss new initiatives of mutual interest with the LEO Foundation in early 2018, and from then on, the development accelerated. We agreed from the beginning that a new and encompassing approach to skin and skin disease research was needed if we are to unravel the complexities of more than 3,000 skin diseases. By approving our ambitious application for DKK 400 million for a new research centre later in the year, the LEO Foundation Board of Trustees made our common vision a reality. And barely two months into 2019, we were able to celebrate the inauguration of SIC.

I am honoured by the confidence the Board has shown us by awarding the University of Copenhagen their largest grant to date. Moreover, I am exceptionally delighted about the scientific endeavours this long-term engagement enables us to pursue.

The Faculty of Health and Medical Sciences at the University of Copenhagen has a long tradition with Centres of Excellence which enables us to specialise in a range of emerging fields within medical science. SIC has already proved that it will be no exception. In 2019, the SIC basic research groups in the Mærsk Tower and our partners in clinical dermatology have expanded and utilised their strong network of expert skills and technologies in and beyond the Faculty to invigorate the encompassing approach of skin immunology research. One year in, I am increasingly enthusiastic about the results that our venture will produce, and I look forward to following SIC’s progress in the years to come.

**Report from the Executive Director**

SIC has now been in operation for a year, and what a year! It has first and foremost been a year of consolidation of a new organisational entity, and identity, at the University of Copenhagen. We have transferred two basic research groups into SIC as the first founding bricks of the new centre. The group leaders of the two basic research groups, alongside a clinical professor from Herlev and Gentofte Hospital’s distinguished dermatology department, now constitute the Center’s Steering Committee and will steer the way for the accumulation of strong and productive clinical and translational insight into some of the world’s most prevalent inflammatory skin diseases.

SIC is located on the 12th floor of the Mærsk Tower in the heart of Copenhagen. Not only does this give us a fantastic view of the city, which is a constant inspiration to all of us, it also gives us an ideal overview of the potentials that lie ahead. With this, I find that we have the best possible framework in place for further expansion, allowing us to take in new capacities that will add to our already strong community of basic immunologists and clinical dermatologists.

It has been a year filled with activities and new initiatives. Hopefully, this annual activity report will give our readers a clear expression of the full scope. However, I would like to highlight two special milestones from the past year.

The inauguration of SIC took place on 25 February 2019. In the morning, the need for a centre focusing specifically on skin immunology research was highlighted in talks by our guest speakers, Professors Christopher Griffiths, Arne Akbar, Tomas Mustelin and Mathias Mann – contributors whose support we still enjoy.

In the afternoon, at the official ceremony, we were honoured by the presence of his Royal Highness Prince Joachim, the Minister for Education and Science Tommy Ahlers, Chairman of the LEO Foundation Lars Olsen and Rector of the University of Copenhagen Henrik C. Wegener. After the ceremony, the four toured our laboratories and talked with our PhD students, learning about the different aspects of the research we carry out. Due to the sincere interest shown by our guests, it was a very big moment for our PhD students.

We have been so fortunate that the LEO Foundation supported us with an add-on grant which made it possible for us to invest in high-end equipment to perform single cell sequencing analysis. The equipment has arrived and is now being installed and tested, and we all look very much forward to using it for novel project investigations into the characterisation of different endotypes of inflammatory skin diseases and the specific cellular impact of treatments.

In 2019, we laid the foundation for this unique centre, and we are excited about the next nine years.

**Group Leader and Professor Charlotte Menné Bonefeld is the acting Executive Director of SIC.**

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

SIC is a separate organisational entity embedded in the Department of Immunology and Microbiology (ISIM) at the Faculty of Health and Medical Sciences at the University of Copenhagen. SIC’s two basic research groups – the T Cell Biology and Skin Inflammation and the Skin Inflammation and Cancer groups – are based at SIC’s headquarters at the Faculty. However, the scientific activities span widely across the Faculty and national and international clinical research units. As a representative of the translational and clinical research milieu, Clinical Professor at Herlev and Gentofte Hospital, Jacob Pontoppidan Thyssen, is a core member of SIC.

STAFF COMPOSITION

By the end of 2019, SIC engaged a total of 45 staff members and students of 14 different nationalities in its two basic research groups. SIC hired eight new scientific staff members (recruitments and extensions) based on the SIC centre grant in 2019. The compositional staff data presented here includes visiting guest researchers, PhD students to whom SIC researchers provide main supervision and internal master thesis students (students conducting their thesis work in SIC’s laboratories). A full list of staff and students engaged in the research groups throughout the year is presented on page 34.

MANAGEMENT

The operational and strategic management of SIC is carried out at four levels: The Daily Leadership Team – comprised of Executive Director Charlotte Menné Bonefeld, ISIM Head of Department Carsten Geisler, Center Administrator Nils Erik Samdal and Center Coordinator Bitten Dalsgaard – executes and oversees the day-to-day operations. SIC’s three core members, including the executive director, make up the Center Steering Committee which proposes and implements strategic scientific initiatives. The executive director and the leadership team meet with Dean of the Faculty Ulla Wewer on a frequent basis to discuss and decide strategic matters related to the continuous development of SIC. Rector of the University of Copenhagen, Henrik C. Wegener, is the grant holder of the SIC centre grant and once a year aligns with the Center Management and the LEO Foundation on strategic progress and development.

SIC currently has three core members: Clinical Professor Jacob Pontoppidan Thyssen from the Department of Dermatology at Herlev and Gentofte Hospital and basic research Group Leaders, Professors Charlotte Menné Bonefeld and Anders Woetmann. As core members, they make up the Center Steering Committee, our key framework for ‘The Team Science Concept’.

The organisation and governance chart reflects that SIC as a minimum aims to double its number of core members through strategic, international recruitment of new principal investigators (PIs) in the coming years.

SIC investigates fundamental questions within skin biology and diseases in an interdisciplinary team of scientists with core competences and insights into basic, translational and clinical skin-related research. We call this ‘The Team Science Concept’.
**YOUNG INVESTIGATOR NETWORK**

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

The network is a self-organising professional and social initiative that meets approximately four times a year in different settings, varying from guest lectures and field trips to relevant institutions and organisations to actual networking sessions to match skills and methods that can produce novel research results.

**GREATER COPENHAGEN HEALTH SCIENCE PARTNERS - CAGS**

Each of the basic research groups at SIC is the driving force of a Clinical Academic Group (CAG) in the Greater Copenhagen Health Science Partners collaboration between the University of Copenhagen, the Technical University of Copenhagen, Region Zealand and the Capital Region of Denmark. A CAG is an academic clinical research group which consists of researchers and clinicians from the universities and hospitals.

A CAG contributes to the health sector with new research and increased quality within the field of clinical practice through a strong professional network. SIC’s group leaders currently hold chairmanship responsibilities of the CAG Allergy, which aims to reduce the increasing number of patients suffering from allergic diseases, including eczema, and the CAG in Cancer Immunotherapy, which aims to develop evidenced-based clinical solutions to the use of breakthrough immunotherapy method in cancer treatment.

**SCIENTIFIC ADVISORY BOARD**

SIC has invited key research leaders within immunology and skin disease research from across the world to become members of SIC’s Scientific Advisory Board (SAB). The SAB provides counselling on the strategic scientific and organisational development of SIC to the dean of the Faculty of Health and Medical Sciences and the executive basic director and meets once a year. Recruitment of a permanent executive director, recruitment of new core member PIs and further developing the ties between basic and clinical research were main themes at the SAB’s constitutive meeting in September 2019. At the meeting, members expressed their appreciation of the overall high scientific quality and relevance of the current scientific projects at SIC. They found that the unprecedented opportunity provided by the centre for strong focus on applying fundamental basic immunological methods and knowledge to skin diseases and translating this knowledge to treatments, will contribute to important scientific progress in the coming decades.

The Planning Group is responsible for planning and holding meetings in the Young Investigator Network. The Planning Group consists of representatives from each participating department.

Currently, the Planning Group consists of the following members:

- Martin Kongskb-Wismsen, Assistant Professor; SIC (Chair)
- Emil Marek Heymanns Pallesen, Postdoc, SIC
- Perrille Lindso Andersen, PhD student, Zealand University Hospital, Roskilde
- Jesper Grenchlund Holm, PhD student, Bispebjerg and Frederiksberg Hospital
- Anne-Sofie Halling-Overgaard, PhD student, Herlev and Gentofte Hospital

ASSOCIATE DEAN WENDY HAVRAN

Scripps Research Institute

Sadly, Professor Havran suffered an untimely death in January 2020. We will remember her as a valued advisor and a generous and inspirational mentor.

PROFESSOR ARNE ACKAR

Division of Infection and Immunity, University College London

Professor Arne Ackar is the driving force of the Clinical Academic Group (CAG) in Cancer Immunotherapy, which aims to develop evidence-based clinical solutions to the use of breakthrough immunotherapy method in cancer treatment.

PROFESSOR MÜBECCEL AKDIS

Swiss Institute of Allergy and Asthma Research, Universität of Zurich

Professor Mu’becel Akdis is the driving force of the CAG in Cancer Immunotherapy, which aims to develop evidence-based clinical solutions to the use of breakthrough immunotherapy method in cancer treatment.

PROFESSOR TOMAS MUSTELIN (CHAIR)

Division of Rheumatology, Department of Medicine, University of Washington

Tomas Mustelin is the driving force of the CAG Allergy, which aims to reduce the increasing number of patients suffering from allergic diseases, including eczema, and the CAG in Cancer Immunotherapy, which aims to develop evidence-based clinical solutions to the use of breakthrough immunotherapy method in cancer treatment.

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CAGs are selected by the Greater Copenhagen Health Science Partners collaboration. Clinical Professor Jeanne Duus Johansen at Herlev and Gentofte Hospital is Chairman of CAG Allergy, and Group Leader at SIC Charlotte Menné Bonefeld is Vice Chairman. Clinical Professor at Herlev and Gentofte Hospital, Inge Marie Svane, is Chairman of the CAG in Cancer Immunotherapy, and SIC Group Leader Anders Woetmann is Vice Chairman.
## Highlights of 2019

A selection of activities throughout the year.

### JANUARY
First joint scientific seminar in the SIC basic research groups

### FEBRUARY
SIC inauguration
Launch of The Proteomic Skin Atlas

### MARCH
Professor inauguration of Charlotte Menné Bonefeld
Joint scientific seminar with LEO Foundation Center for Cutaneous Drug Delivery

### APRIL
SIC delegation at the 13th World Immune Regulation Meeting in Davos
Guest seminar by Research Associate Emma Chambers, University College London
Guest seminar by Associate Professor Mads Gyrd-Hansen, Oxford University

### MAY
Professor Niels Ødum talks at the Bloom festival

### JUNE
DKK 15 million grant for a single cell sequencing facility by the LEO Foundation
PhD defence by Tengpeng Hu
Training of eight social media ambassadors
Kick-off meeting in the Young Investigator Network
Guest seminar by Associate Professor Marta Polak, University of Southampton

### JULY
Guest seminar by Professor Mariusz Wasik, Fox Chase Cancer Center

### AUGUST
Annual Meeting of the Graduate Programme in Immunology and Infectious Diseases

### SEPTEMBER
Constitutive meeting of the Scientific Advisory Board
SIC delegation at the 49th Annual ESDR Meeting
Guest seminar by Professor Vincenzo Bronte, Verona University
Guest seminar by Professor Mübeccel Akdis, University of Zurich
Guest seminar by Professor Susan Bates, Colombia University

### OCTOBER
PhD defence by Edda Blümel
Guest seminar by Associate Professor Amanda MacLeod, Duke University
SIC delegation at Cutaneous Allergy Research Group Organisation (CARGO) meeting in Paris

### NOVEMBER
PhD defence by Anne-Sofie Østergaard Gadsbøll

### DECEMBER
PhD defence by Sanne Steengaard Meisser

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1. The Proteomic Skin Atlas was launched at the inauguration of SIC and received international media attention. Read more online at skin.science.

2. Charlotte Menné Bonefeld with long-term colleague Carsten Geisler, Head of Department, as she celebrated her inauguration as professor in skin immunology.

3. Postdoc Terkild Brink Buus received the 'Best Workshop Presentation Award' at the 13th World Immune Regulation Meeting in Davos.

4. Professor Niels Ødum took on the initial role as Executive Director of SIC. He did an excellent job communicating the need for advanced skin immunology research at numerous occasions throughout the year – here at the Bloom festival.

5. The Young Investigator Network was kicked off with an inspiration workshop on synergies in basic/clinical collaborations.

6. SIC’s Scientific Advisory Board met for their constitutive meeting at the top of the Marsk Tower.

7. SIC has trained ambassadors in research dissemination on social media. Twitter account @skinucph took off at the 49th Annual ESDR Meeting in Bordeaux.

8. Anne-Sofie Østergaard Gadsbøll published research results from her PhD thesis in Journal of Investigative Dermatology.
T cell biology and skin inflammation

The T Cell Biology and Skin Inflammation basic research group investigates the aspects of T cell biology in connection with the skin, including the interplay between the skin, thymus and T cell development, and how different skin-related factors regulate the activation and differentiation of naïve T cells to effector and memory T cells. The group is headed by Group Leader and Professor Charlotte Menné Bonefeld.

Lymphocytes (T cells) play a central role in the immune system and are needed for a healthy life. The precursors for T cells originate in the bone marrow, and T cell development takes place in the thymus. After having undergone a complex selection process, naïve T cells leave the thymus and start their circulation in the body via the blood and lymph vessels. Upon encountering specific antigens, naïve T cells are activated and differentiate into effector and memory T cells. It has recently become clear that twice as many T cells are found in the skin as in the circulation and that the majority of the T cells in the skin is memory T cells.

In 2019, our focus has been on how regulators of anti-oxidants and vitamin D affect T cell activation and differentiation. We found that vitamin D has a profound effect on key molecules expressed by the T cells and involved in inflammatory skin diseases. In addition, we found that tumor necrosis factor (TNF) induces rapid down-regulation of the thioredoxin interacting protein (TXNIP) and a concomitant increase in glucose uptake in naïve T cells. TNF-induced TXNIP down-regulation is almost completely blocked by caspase inhibitors indicating a mechanism involving caspase-mediated cleavage of TXNIP. Our data indicate that TNF might act as a co-stimulatory molecule for T cells by inducing down-regulation of TXNIP.

We have also investigated the effect of contact allergens on the expression of various stress molecules in the form of keratinocytes and epidermal T cells. Our preliminary data suggests that various stress molecules play a role in activation of epidermal T cells during the response to contact allergens.

Finally, we have investigated the regulation of the epidermal T cell composition following exposure of the skin to contact allergens and the role of epidermal memory T cells in the immune response to contact allergens. We have shown that exposure to contact allergens results in the generation of epidermal memory CD8+ T cells and that the generation of these induces a displacement of a subset of epidermal-resident γδ T cells. This showed us that exposure of the skin to contact allergens results in an alteration of the epidermal T cell composition. We demonstrated that the epidermal memory CD8+ T cells have an increased responsiveness to contact allergens compared to the epidermal-resident γδ T cells. As such, the magnitude of the rapid response to contact allergens correlates with the frequency of the epidermal memory CD8+ T cells. Furthermore, we found that the pathogenic epidermal memory CD8+ T cells might out-compete the epidermal-resident γδ T cells due to a superior metabolic fitness.

Based on this, we suggest that local immunomodulatory therapy targeting the metabolism of epidermal memory CD8+ T cells could provide a novel therapeutic strategy for the treatment of allergic contact dermatitis, and we will continue to build on this approach in 2020.

PROFESSORS
- Charlotte Menné Bonefeld
- Carsten Geisler

ASSISTANT PROFESSORS AND POSTDOCS
- Anne-Sofie Østergaard Gadsbøll
- Martin Kongsbak-Wismann

ASSOCIATED ASSISTANT PROFESSOR
- Beatrice Dyring-Andersen

PHD STUDENTS
- Anders Boustrup Funch
- Anna Kathrine Obelitz Rode
- Daniel Villalba Lopez
- Fatima Abdul Hassan Al-Jaberi
- Mia Hamilton Jee
- Veronika Mraz

STUDENT ASSISTANT
- Gustav Ørting Jørgensen

INTERNAL MASTER’S THESIS STUDENTS
- Tinghuai Song
- Søren Vester Kofoed

LAB MANAGERS
- Louise Mørk
- Julie Friis Weber
Skin inflammation and cancer

The key research themes of the Skin Inflammation and Cancer basic research group are skin inflammation, microbes and cancer with special focus on how bacteria and bacterial toxins and metabolites influence T cell regulation, homeostasis and T cell malignancy. The group is headed by Group Leader and Professor Anders Woetmann.

The Skin Inflammation and Cancer group works to unravel the interplay between immunity, skin cells and the microbiota to understand what drives disease progression and resistance to treatment. As inflammation damages the skin barrier, it paves the way for microbial colonisation that fuels more inflammation and disease progression.

In 2019 in particular, we have investigated how disease mechanisms such as aberrant signalling and production of inflammatory factors are influenced by the metabolic state, cross-talk between immune cells and keratinocytes and bacterial products. Our hypothesis is that bacterial toxins and metabolites influence the inflammatory milieu leading to reduced anti-tumour responses, decreased barrier function and increased tumour burden. Furthermore, we have investigated how the balance between mitochondrial and aerobic glycolytic metabolism affects T cell activation, proliferation and function. Our hypothesis is that mitochondrial metabolism is needed for proper T cell function. Understanding this might allow for identification of novel therapeutic targets for treatment of T cell driven inflammatory skin diseases.

We have also worked to identify novel T cell subpopulations believed to play a role in chronic skin inflammation and diseases, such as psoriasis, as well as in non-canonical functions of Janus kinases. Our preliminary data suggests that several novel T cell subsets exist, and we hypothesise that they play important roles in development and/or maintenance of inflammatory skin diseases.

We are currently working to establish novel methods and techniques to address the importance of T cell senescence in deregulated cytokine expression and skin inflammation and cancer. This will allow us to investigate whether senescence plays a role in either benign or malignant skin diseases.

We have achieved a series of important results this year. We discovered that antibiotics inhibit T cell lymphoma of the skin, and we provided the first direct evidence that bacteria fuel the disease through changes in the tumour microenvironment. Moreover, we discovered that a staphylococcus aureus toxin selectively kills healthy CD4+ T cells while sparing malignant T cells due to a cancer-associated resistance, partly mediated by deficient expression or function of the toxin receptor ADAM10 by malignant T cells.

In the coming period, we will build on these results to explore treatment targets and principles such as novel kinase inhibitors, anti-microbial peptides and non-antibiotic drugs – in order to inhibit bacteria and better understand how environmental factors such as bacteria and metabolites influence drug resistance.

Tumour microenvironment in the skin.
Antibiotics inhibit lymphoma of the skin

Cutaneous T-cell lymphoma (CTCL) is a cancer in the T cells in the immune system that shows in the skin. As the patient’s immune system is weakened, the skin is less resistant to bacteria, and patients often get bacterial skin infections. In laboratory experiments, we have recently discovered that surprisingly, staphylococcal bacteria promote growth of cancer cells. This prompted the initiation of a clinical pilot study to address whether bacteria also stimulate cancer disease activity in patients. We discovered that by treating patients with aggressive antibiotics, we can indeed inhibit disease activity in the skin of CTCL patients. When we inhibit the staphylococcal bacteria with antibiotics, we simultaneously remove the activation of the immune cells. This means that they produce fewer cytokines, used by the cancer cells as fuel to accelerate their own growth. As a result, the cancer cells are inhibited from growing as fast as they did during the bacterial attack. This is the first direct link between bacterial infection and cancer cells in patients.

The study was conducted in a collaboration between:

Niels Ødum at SIC
Maria Kamstrup at Bispebjerg and Frederiksberg Hospital
Lars Iversen and Lise Lindahl at Aarhus University Hospital
Lise-Mette Rahbek Gjerdrum at Zealand University Hospital.

The effects of age and environment on the epidermis

It is well known that the outmost layer of the skin, the epidermis, provides us with an important physical barrier protecting us against the outside world. In addition to being a physical barrier, the epidermis also provides an immunological barrier. Epidermal T cells are a central part of the immunological barrier. The epidermal T cell composition found in skin from adult humans and laboratory mice that have never been exposed to antigen are very different. But as very little is known about the epidermal T cell composition in infant human skin, it is unknown whether these differences simply are a question of inborn species differences or rather a matter of the degree of antigen-experience. In a study, we found that the composition of epidermal T cells significantly changes with age in humans, whereas it remains constant in antigen-inexperienced laboratory mice. However, when we exposed mice to antigen, their epidermal T cell composition changed dramatically in a way that mimic the composition found in adult human epidermis. Based on our findings, we therefore suggest that antigen-experienced mice might be better models than antigen-inexperienced mice for investigating inflammatory skin diseases in humans. The study was carried out in a collaboration between Charlotte Bonefeld at SIC and Malin G. Ahlström, Beatrice Dyring-Andersen and Jeanne Duus Johansen at Herlev and Gentofte Hospital.

SIC Annual Activity Report 2019

Translational and clinical research

SIC is strongly committed to integrating the basic research groups at the SIC headquarters at the Faculty of Health and Medical Sciences with translational and clinical research forces in dermatology departments nationally and internationally. This approach translates basic discoveries to the patients, and it ensures that observations and questions arising in the clinic are referred back to the laboratory. On these pages, we highlight but a few examples of translational and clinical research projects that have resulted from the ‘Team Science Concept’ as adapted by basic and clinical researchers in and associated with SIC.

SIC collaborates with numerous clinical departments nationally and internationally. Professors Lone Skov and Jacob Pontoppidan Thyssen, Herlev and Gentofte Hospital, are SIC’s clinical representatives as Chair of the Clinical Task Force and Center Steering Committee member, respectively.

An aggressive antibiotics treatment inhibits the staphylococcus infection and makes the immune cells produce fewer cytokines. Thereby, the cancer cells cannot use the cytokines to grow faster than normal.
The skin is a complex organ, comprising multiple layers and cell types that are functionally distinct. The ability to define the skin at the molecular level of proteins, the functional biological entities in cells, is an important and unmet need. Recent technological advances in the field of mass spectrometry-based proteomics have made it a sensitive and accurate method for large-scale and unbiased proteomic analyses. This enables characterisation of nearly complete proteomes. Using healthy skin discarded from plastic surgeries and state-of-the-art MS-based proteomics, we have now created a global overview of the protein composition in healthy human skin layers and cell types that are functionally distinct.

The aim of the project is to establish models to study these interactions. Initially, we aim to establish a two-dimensional in vitro co-culture system to understand how humoral factors secreted by immune cells affect keratinocyte biology. In addition, we want to introduce skin bacteria to this model and measure changes in bacterial colonisation when keratinocytes are grown with humoral factors harvested from immune cells that have been isolated from different immune-mediated skin diseases. We have preliminary results showing that the two-dimensional co-culture system combining keratinocytes and humoral factors from malignant T cell supernatants can mimic the characteristic protein changes identified in several immune-mediated skin diseases, exemplified by the reduced filaggrin expression seen in the lesional skin of CTCL patients. We hope to further advance our co-culture system and convert the system into a three-dimensional model using either reconstructed epithelial models, organotypic human skin models or ex vivo human skin. The ability to model immune-mediated skin diseases in two dimensions enables us to better understand the humoral factors produced by T cells which cause the changes in gene expression and the insufficient barrier formation.

Using a skin model that includes a proper epithelial barrier will aid in answering questions related to changes in barrier formation and whether humoral factors are sufficient to cause the barrier defects seen in immune-mediated skin diseases. In addition, co-culture systems with skin models, including all skin layers, will allow us to get a better understanding of microbial colonisation in immune-mediated skin diseases.
Many skin diseases share symptoms such as rash, itchiness, red swelling and cracked skin. This results in challenges to provide the right diagnosis, and thereby the right treatment.

With the era of genetics, we now have the ability to do population wide genomic studies and thereby discover underlying genetic mechanisms for diseases. From the amount of genetic data, we have collected so far, we know that the underlying mechanisms for a disease vary as much as our physical appearance. One disease will affect two people in different ways, and treatment could therefore be different for each individual. The use of an individual’s genomic data and other relevant information – such as information from blood samples – is termed precision medicine. This project combines a multitude of fields of expertise to improve precision medicine in skin diseases.

The particular focus of the project is atopic dermatitis. It affects up to 20% of the human population in the course of their lives, and the disease can become chronic. Not much is known about the disease course, but atopic dermatitis is often followed by asthma or allergic rhinitis.

The project is established in collaboration between SIC, Novo Nordisk Foundation Center for Protein Research at the University of Copenhagen, the Copenhagen Hospital Biobank, Rigshospitalet and deCODE genetics in Iceland.
Based on a DKK 15.3 million add-on grant, SIC is now building a state-of-the-art facility for single cell sequencing. The facility is an important addition to the advanced equipment and technologies available to SIC at the Faculty of Health and Medical Sciences, including microscopy, animal facilities, supercomputing and proteomics.

In the coming years, the invention of novel, advanced technologies for single cell analysis is expected to revolutionise cellular biology and, in particular, the fields of immunology, cell cybernetics, inflammation and cancer. Thus, single cell analysis provides an unprecedented opportunity to investigate the extreme complexity of cells during immune responses, the interplay between skin and immune cells and the dynamics of skin diseases.

Moving from investigating an average of molecular changes in thousands or millions of cells to the study of changes in the transcriptome in single cells is critical to obtain a deeper and more precise understanding of disease heterogeneity and novel disease mechanisms. Based on the significant add-on grant, SIC was able to acquire the advanced equipment for single cell analysis presently available to conduct state-of-the-art single cell analysis in the key areas of the research focus of SIC.

In 2020, SIC researchers will initiate research projects that include single cell analysis of skin in healthy individuals and patients with atopic and contact dermatitis, psoriasis and cutaneous T cell lymphoma.

The single cell sequencing equipment will be integrated into the existing Core Facility for Flow Cytometry, a core facility at the Department of Immunology and Microbiology (ISIM) with 8 years of experience in operating and supporting shared advanced equipment for users, both internally at SUND and externally. The facility, located on the 14th floor of the Mærsk Tower, has undergone construction to accommodate the new advanced equipment. The reconstructed facility will be launched at an official, open event on 6 May 2020 under its new name: Core Facility for Flow Cytometry and Single Cell Sequencing.

The equipment for single cell sequencing includes:
- ImageStream
- 10X System
- MiSeq
- NovaSeq
- Smaller support equipment
In 2019, SIC researchers:
- Delivered 93 teaching hours at bachelor’s and master’s degree level
- Conducted 282 exams at bachelor’s and master’s degree level
- Supervised 19 PhD students

Top three teaching programmes:
1. Immunology and Inflammation
2. Medicine
3. Human Biology

SIC invests heavily in training the next generation of immunologists. At the graduate level, SIC trains specialists in immunological and infectious diseases as a stepping stone for careers in academia or the life science industry. At bachelor’s and master’s degree level, SIC researchers provide teaching in basic and advanced immunological skills to a range of educational programmes within health and medical sciences. As a result of the inauguration of SIC, a new elective course focusing especially on the immunology of the skin will open in spring 2020.

Tengpeng Hu
Thesis: Kv1.3 Potassium Channel in Cutaneous T-cell Lymphoma
Next destination: PhD Tengpeng Hu pursues a clinical career as a medical doctor in China.

Edda Blümel
Thesis: Staphylococcal alpha-toxin selects for malignant cells in cutaneous T-cell lymphoma
Next destination: PhD Edda Blümel pursues an academic career in Germany.

Anne-Sofie Østergaard Gadsbøll
Thesis: Epidermal T cells – Studies on distribution and activation
Next destination: PhD continues her academic career as a postdoc at SIC.

Sanne Steengaard Meisser
Thesis: Allergic contact dermatitis to para-phenylenediamine and the immunology involved
Next destination: PhD Sanne Steengaard Meisser pursues an academic career in Switzerland.

Graduate programme in Immunology and Infectious Diseases

The research programme in Immunology and Infectious Diseases was established in 2006 to promote excellent research at the PhD level within these specific fields. The students choose training courses within the area of immunology. The students also receive training in research methods and techniques such as microscopy, flow cytometry and cell sorting and laboratory animal science needed to conduct their concurrent and independent thesis project in the laboratory. Every year, the programme hosts an annual meeting with Danish and international expert speakers. At the end of the three-year programme, the students defend their thesis to be awarded the PhD title.

Education and career development
SKIN IMMUNOLOGY COURSE

From spring 2020, SIC offers a new elective course in Skin Immunology (7.5 ECTS). Here, students at the Master in Immunology and Inflammation programme will get a deeper understanding of the immunology of the body’s largest organ, the skin. Students will be taught immunology of healthy and diseased skin, including the response to infections and allergens, in autoimmunity and upon wounding of the skin. The course in Skin Immunology will be a mixture of lectures, case studies and student interactive teaching.

TEACHING THEMES
- Structure and cells of healthy and diseased skin
- Skin infections
- Wound healing of the skin
- How to investigate the immune system of healthy and diseased skin
- Skin diseases – immunology, prevention and treatment

METHODS
- Lectures
- Student presentations
- Case-based teaching
- Quizzes

MASTER OF SCIENCE IN IMMUNOLOGY AND INFLAMMATION

The Master of Science in Immunology and Inflammation was added at the University of Copenhagen in 2017. The Master is unique in Europe as it is the only Master in Immunology taught in continental English, making it a highly coveted international programme. Each year, approximately 30 students of more than 10 nationalities are enrolled in the programme. The students receive mandatory training in advanced immunology involving infectious immunology, tumour immunology and immunological diseases. In addition, the students can choose between various elective courses. The last year of the programme is spent in the laboratory where the students complete their master’s thesis project.

In 2019, SIC supervised 13 master’s thesis students – nine students from the Master of Science in Immunology and Inflammation programme and four students from other master’s programmes.

SUMMER SCHOOL 2020

SIC has invited young and talented researchers from across the world to join an intense three-day learning experience on skin and immunological skin disease research at its first international Summer School on 20–22 April, 2020. The Summer School offers 1:1 interaction with and feedback from 14 leading experts on ‘The Skin Barrier’ as the main theme of the year. SIC intends for the Summer School to grow into an annual flagship learning opportunity for the next generation of skin immunology researchers.

14 EXPERT SPEAKERS
- Liam O’Mahony, National University of Ireland
- Padraic G. Fallon, Trinity College Dublin
- Tiffany C. Scharschmidt, University of California, San Francisco
- John E. Common, Skin Research Institute of Singapore
- Sanja Kezic, Academic Medical Center, Amsterdam
- Cezmi A. Akdis, SIAF, University of Zurich
- Mads Gyrd Hansen, University of Oxford
- Muzlifah Haniffa, Newcastle University
- Liv Eidmo, Karolinska Institutet
- Michael Rosenblum, University of California, San Francisco
- Bernhard Homy, University of Duesseldorf
- Mübeccel Akdis, SIAF, University of Zurich
- Niels Ødum, SIC, University of Copenhagen
- Christian Antoni, LEO Pharma

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

SIC received 95 applications for participation in the 2020 Summer School. The applicants represented universities and hospitals in 21 countries.
Outreach and communication

SIC deliberately works on the basis of four pillars of strategic communication and outreach. The communicative initiatives highlight the continued need for advances in skin disease research and disseminate research results to our large network of collaborators. In 2019, SIC also opened its doors to delegation visits and guest lectures to spark 1:1 dialogue.

The inauguration SIC – with participation by His Royal Highness Prince Joachim – provided a unique opportunity in 2019 to promote SIC and its ambition of being an international research powerhouse for research in skin diseases and immunology. In the Danish media, the inauguration put the spotlight on SIC and its research. This included articles in national papers such as Berlingske, Kristeligt Dagblad and Information, with additional publicity through both MedWatch and Science Report and culminating in a spot on the local network TV2 Lorry. Add to this, exposure on SoMe, where SIC had massive outreach through the websites of The Royal House and the University of Copenhagen as well as the LEO Foundation’s digital platforms.

As for research dissemination, SIC has made use of SoMe, press liaisons and videos. This led to international acclaim in Science Daily, ScienMag and News Medical as well as posts on EurekAlert and Futurity. Another great outreach success in 2019 was the participation in the Bloom nature and science festival, in which SIC intrigued audiences and coined 2020 as the launch of ‘The Decade of the Skin’. In 2019, SIC’s ‘Join us’ webpage expanded significantly, set to work together with employer branding training of researchers and recruitment campaigns at LinkedIn.

In 2020, strategic initiatives will support the recruitment of a new executive director and the continued recruitment of talented researchers and students. Additional communication efforts will be made to establish SIC as a visible public voice on skin, skin diseases and immunology – including the use of an explanatory long read on skin and skin disease, the continued use of social media and research dissemination via national and international media.

Find us on social media

**TWITTER**
@skinucph

**LINKEDIN**
LEO Foundation Skin Immunology Research Center

The four pillars of SIC’s communication and outreach strategy

**COMMUNICATION PILARS**

- Establish digital platforms
- Train ambassadors
- Stakeholder collaboration
- Research dissemination

DELEGATION VISITS
- DIS – Danish Institute for Study Abroad students’ groups
- LEO Pharma units and leadership
- Cambridge University
- Healthcare Denmark – international healthcare ambassadors

INVITED GUEST LECTURERS
- Research Associate Emma Chambers, University College London
- Associate Professor Mads Gyrld-Hansen, University of Oxford
- Associate Professor Marta Polak, University of Southampton
- Professor Mariusz Wasiak, Fox Chase Cancer Center
- Professor Vincenzo Bronte, Verona University
- Professor Mübeccel Akdis, University of Zurich
- Professor Susan Bates, Colombia University
- Associate Professor Amanda MacLeod, Duke University

His Royal Highness Prince Joachim attended the inauguration of SIC in February 2019. The event created a unique opportunity to promote SIC’s ambition to become a world leader in skin and skin disease research.
Funding and awards

SIC was awarded DKK 400 million from the LEO Foundation for centre 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 79 million in 2019. In addition, SIC acquired single cell sequencing equipment at a value of DKK 417 million in new funding from six external research grants.

<table>
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<tr>
<th>EXTERNAL RESEARCH GRANTS AWARDED IN 2019</th>
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<td>FUNDER</td>
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<td>The A.P. Møller Foundation for the Advancement of Medical Science (Fonden til Langevidenskabens Fremme)</td>
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<td>The Aase and Ejnar Danielsen Foundation</td>
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Scientific output

SIC researchers authored 25 scientific publications in peer-reviewed journals in 2019. Bibliometric data of senior scientists and publications of the year are listed here.

Sources: Web of Science, Scopus

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<th>H-INDEX OF SENIOR SCIENTISTS</th>
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<tr>
<td>RESEARCHER</td>
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<tr>
<td>Professor Anders Woetmann</td>
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<td>Professor Carsten Geisler</td>
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<td>Professor Charlotte Menné Bonefeld</td>
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<td>Professor Niels Ødum</td>
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<td>Associate Professor Thorbjørn Krejsgaard</td>
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<td>Antibiotics inhibit tumor and disease activity in cutaneous T-cell lymphoma</td>
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<tr>
<td>Anti-regulatory T cells are natural regulatory effector T cells</td>
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<tr>
<td>Ødum N. Cell Stress. 2019 Oct 8;3(10):310-311. (Not yet available)</td>
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<tr>
<td>Clinical and Histological Characteristics of Mycosis Fungoides and Sézary Syndrome: A Retrospective, Single-centre Study of 45 Patients from Eastern Denmark</td>
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</table>
Inflammation induced PD-L1-specific T cells

Cell Stress. 2019 Sep 13;10(9):319-327. (Not yet available)

Low SATB1 Expression Promotes IL-5 and IL-9 Expression in Ségaz Syndrome


Mice with epidermal filamentin deficiency show increased immune reactivity to nickel
Petersen TH, Jee MH, Gadsbøll AD, Schmidt JD, Sloth JJ, Sonnenberg GF, Geisler C, Thyssen JP, Bonefeld CM.

Contact Dermatitis. 2019 Mar;80(3):129-138. 2.46

OMIP-037: Mouse Y T-Cell Development Characterized by a 14 Color Flow Cytometry Panel
Buus TB, Jee MH, Ødum N.

Cytometry A. 2019 Jul;95(7):726-729. 3.43

Pathogenic CD8+ Epidermis-Resident Memory T Cells Displace Dendritic Epidermal T Cells in Allergic Dermatitis


Peptidylarginine deiminase-4 gene polymorphisms are associated with systemic lupus erythematosus and lupus nephritis
Massarenti L, Enevold C, Damgaard D, Ødum N, Nielsen CH, Jacobsen JD.


Skin barrier damage after exposure to para-phenylenediamine
Meisser J, Altmunialaki C, Bandier J, Opstrup MS, Castro-Giner F, Akdim M, Bonefeld CM, Johansen JD, Akdim CA.


Skin tape stripping: Which layers of the epidermis are removed?
Selberg J, Ulrich NH, Krustrup D, Aalstrøm MG, Thyssen JP, Menné T, Bonefeld CM, Gadsbøll AD, Bølløv E, Johansen JD.

Contact Dermatitis. 2019 May;80(5):319-321. 2.46

Staphylococcal alpha-toxin tilts the balance between malignant and non-malignant CD8+ T cells in cutaneous T-cell lymphoma

Oncomunology. 2019 Jul 17;8(11):e1641387. 4.91

STAT-3 Dysregulation in Mature T and NK Cell Lymphomas
Seiffens A, Herrerra A, Tegla C, Buus TB, Hymes KB, Ødum N, Geskin LJ, Korolov SB.


The Escherichia coli protein toxin cytotoxic necrotizing factor 1 induces epithelial mesenchymal transition

Cell Microbiol. 2019 Nov 7;21(13):4.06

The functional interlink between AR and MMP9/VEGF signaling axis is mediated through PIP5K1α/PKR in prostate cancer


The MicroRNA Expression Profile Differences Between Erythromyeloid Mycosis Fungoides and Sézary Syndrome

Acta Derm Venereol. 2019 Nov 19;109(12):1148-1153. 3.53

The role of PIP5K1α/PKR and targeted inhibition of growth of subtypes of breast cancer using PIP5K1α inhibitor


The Skin Reservoir Model: A Tool for Evaluating Microdialysis Sampling of Large Biomarkers from Human Skin
Baumann K, Falkencreme S, Krudsen NP, Woetmann A, Dabelsteen S, Skov PS.

Acta Derm Venereol. 2019 Oct 18. 3.53

Tumor necrosis factor induces rapid down-regulation of TNF1 in human T cells


Increase in Vitamin D but not Regulatory T Cells following Ultraviolet B Phototherapy of Patients with Atopic Dermatitis
Simonsen S, Bonefeld CM, Thyssen JP, Geisler C, Skov L.

Acta Derm Venereol. 2019 Feb;99(2):139-145. 3.53
Full staff list

PROFESSORS
- Charlotte Menné Bonefeld
- Carsten Geisler
- Anders Woetmann
- Niels Ødum

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- Andreas Willerslev-Olsen
- Claudia Nastasi
- Emil Marek Heymans Fallesen
- Nicolai Skovbjerg Arildsen
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- Cheng Chi
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- Mia Hamilton Jee
- Veronica Mraz
- Eileen Donohue
- Katrine Yderstraede Baumann
- Laura Massarenti
- Lukas Peiffer
- Maria Giud Grendahl
- Maria Teresa Martin Monreal
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- Oliver Krigslund
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- Sara Torres Rusillo

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- Gustav Øring Jørgensen

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- Søren Vester Kofoed
- Chella Krishna Vadhivel
- Lisa Harth
- Siri Svarre Haselager

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- Julie Weber Friis
- Sana Ahmad

ADMINISTRATION
- Nils Erik Samdal
- Mette Malene Odgaard
- Bitten Dalsgaard

By the end of 2019, SIC engaged a total of 45 staff members and students of 14 different nationalities in its two basic research groups.