



# Strategy 2020 and annual report

Focused Research Unit for Molecular Diagnostic and Clinical Research (MOK)-Vibeke Andersen's group  
IRS-Center Soenderjylland  
University Hospital of Southern Denmark

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## Welcome

This report provides a snapshot of the research that has been performed in the Focused Research Unit for Molecular Diagnostic and Clinical Research (MOK) – Vibeke Andersen's group in 2019. The report presents the people, projects, grants achieved and activities in 2019.

Importantly, we also present plans as well as expectations for the coming years.

The overall aim of the health care system is to normalize the quality of lives of patients and to prevent healthy individuals from becoming ill. As we move into 2020 we will maintain this focus on multidisciplinary collaboration in order to produce results that support this aim.

Vibeke Andersen

Professor and Research Leader

## **MOK-Vibeke Andersen's group**

Focused Research Unit for Molecular Diagnostic and Clinical Research (MOK) is organized with a steering committee, a research leader, and two research groups. Senior Consultant, associate professor Ming Chen is the leader of the research group focusing on microbiology and Professor Vibeke Andersen is the leader of the group focusing on chronic inflammatory diseases. This is the annual report of Vibeke Andersen's (MOK-VA) research group.

MOK-VA is a part of the Biochemical and Immunological Department of the Hospital of Southern Jutland (SHS), the IRS-Center Soenderjylland, Institute of Regional Health Research, University of Southern Denmark, and the Institute of Molecular Medicine, University of Southern Denmark. The hospital is a part of the University Hospital of Southern Denmark and includes all of the hospitals in the Region of Southern Denmark.

## Vision

Our vision is to produce research results that support the health care system, normalize the quality of lives of patients and prevent healthy individuals from becoming ill.

Inflammation is involved in a wide variety of mental and physical health problems that dominate morbidity and mortality worldwide. In fact, more than 50% of all deaths can be attributed to chronic inflammatory diseases such as autoimmune conditions, ischemic heart disease and diabetes mellitus and several others<sup>1</sup>.

The vision and goal of our research group is to improve the health and the quality of life of patients suffering from chronic inflammatory diseases. We focus specifically on inflammatory bowel disease, rheumatic arthritis, psoriatic arthritis, spondylarthritis and psoriasis. These are common diseases affecting many people for long periods of their lives. Our aim is to produce evidence-based tools for diagnosis, prediction of prognosis, selection of treatment strategy and prevention of these chronic inflammatory diseases. Importantly, this may include disease reclassification taken the heterogeneity of many chronic diseases into account.

A “tool” with great potential is the framework of “Personalised Medicine”. *“Personalised medicine uses information specific to an individual to target therapeutic and prevention strategies more accurately, putting citizens and patients at the center of healthcare and innovation. Recent developments in areas such as molecular profiling, medical imaging, and diagnostics are making PM a reality in healthcare.”*<sup>2</sup>

As a result of massive investments from the EU and other funders, personalized medicine is already a reality within the treatment of many cancer diseases and will extend to many other common diseases within the next few years. However, a large challenge is that personalized medicine often does not reach all relevant patients. It is estimated that only 20% of those who will benefit from treatment are reached<sup>2</sup>.

We want to change this.

In order to reach real improvements for patients, collaboration is vital. Collaboration need to occur on many different levels including with patients and their carers in order to understand needs; transdisciplinary collaboration to achieve in-depth understanding of disease mechanisms necessary for providing evidence-based information and for translation of research results to clinical use; national and international collaboration in order to achieve high levels of research, adequate funding, and a sufficient number of well-characterized patients for investigation.

We have international, national, regional, and local collaboration partners. For example, we are a partner of the EU funded consortium SYSCID (syscid.eu) initiated in 2017, aimed at improving the treatment of chronic diseases. Furthermore, we are a partner of the regional IBD-CARE group, situated at the University Hospital of Southern Denmark (SHS), receiving funding from the region of Southern Denmark in 2018 and 2019. We also take part in the working group PreMedico at Odense University Hospital in order to implement personalized medicine on a more local level.

Thus, we are in line with the European and national strategies for personalized medicine; 1) “The International Consortium for Personalised Medicine<sup>3</sup>” - a platform of over 30 European and international partners representing ministries, funding agencies, and the European Commission, 2) “Personalised

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<sup>1</sup> Furman, D., et al., *Chronic inflammation in the etiology of disease across the life span*. Nat Med, 2019. 25(12): p. 1822-1832.

<sup>2</sup> ICPeMed ActionPlan, icpermed.eu

<sup>3</sup> “The International Consortium for Personalised Medicine”, ICPeMed, icpermed.eu

Medicine for the Benefit of Patients” - The Danish National Strategy For Personalised Medicine 2017-2020 and 3) “Et sygehus, der forsker, er et sygehus, der forbereder sig på fremtiden”<sup>4</sup> - the local hospital.

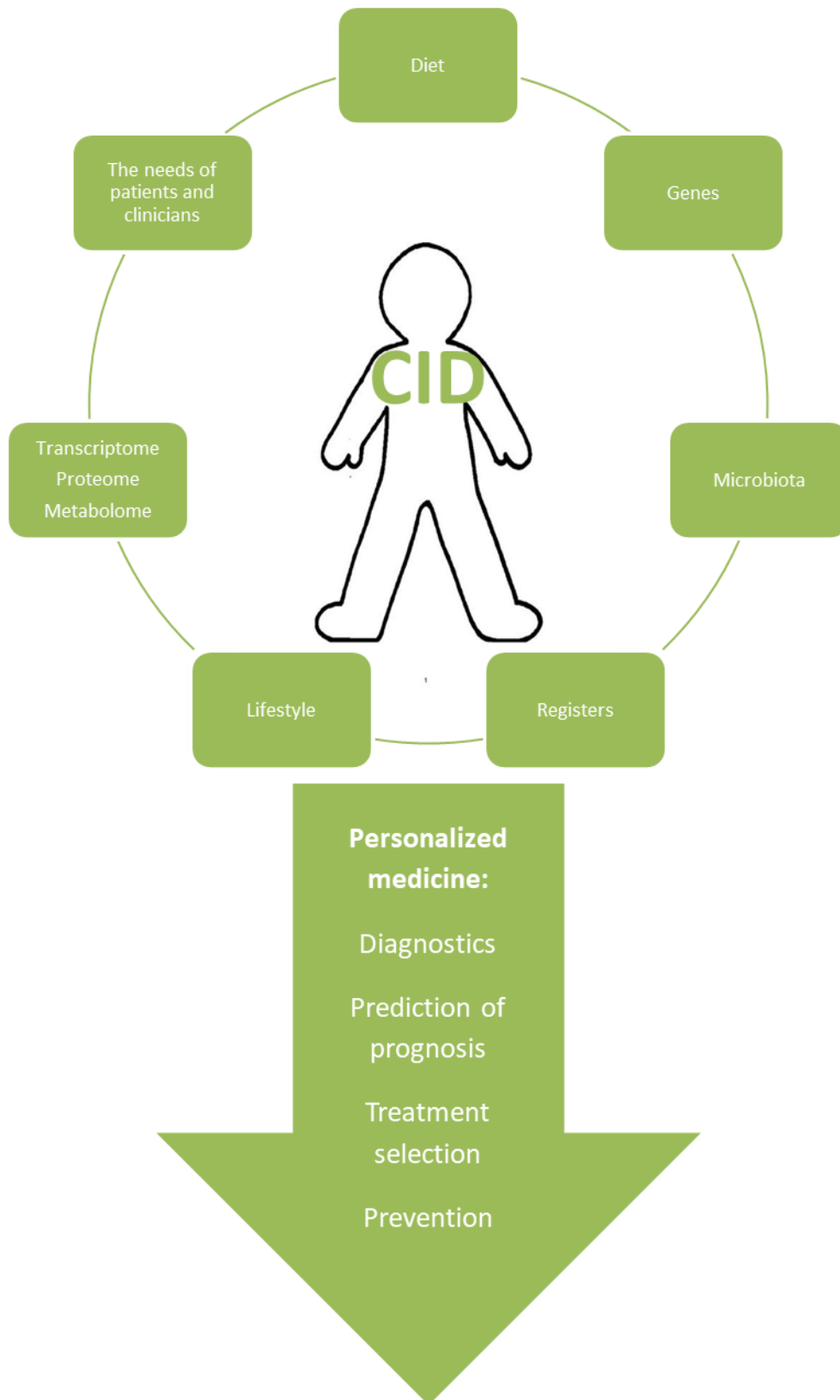
We have have many projects within the framework of personalised medicine. Our four largest projects include BELIEVE, TARCID, TWIBD and NORDTREAT (see description on page 12-13).

In summary, our vision is to create research that can help prevent the development of chronic inflammatory diseases among the citizens and normalize the quality of life of the patients within and outside the Region of Southern Denmark. Research at a high international level is needed to produce results that can be translated into clinical and/or preventative purposes.

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<sup>4</sup> “A hospital performing research is preparing for the future” from the hospital research strategy (Sygehus Sønderjylland Forskningsstrategi 2018-2019)

## The patient centered research approach in MOK



**Figure.** Overview of our patient-centered research approach (\*CID: chronic inflammatory diseases which include IBD, rheumatoid arthritis, psoriatic arthritis, spondylarthritis and psoriasis)

## Who are we? – members of MOK

- **Signe Bek Sørensen**, Post. doc., Molecular Biologist  
Signe.Bek.Sorensen@rsyd.dk  
Signe works as a project leader and coordinator and is associated with almost every project in the research group.  
**Projects:** TARCID, BELIEVE, NORDTREAT, TWIN Study, sCRC
- **Steffen Bank**, Post. Doc., Molecular Biologist  
Steffen.Bank@rsyd.dk  
**Project:** TARCID
- **Tina Jean Larsen**, Lab Technician  
Tina.Larsen1@rsyd.dk
- **Mohamad Jawhara**, PhD student, Medical Doctor  
Mohamad.jawhara@rsyd.dk  
**Project:** BELIEVE (controls)
- **Silja Hvid Overgaard**, PhD student, Cand. Scient. in Human Nutrition  
Silja.Hvid.Overgaard@rsyd.dk  
**Project:** BELIEVE
- **Nathalie Fogh Rasmussen**, PhD student from primo 2020, Cand. Scient. San. Publ.  
Nathalie.Fogh.Rasmussen@rsyd.dk  
**Project:** R-IBD
- **Agnete Donskov Overgaard**, young researcher, medical doctor  
**Project:** R-IBD
- **Vibeke Andersen**, Professor, Research leader and Medical Doctor.  
va@rsyd.dk  
Main PhD supervisor for Mohamad, Silja and Nathalie  
Co-supervisor for 6 additional PhD students

### Associated Professor

**David Ellinghaus**, Associate Professor, Bioinformatician, Geneticist.

### Associated from the hospital

**Majbritt Petersen**. Assistant at the Department of economy, planning, and communication.

**Idriz Katana**. Systems Administrator.

### The leader of the Biochemical Department

**Susan Cording**, Leader of the Biochemical Department.



## Current Student projects

- **Caroline Moos.** Pregraduate student, Master of Science in public health  
[caroline.moos@rsyd.dk](mailto:caroline.moos@rsyd.dk)  
*'Prenatal exposure to Vitamin D and the risk of Coeliac Disease'.*

### Associated pregraduate project:

- **Katrine Duus.** Pregraduate student, master in public health  
[katrinesideniusduus@gmail.com](mailto:katrinesideniusduus@gmail.com)  
*'Prenatal exposure to vitamin D and risk of Inflammatory Bowel Disease'.*

## PhD and student projects finalized in 2019

### PhD projects:

- **Lina Almind Knudsen, M.Sc. Human biology, Ph.D. student**  
*'Identification of components in the gut microbiota with effects on inflammation in the gut'.*

### Student projects:

- **Emma Olivia Schultz Harringer, BSc.med.**  
*'Gluten's effect on Ulcerative Colitis'.*
- **Nathalie Fogh Rasmussen, Pre-graduate student in Public Health at Aarhus University**  
*'Impact of leisure time physical activity on risk of late-onset chronic inflammatory bowel disease: a prospective cohort study on prognostic factors using the Danish "Diet, Cancer and Health" cohort'.*
- **Catalina Christensen, Pre-graduate student, Bachelor in biochemistry and molecular biology**  
*'Nutritional effects on the microbiome and the development of inflammatory bowel diseases'.*
- **Lea Gleie, Pregraduate student, master in public health.**  
*'Feasibility of a cohort study on sleep quality and the impact on quality of life in patients with colitis ulcerative disease'.*

## Collaboration

# Collaboration Partners

International Partners, Research Consortia	National Partners	University of Southern Denmark (SDU)	Regional Partners	Local Partners at the Hospital	Private Partners	Individual Researchers
<ul style="list-style-type: none"> <li>• ibdgc (ibdgenetics.org)</li> <li>• icpermed (icpermed.eu)</li> <li>• igenomed (medgeni.org/projects/igenomed)</li> <li>• SYSCID (syscid.eu)</li> <li>• EPIC-IBD (epic.iarc.fr/)</li> <li>• ECCO (ecco-ibd.eu)</li> <li>• NORDTREAT</li> </ul>	<ul style="list-style-type: none"> <li>• Medical / gastroenterol Dept</li> <li>• Rheumatol Dept</li> <li>• Dermatol Dept</li> <li>• Biochem Dept</li> <li>• University of Aarhus (AU)</li> <li>• University of Copenhagen (KU)</li> <li>• University of Aalborg (AAU)</li> <li>• Technical University of Denmark (DTU)</li> <li>• University of Roskilde (RUC)</li> </ul>	<ul style="list-style-type: none"> <li>- Institute of Regional Research (IRS)</li> <li>- Institute of Molecular Medicine (IMM)</li> <li>- Epidemiology, Biostatistics and Biodemography (EBB)</li> <li>- Odense Patient data Explorative Network (OPEN)</li> </ul>	<ul style="list-style-type: none"> <li>• Odense University Hospital (OUH)</li> <li>• Hospital of Southwest Jutland (SVS)</li> <li>• Hospital Lillebaelt (SLB)</li> <li>• Alsion</li> <li>• PREmedico Working Group</li> <li>• IBD-CARE working group</li> </ul>	<ul style="list-style-type: none"> <li>• Medical Research Unit</li> <li>• Focused Research Unit within Acute Medicine</li> <li>• Focused Research Unit within Neurology</li> <li>• Focused Research Unit within Rheumatology</li> </ul>	<ul style="list-style-type: none"> <li>• Nordic Bioscience</li> <li>• The Cancer Institute (Kræftens Bekæmpelse)</li> </ul>	<ul style="list-style-type: none"> <li>• Professor Jack Satsangi, Oxford</li> <li>• Professor Andre Franke, Kiel</li> <li>• Professor Stefan Schreiber, Kiel</li> <li>• Professor Marcus Harbord, London</li> <li>• Ass. Professor Jonas Halfvorsson, Örebro</li> <li>• Professor Ulla Vogel, Copenhagen</li> <li>• Professor Gordon Lauc, Zagreb</li> </ul>

## Research projects in MOK

**BELIEVE** – A prospective cohort study of prognostic factors and personalized medicine in chronic inflammatory diseases. The aim is to identify lifestyle factors and biomarkers that may improve the outcome of targeted therapy. Collaboration partners include SYSCID, Danish medical, gastroenterological, rheumatological, and dermatological departments. The national recruitment of patients is on-going but is expected to be finalized in summer 2020. The recruitment of control patients (referred to endoscopy for other reasons than IBD) has been finalized, and analysis on e.g. mucosal thickness in relation to diet is on-going (Mohamad Jawhara).

**TARCID** - Predicting the outcome of targeted therapy in chronic inflammatory diseases. Genetic analysis of more than 8.000 patients and 100.000 controls with the aim of identifying molecular markers that can predict the expected outcome from targeted therapy in the individual patient. Collaboration partners include partners from Region Sjælland and Kiel, as well as DECODE (Reykjavik), PercisionLife, Danbio, Dermbio, Danish medical departments, laboratories, and research groups from Korea and Austria among others.

**TWIBD** – A working group aiming at understanding the interaction of diet, gut microbes and disease mechanisms investigating clinical and biological material from our cohort of identical twins whereof one has IBD. Furthermore, a mouse IBD model is produced based on transferring the feces from the identical twins (one with IBD and one without) to the mice. In 2020, we will focus on characterizing the gut microbiota from identical twins with and without IBD. Metagenom-analyses will be carried out in addition to analyses on the viral component on the suspicion that it controls some of the processes between the host and the microbiome. Furthermore, we will analyse the microbiome of saliva to investigate whether certain enzyme-producing bacteria are involved in the development of IBD for a subgroup of the patients.

**NORDTREAT** – A clinical study evaluating a biomarker aimed at stratifying Inflammatory Bowel Disease patients according to their need for intensive medical treatment. Funded by Nordforsk. A collaboration between Nordic countries.

**IBD-CARE** - A working group of clinicians and researchers in the Region of Southern Denmark working with inflammatory bowel disease. The aim is to improve the lives of the patients through research and implementation of evidence-based tools in a clinical setting. Collaboration partners include OUH, SDU, SVS, SLB.

**IBD-register (New)** - We are in the process of developing an IBD-register in our research unit. Coming PhD student Nathalie Fogh Rasmussen will be the coordinator for this project. One aspect of the project is to examine the information which forms the basis for the decision regarding IBD patients according to registries (which data is available for clinicians when making decisions on personalised medicine; diagnosis, treatment decisions, treatment shift etc ). Dr. Agnete Overgaard Donskov from the medical department at the hospital is affiliated with this project along with with researchers from SDU (Professor Lau Caspar Thygesen, Kim Rose Olsen and Professor Anders Green).

**IBD-SUR-TCR** – Trying to find a specific mechanism underlying Inflammatory Bowel Disease (IBD) in similarity with gluten in coeliac disease. Collaboration partners IBD-CARE and Kiel.

**SYSCID** – A Systems medicine approach to chronic inflammatory diseases (syscid.eu). The SYSCID consortium aims to develop a systems medicine approach for predictions in chronic inflammatory diseases (CID). The

overall goal is to create a prediction framework for disease outcome to guide therapy decisions on an individual patient level enabling the choice of the right therapy at the right time. Furthermore, the SYSCID consortium targets new therapy approaches by “reprogramming” disease through epigenome editing. The SYSCID consortium consists of 15 partners from Europe.

**PROCID** - Prospective cohort studies of prognostic factors in CIDs. The aim is to identify lifestyle factors involved in developing chronic inflammatory diseases and to evaluate the underlying biological mechanisms through gene-environment interaction analyses. Collaboration partners are the Danish Cancer Society, UKBiobank, SDU (Epidemiology, Biostatistics, and Biodemography, OPEN), Kiel among others.

**IIBDGC** – An International study group of GWAS study of IBD patients with the aim of identifying underlying genetics and thereby disease mechanisms in IBD.

**EPIC-IBD** – An international working group aiming at identifying factors involved in developing IBD.

**Abcb1**- A working group aiming at identifying factors involved in disease mechanisms in IBD using a mouse IBD model fed red meat. Collaboration partners Aalborg and Copenhagen universities.

**PIG IBD model** - A working group that has established a pig IBD model. The model has been used for identifying factors involved in disease mechanisms in IBD model when fed red meat. The model is intended for future evaluation of treatment strategies of IBD. Collaboration partners: Aarhus and Copenhagen universities.

**CRC-GxE** – A working group identifying underlying mechanisms for the development of colorectal cancer by investigating gene-environment interactions on the prospective “Diet, Cancer and Health” cohort owned by the Danish Cancer Society.

**sCRC** – A working group investigating the effect of the screening program for Colorectal Cancer (sCRC) and searching to identify biomarkers in the fecal samples that may improve the program. The project is funded by the PROCRIN and Region of Southern Denmark.

## Plans for the coming 5 years

- **Collaboration**

- *Within the Region of Southern Denmark (RSD)*

We want to contribute to the further development of collaboration between different entities in the region and the university with a focus on translational research within the common diseases in the region specifically chronic inflammatory diseases, via e.g. the IBD-CARE group. The IBD-CARE group are composed of clinicians and researchers from the Region of Southern Denmark with the aim of integrating the fast translation of evidenced-based knowledge and tools into clinical use using inflammatory bowel disease as a model disease for chronic inflammatory diseases. IBD-CARE received funding for an additional year at the end of 2019 and will apply for a further 5 year funding in 2020.

- *At the University Hospital of Southern Denmark-Soenderjylland*

There will be a greater focus on research collaboration within the hospital, and on smaller projects. We want to contribute to develop and expand the research at the hospital, including the development of the research facilities, which will also help in the fulfilment of our new responsibilities of supervising the projects of more masters student. Furthermore, improving the research facilities will help recruit and maintain qualified staff.

Our goal is to increase interaction with clinicians whom will be affiliated with our research unit and have the resources to do research. A basis has been established with the the gastroenterological, surgical and medical departments as well as with rheumatologists from the Danish Gigt hospital (Det Danske Gighthospital). This focus aligns well with the main themes of the research strategy of RSD ("Research for the clinic").

- *International*

We will maintain and develop relationships and collaboration with our international partners in order to secure high-level research. E.g. we are a member of the SYSCID consortium which is an EU funded project within personalized medicine which runs until the end of 2021. This project is financing BELIEVE. Furthermore, NORDTREAT is a collaboration within the Nordic countries.

- *Transdisciplinary*

We will continue to work transdisciplinary in order to secure high quality and in-depth knowledge. Thus, we collaborate with clinicians, patient organisations, pre-clinical research units, molecular biologist, etc. In fact, this transdisciplinary approach is also reflected in our own research unit.

- **Development of the research unit**

There is a continuous focus on developing the research unit. The vision is to expand the group, thus creating a greater critical mass of qualified researchers for scientific discussions and mutual personal and professional development.

- **Involvement of the end-users of the research results**

In the research strategy of the Region of Southern Denmark a main theme is "Research for the patient" – it is important to make sure that we do research on topics that are important for the patients. We have collaborated with the Colitis-Crohn Association, the Psoriasis Association, and the Danish Patient Association for several years and we will work to continuously involve patient organisations etc. in the planning of future projects.

MOKs project proposal for the annual RSD competition (“SUND i SYD”) is a citizen science project, where the citizens are involved in defining the relevant research questions and execution of the project.

## Publications in 2019

[http://findresearcher.sdu.dk/portal/da/persons/vibeke-andersen\(13a7e111-7511-412b-9e1e-4c3bc8982e21\)/publications.html?filter=research](http://findresearcher.sdu.dk/portal/da/persons/vibeke-andersen(13a7e111-7511-412b-9e1e-4c3bc8982e21)/publications.html?filter=research)

1. Andersen, V., et al., *No Interaction between Polymorphisms Related to Vitamin A Metabolism and Vitamin A Intake in Relation to Colorectal Cancer in a Prospective Danish Cohort*. *Nutrients*, 2019. **11**(6).
2. Andersen, V., et al., *Intake of Red and Processed Meat, Use of Non-Steroid Anti-Inflammatory Drugs, Genetic Variants and Risk of Colorectal Cancer: A Prospective Study of the Danish "Diet, Cancer and Health" Cohort*. *Int J Mol Sci*, 2019. **20**(5).
3. Bank, S., et al., *Polymorphisms in the NFkB, TNF-alpha, IL-1beta, and IL-18 pathways are associated with response to anti-TNF therapy in Danish patients with inflammatory bowel disease*. *Aliment Pharmacol Ther*, 2019. **49**(7): p. 890-903.
4. Burisch, J., et al., *Natural Disease Course of Ulcerative Colitis During the First Five Years of Follow-up in a European Population-based Inception Cohort-An Epi-IBD Study*. *J Crohns Colitis*, 2019. **13**(2): p. 198-208.
5. Burisch, J., et al., *Disease course of inflammatory bowel disease unclassified in a European population-based inception cohort: An Epi-IBD study*. *J Gastroenterol Hepatol*, 2019. **34**(6): p. 996-1003.
6. Campa, D., et al., *Genetic polymorphisms in genes of class switch recombination and multiple myeloma risk and survival: an IMMEnSE study*. *Leuk Lymphoma*, 2019. **60**(7): p. 1803-1811.
7. Canet, L.M., et al., *Polymorphisms at phase I-metabolizing enzyme and hormone receptor loci influence the response to anti-TNF therapy in rheumatoid arthritis patients*. *Pharmacogenomics J*, 2019. **19**(1): p. 83-96.
8. Canet, L.M., et al., *Correction: Polymorphisms at phase I-metabolizing enzyme and hormone receptor loci influence the response to anti-TNF therapy in rheumatoid arthritis patients*. *Pharmacogenomics J*, 2019. **19**(6): p. 582.
9. Jawhara, M., et al., *Biomarkers of Whole-Grain and Cereal-Fiber Intake in Human Studies: A Systematic Review of the Available Evidence and Perspectives*. *Nutrients*, 2019. **11**(12).
10. Kirov, S., et al., *Degradation of the extracellular matrix is part of the pathology of ulcerative colitis*. *Mol Omics*, 2019. **15**(1): p. 67-76.
11. Rasmussen, N.F., et al., *Impact of red meat, processed meat and fibre intake on risk of late-onset chronic inflammatory diseases: prospective cohort study on lifestyle factors using the Danish 'Diet, Cancer and Health' cohort (PROCID-DCH): protocol*. *BMJ Open*, 2019. **9**(3): p. e024555.
12. Rosati, E., et al., *Identification of disease-associated traits and clonotypes in the T-cell receptor repertoire of monozygotic twins affected by inflammatory bowel diseases*. *J Crohns Colitis*, 2019.
13. Skyum, F., et al., *Risk factors for contagious gastroenteritis in adult patients with diarrhoea in the emergency department - a prospective observational multicentre study*. *BMC Infect Dis*, 2019. **19**(1): p. 133.
14. Walker, G.J., et al., *Association of Genetic Variants in NUDT15 With Thiopurine-Induced Myelosuppression in Patients With Inflammatory Bowel Disease*. *Jama*, 2019. **321**(8): p. 773-785.

## Activities in 2019

16<sup>th</sup> of January, Seminar, Aabenraa

5<sup>th</sup>-7<sup>th</sup> of February, Wellcome Trust, Immunogenomics of Disease: Accelerating patient benefit, Cambridge

3<sup>rd</sup>-5<sup>th</sup> of April, Symposium SYSCID, Croatia

23<sup>rd</sup> -30<sup>th</sup> of May, Visit Prof. Susan Lynch, UCLA, California University, The DARE program, San Francisco

6<sup>th</sup> of June, PhD thesis defence, Bergen

9<sup>th</sup> of June, PhD thesis defence, Aabenraa

11<sup>th</sup> and 12<sup>th</sup> of September, SYMPOSIUM NORDTREAT, Ørebro

17<sup>th</sup> and 18<sup>th</sup> of September, Symposium NORDFORSK, Oslo

4<sup>th</sup> of October, PhD thesis defence, Copenhagen

12<sup>th</sup> and 13<sup>th</sup> of December, Symposium deCODE, Reykjavik

Autumn and winter: participation in the course "Effective Research by choice, Odense University Hospital



## **Presentations in 2019**

18<sup>th</sup> of september, Danske Bioanalytikere: Personlig Medicin

12<sup>th</sup> of December, deCODE, Reykjavik, Iceland: TARCID – predicting outcome from TARgeted therapy in Chronic Inflammatory Diseases; a Danish case-control study

## **Grants received in 2019**

The project NORDTREAT was granted funding from NORDFORSK (in total 30 mio S kr, 5 DKK mio for Denmark). The project is a collaboration between the Nordic countries and starts in September 2020.

The project IBD-CARE was granted 1 mio DKK.

The Region of Southern Denmark granted 927.300 DKK for a PhD project within BELIEVE.

Furthermore, “Knud and Edith Eriksens Mindefond” has granted a total of 75.000 DKK for projects in MOK.

## Contact

Please feel free to contact us if you are interested in hearing more about our research or if you are interested in collaboration.

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IRS-Center Soenderjylland  
University Hospital of Southern Denmark – Hospital Sønderjylland