

# The Hematology Research Unit



## Annual report 2021

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# Introduction

This is the first annual report from the Hematology Research Unit at the Department of Hematology, Odense University Hospital (OUH) and Department of Clinical Research, University of Southern Denmark (SDU).

The Hematology Research Unit was established in 2004 following the establishment of an independent Department of Hematology in 2002 by separation from the Department of Oncology, OUH. There has been a sustained development and growth of the Research Unit as described in the report. Some prior important milestones deserve to be high-lighted:

- 2010, Head of Research, Niels Abildgaard appointed clinical professor at SDU
- 2014, Hematology-Pathology Research Laboratory established in collaboration with the Pathology Department
- 2016, Molecular biologist, Charlotte Guldberg Nyvold appointed professor of molecular hematology at SDU and employed as Head of the Hematology-Pathology Research Laboratory
- 2017, Odense Amyloidosis Centre, AMYC OUH, hosted at the Department of Hematology and the Hematology Research Unit awarded Centre of Clinical Excellence by the Health Region of Southern Denmark
- 2017, the Quality of Life Research Center, QOL Research OUH, established at the Hematology Research Unit
- 2018, professor Madeleine King, Sydney University, appointed adjunct professor at SDU and QOL Research OUH, Hematology Research Unit
- 2018, Ole Weis Bjerrum, Copenhagen, appointed adjunct professor at SDU and the Hematology Research Unit
- 2018, Henrik Frederiksen, consultant hematologist appointed clinical professor at SDU

More recent news and achievements can be found in the report.

# Latest achievements in 2021

- Nana Hyldig, nurse, MSc, PhD, appointed associate professor in nursing at SDU and employed as senior researcher at the Department of Hematology
- Lene Granfeldt Østgaard, MD, consultant, PhD, appointed associate professor at SDU
- Henrik Eshøj, physiotherapist, PhD, and project leader at Quality of Life Research Centre OUH, appointed assistant professor at SDU
- We initiated our first "first-in-human" trial after an accreditation process by the national health authorities (Lægemiddelstyrelsen).
- 3 finalized PhD-studies in 2021 by
  - Emelie Rotbain, MD: "Comorbidity and survival in chronic lymphocytic leukemia"
  - Marcus Høy Hansen, MSc: *"Development of clinically applicable next-generation bioinformatics"*
  - Simone Valentine Hansen, MSc: *"Impact of molecular heterogeneity in B cell malignancies"*

Find the theses at <https://www.sdu.dk/en/forskning/haematologi/phd-projekter>

# About this report

We have managed to reach our major goals for research activity and production in 2021. The following pages summarize our

- Organization
- Research teams
- User Council for Research
- Clinical trial activity
- Research production
- Research granting
- PhD projects
- List of peer-reviewed publications in 2021

# Our organization

Our human resources in 2021 counted a total of 40 employees, including TAPs and named VIPs

- 3 professors Niels Abildgaard (head of Research), Henrik Frederiksen, Charlotte Guldborg Nyvold
- 5 associate professors (clinical lecturers) Thomas Stauffer Larsen, Thomas Lund, Claus Marcher, Duruta Weber, Lene Granfeldt Østgaard
- Associate professor in Nursing Research Nana Hyldig
- Assistant professor in Quality of Life Research Henrik Eshøj
- 2 adjunct professors Madeleine King and Ole Weiss Bjerrum
- 3 Post docs – Jakub Krejcik, Lene Kongsgaard Nielsen, Rikke Faebo Larsen
- 9 PhD students - hereof 3 finalizing their study in 2021
- Research coordinator/fundraiser Tine Rosenberg
- Specialist senior consultant Sally Grant
- 1 clinical nurse and 12 study coordinators, including daily manager Pia K. Pedersen
- 2 secretaries, including research secretary Vickie Svane Kristensen

# Plasma cell dyscrasia



The research team is headed by Professor Niels Abildgaard.

Primary research areas of the team are multiple myeloma, AL amyloidosis, and Waldenstrom macroglobulinemia. The research includes clinical research, basic laboratory research, and research within the fields of health-related quality of life, patient-reported outcome (PRO), and health economics.

Diagnostics and treatment of multiple myeloma bone disease and AL amyloidosis are areas of particular interest. Niels Abildgaard heads Odense Amyloidosis Centre, AmyC OUH, appointed as center of clinical excellence.

Senior researchers in the team are associate professor, consultant, PhD Thomas Lund; consultant, PhD Charlotte Toftmann Hansen, and staff specialist, PhD Ida Bruun Kristensen. Three PhD-studies are ongoing, and three part-time post docs are active within the team.

The team is represented in several academic study groups including the Danish Myeloma Study Group (DMSG), the Nordic Myeloma Study Group (NMSG), the European Myeloma Network (EMN), and the International Myeloma Working Group (IMWG). Through these collaborations, the department participates in several research protocols.



# Benign hematology and epidemiology

The team is headed by Professor Henrik Frederiksen.

Primary research areas of the team are frequency and complications of a variety of benign hematological diseases, including hemolytic anemias, congenital erythrocyte diseases, immune thrombocytopenia, and TTP. Moreover, age, comorbidity and complications of hematological cancer as well as risk of new cancer are studied. Randomized, controlled studies are conducted together with studies on Quality of Life. Other methods include mathematical modeling and artificial intelligence/machine learning (coming up).

Senior researchers in the team are MD, PhD Dennis Lund Hansen and MD, PhD Emelie Rotbain. Two PhD-studies and two pre-graduate projects are ongoing.

The team collaborates with national researchers and groups across Denmark within epidemiology, biostatistics, and hematology. International collaborations extend to France, Italy, Norway, Holland, UK, and USA. Through these collaborations, the department also participates in several clinical research protocols.



# Malignant lymphomas



MD, PhD, Associate Professor Thomas Stauffer Larsen heads the research team.

Other senior researchers are Professor, Henrik Frederiksen; staff specialist, PhD Karen Juul-Jensen, staff specialist, PhD Peter Brændstrup, and consultant, PhD Jacob Haaber Christensen.

The primary research area of the team is B-cell lymphomas, which are explored through both clinical and basic laboratory research. In addition, register-based research is conducted to uncover the prevalence and prognosis of different lymphoma subtypes. One PhD study is currently ongoing. Moreover, the team runs a large number of clinical trials, covering early phase 1 to post-registration, phase 4 trials.

The team is represented in the Danish Lymphoma Group (DLG) and the Nordic Lymphoma Group (NLG) and is engaged in international collaborative groups conducting clinical trials, such as European Mantle Cell Network and International Extranodal Lymphoma Study Group (IELSG). Further, the team actively participates in collaborations with the Centre for Cellular Immunotherapy of Hematological Cancer Odense (CITCO) and the Academy of Geriatric Cancer Research (AgeCare) at OUH.



# Myeloid disorders

The research team is headed by MD, PhD, Associate Professor Claus W. Marcher.

Primary research areas of the team are myelodysplastic syndrome, acute leukemia, mastocytosis, and hypereosinophilic syndrome. The research includes clinical research, stem cell research, register-based research, and basic laboratory research.

Other senior researchers include associate professor, consultant, PhD Dutura Weber; associate professor, consultant, DMSc, PhD, Lene Østgaard Granfeldt; staff specialist, PhD Lene Østergaard Jepsen and Head of department, PhD Hanne Vestergaard;. Further, Professor, DMSc Ole Weiss-Bjerrum from Rigshospitalet is associated as adjunct Professor.

The team actively participates in the Mastocytosis Center OUH (MastOUH) and the Center for Eosinophilia Odense (CEOS). Moreover, the team is represented in several academic study groups including the Acute Leukemia Group (ALG), the Danish Society for Chronic Myeloproliferative Diseases (DSKMS), the Nordic CML Study Group, the Nordic MDS Group (NMDS), and the Nordic AML Group (NAMLG).

# Cancer biology and molecular hematology



Professor Charlotte Guldborg Nyvold heads the Hematology-Pathology Research Laboratory, HPF (HPRL).

At HPF, the research team conducts laboratory research within the field of hematology in close collaboration with hematologists at the Department of Hematology and hematopathologists and laboratory technicians at the Department of Pathology. The molecular heterogeneity of malignant B-cell diseases, specifically, malignant B cell lymphomas and multiple myeloma is of particular interest. The research team possess expertise in a wide range of molecular techniques, such as biobanking, flow cytometry, cell sorting, functional cell culture studies, and sequencing, including next generation sequencing, exome and whole genome sequencing, transcriptome sequencing, and single cell sequencing.

Senior researchers in the team are molecular biologist and bioinformatician, PhD Marcus Høy Hansen, molecular biologist, PhD Oriane Cédile, and molecular biologist, PhD Simone Valentin Hansen. Three PhD-studies and three pre-graduate projects are ongoing as well as the daily management of our biobank.

The team is represented in several academic study groups including the Nordic Myeloma Study Group (NMSG) and is involved in both national and international collaborations.



# Health related Quality of Life and Patient Reported Outcomes

Project Manager, assistant professor, PhD Henrik Eshøj heads the research team.

Using both quantitative and qualitative methods, the research team studies Health-related Quality of Life (HRQL) in patients with hematological cancer. Quantitative research methods include validated questionnaires while qualitative research is conducted e.g. by interviews. In addition, the team develops and validates new instruments for collecting self-reported data.

Senior researchers in the team are Professor Niels Abildgaard, Professor Henrik Frederiksen, associate professor, Nana Hyldig, and associate professor, consultant, Lene Kongsgaard Nielsen. Further, Professor Madeleine King from University of Sydney is associated as adjunct Professor.

The team is represented in various academic study groups including Nordic Myeloma Study Group (NMSG) and Danish Comprehensive Cancer Center - DANish OncoGERiatric network (DCCC AGE). In addition, the team has several international collaborators including Senior Researcher, Jessica Roydhouse from Menzies Institute for Medical Research, University of Tasmania, Australia & Brown University School of Public Health, USA, and Professor Sam Salek from School of Life and Medical Sciences, University of Hertfordshire, UK.

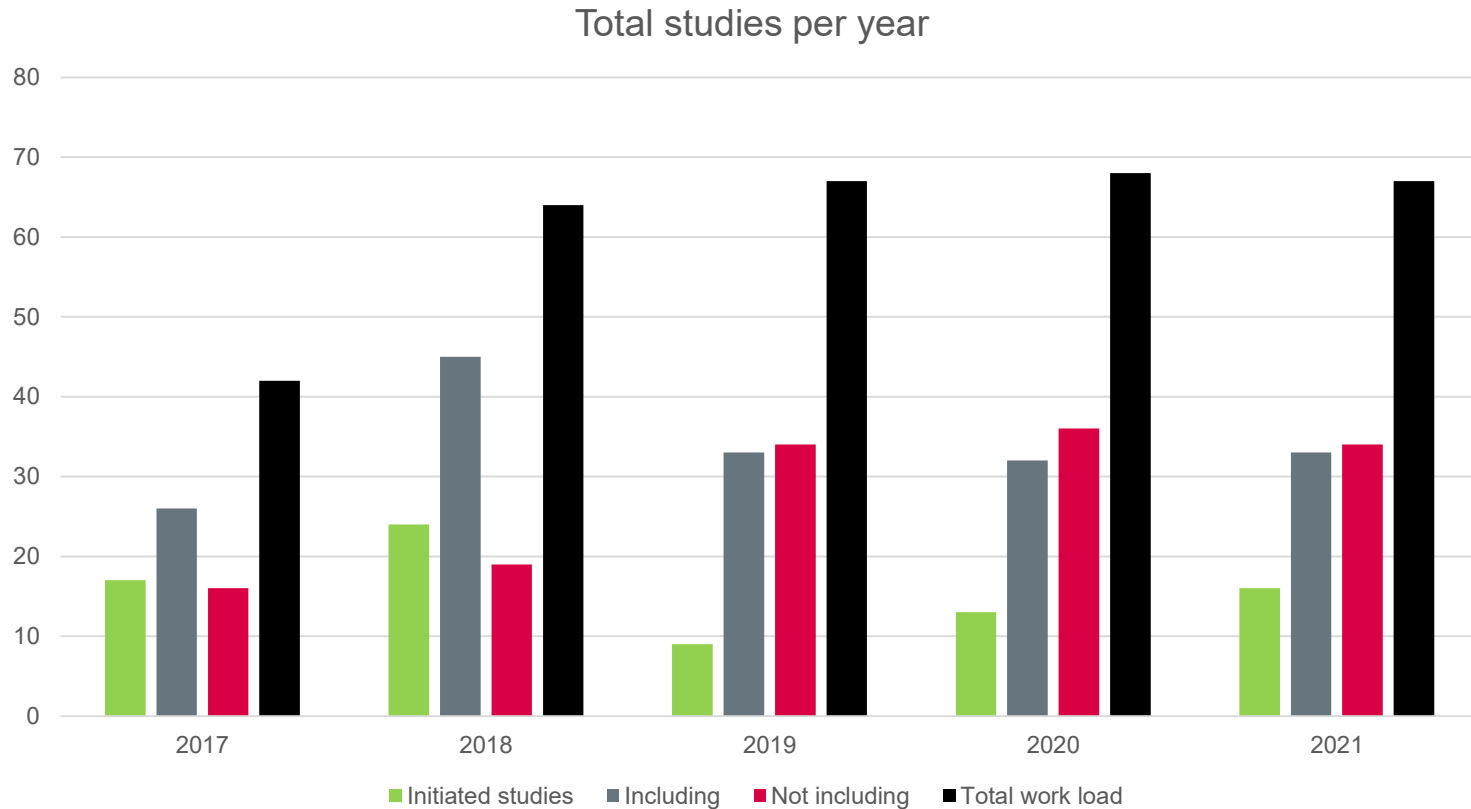
# User Council for Research

To strengthen the dialogue and collaboration with patients and relatives, we established a User Council for Research at the Department of Hematology in 2017. Currently, six patients and one relative comprise the Council.

Twice a year, the Council is invited to dialogue meetings at the department where upcoming and ongoing projects are discussed, and the Council is asked for input. Between meetings, our researchers contact the council for input on layman paragraphs for e.g. grant applications and on patient information material, among other things, and we keep the council members informed of the department's activities. In 2021, the council was also represented at two job interviews in the research unit.

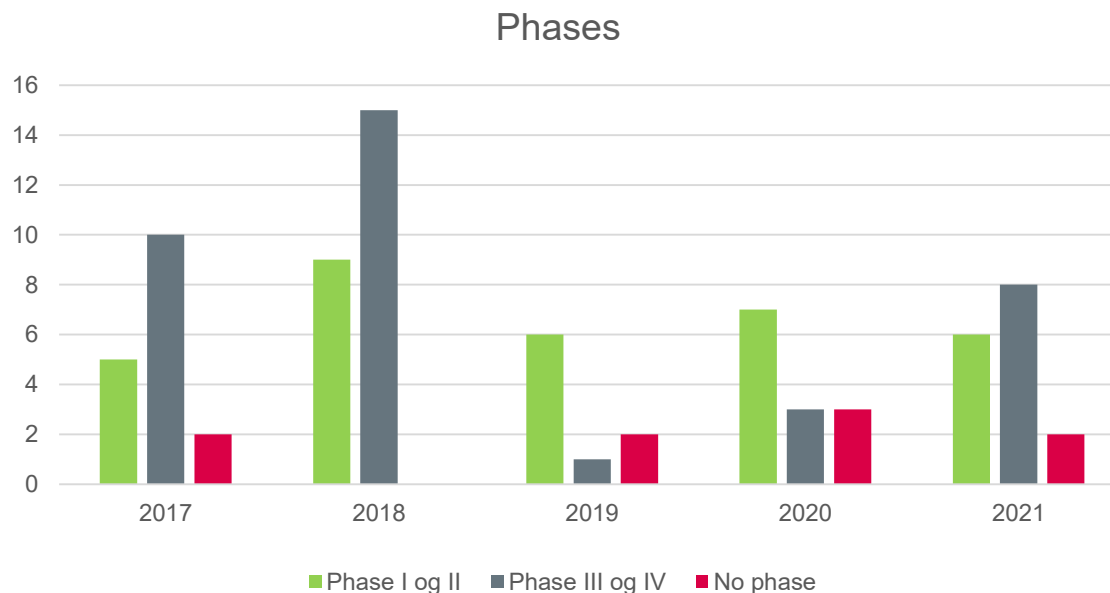
In the coming years, we will focus on more systematic involvement of the council and work towards involving the council at an earlier stage of our projects.

# 2017-2021 Clinical Trials



We have continued high activity in initiating and running clinical trials. Only a minor decrease in activity could be noticed during the Corona pandemic.

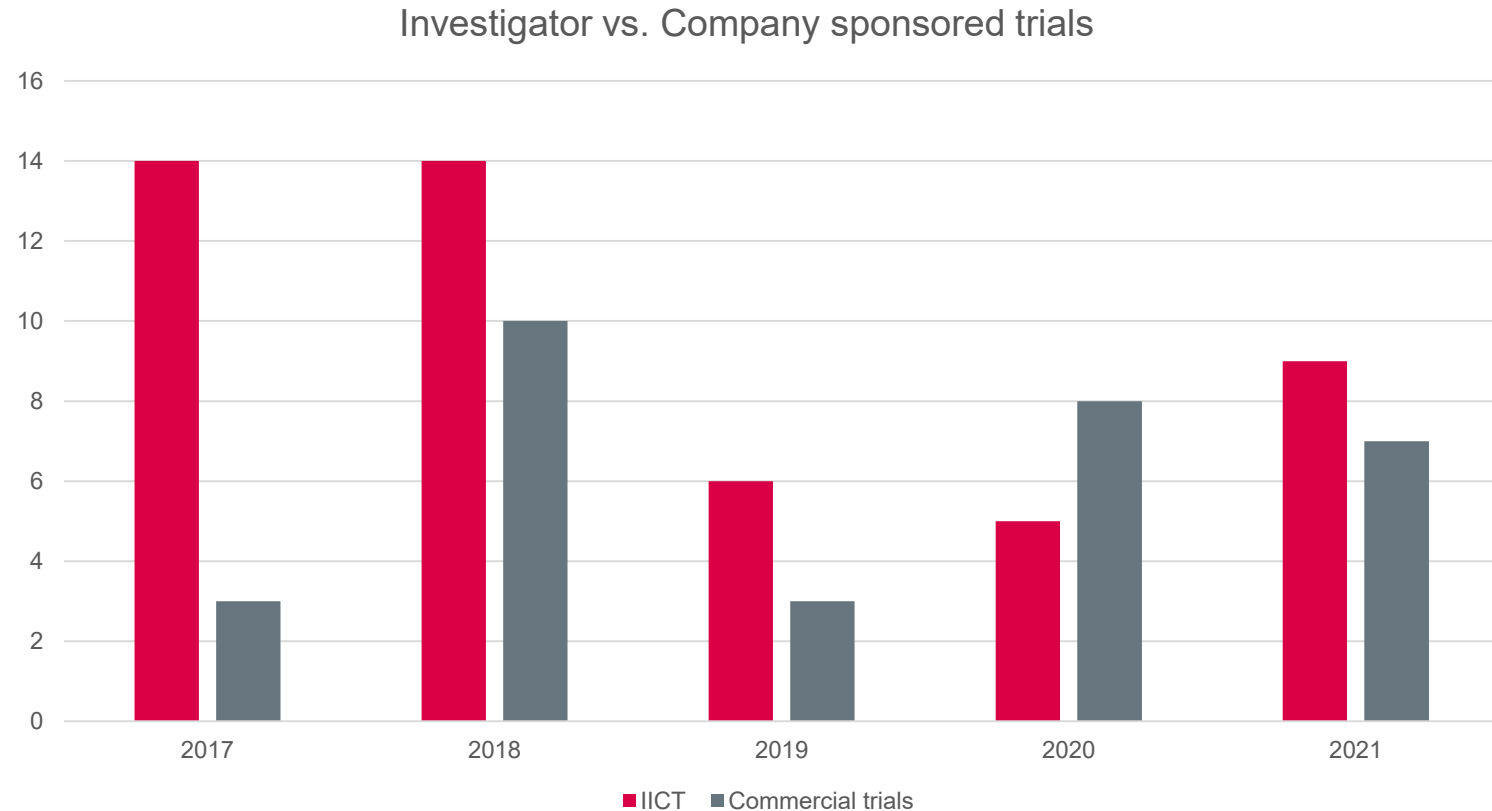
# 2017-2021 Trial categories



In recent years, it has been our strategy to increase the number of early phase 1-2 clinical trials, which typically involve treatment with new therapeutics. In 2021, we initiated our first "first-in-human" trial after an accreditation process by the national health authorities (Lægemiddelstyrelsen).

We are in the process of setting up a "Phase 1 Unit", which will allow us to formalize the running of early phase studies.

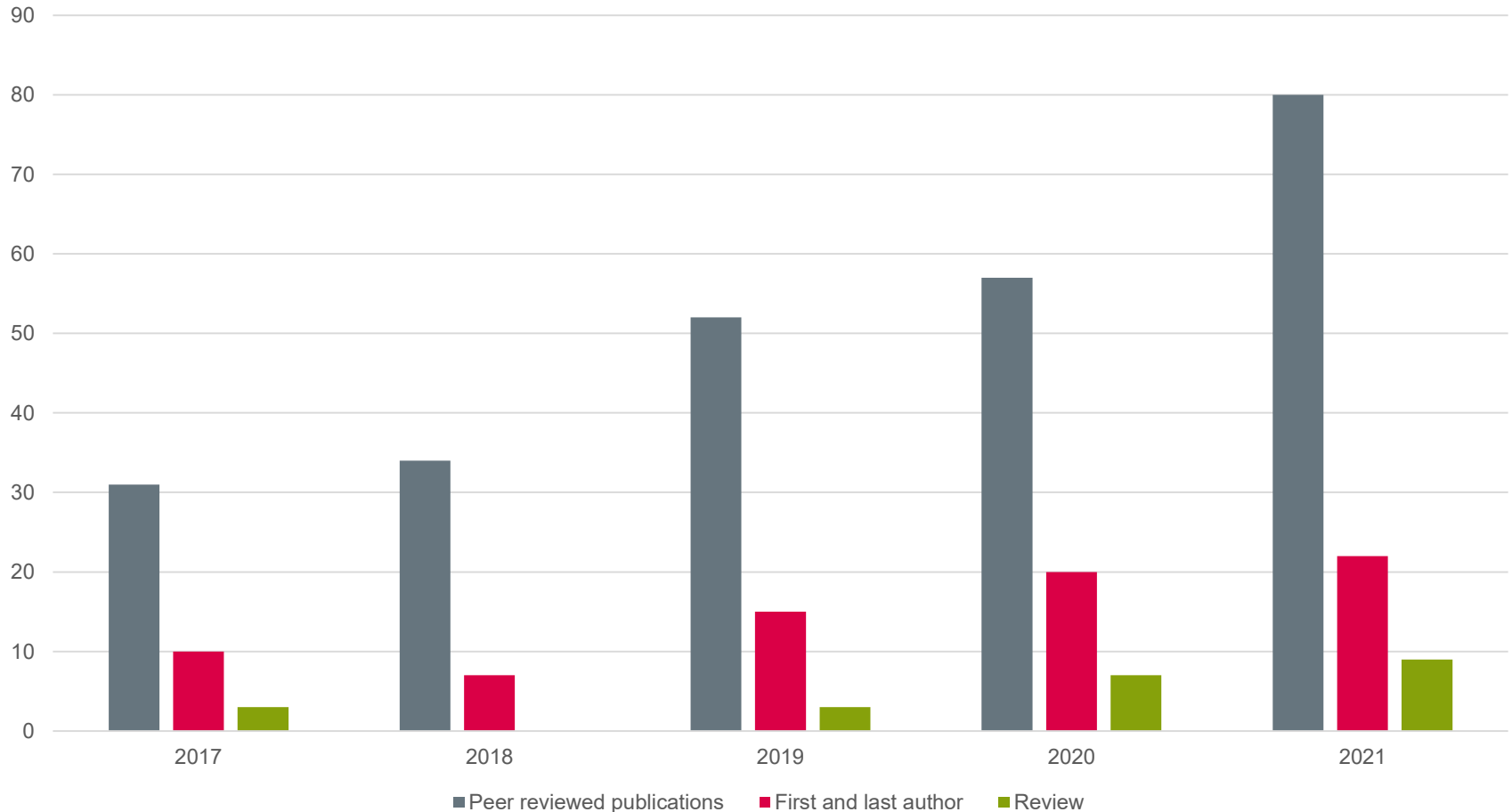
# 2017-2021 Trial categories



It is our goal to balance initiation of investigator-initiated clinical trials (IICT) and trials that are initiated and sponsored by pharmaceutical companies. As expected, there is some year-to-year variation in this.



# 2017-2021 Publications



We have been successful in increasing the annual number of peer-reviewed publications. There is an increasing number of first and/or last authorships too. Moreover, it is our goal to increase the number of systematic reviews.

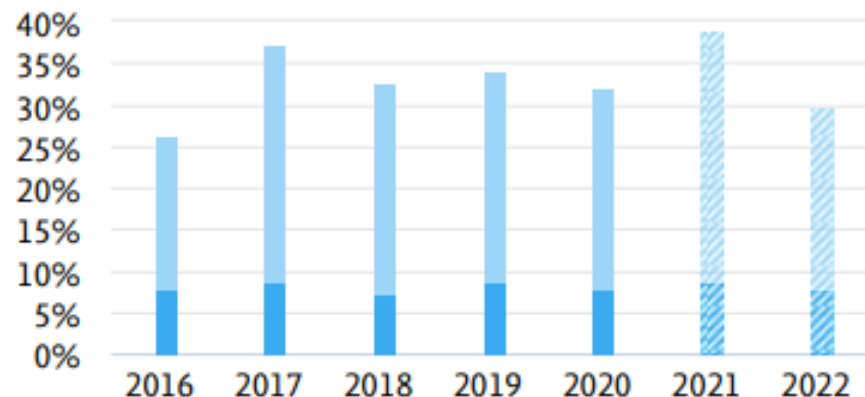
# Journal ranking

## Publications in Top Journal Percentiles by SJR

Entity: OUH Haematology March 2022 · Year range: 2016 to 2022 · Data source: Scopus, up to 30 Mar 2022 ·

Filters: Only Scholarly Output published at University of Southern Denmark included ·

### Share of publications in OUH Haematology March 2022 that are in the top journals by SJR



**114 (33.8%)**

number of publications in the top 10% journals by SJR

- % publications in top 10% journals
- % publications in top 1% journals
- ▨ Incomplete year

According to OUH/SDU goals, 40% of publications should be in Scimago Journal Rank top 10%. This has nearly been achieved.

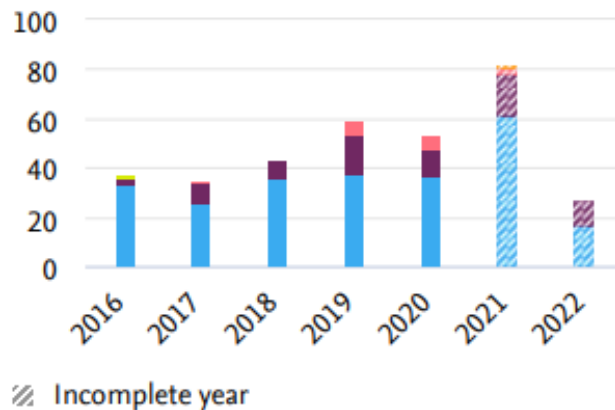
# Journal ranking

## Publications by Journal quartile

Entity: OUH Haematology March 2022 · Year range: 2016 to 2022 · Data source: Scopus, up to 30 Mar 2022 ·

Filters: Only Scholarly Output published at University of Southern Denmark included ·

### Share of publications per Journal quartile by SJR



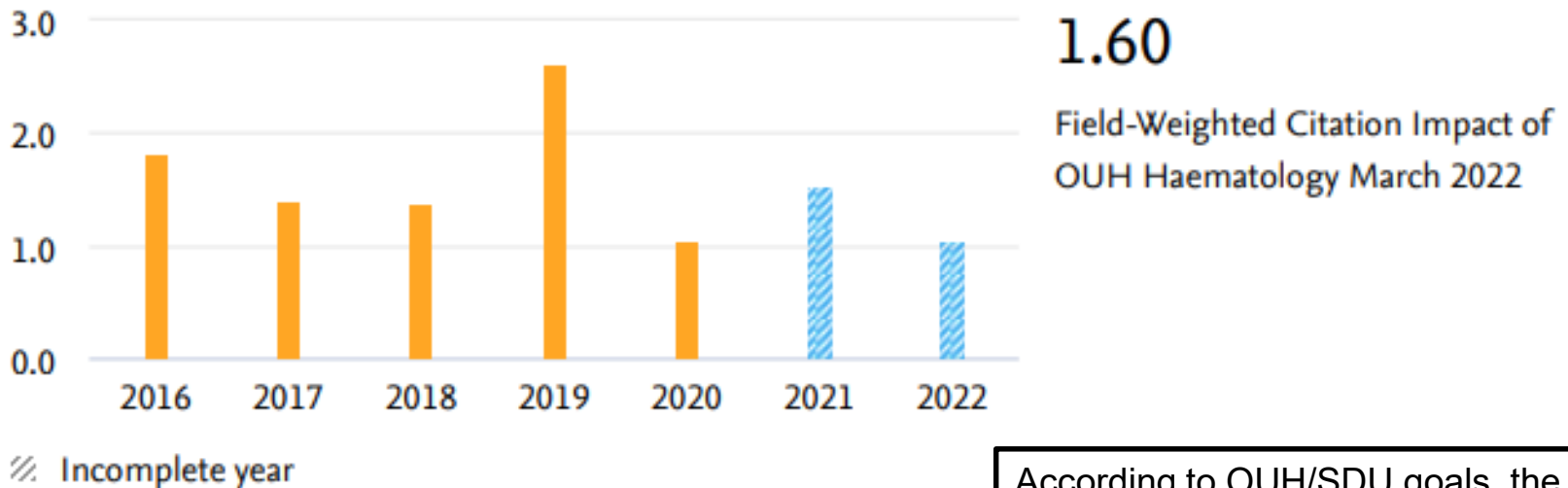
According to OUH/SDU goals, 80% of publications should be in Scimago Journal Rank top 25%. This was nearly reached in 2021.

Quartiles	Publications	Publication share (%)
■ Q1 (top 25%)	248	73.6
■ Q2 (26% - 50%)	73	21.7
■ Q3 (51% - 75%)	13	3.9
■ Q4 (76% - 100%)	3	0.9
Cumulative shares	Publications	Publication share (%)
Q1 to Q2 (top 50%)	321	95.3

# Journal ranking

## Field-Weighted Citation Impact

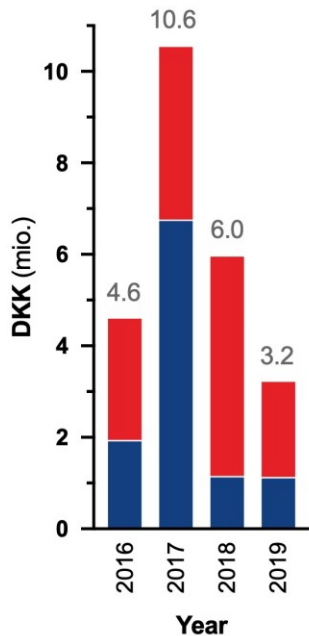
Entity: OUH Haematology March 2022 · Year range: 2016 to 2022 · Data source: Scopus, up to 30 Mar 2022 ·  
Filters: Only Scholarly Output published at University of Southern Denmark included ·



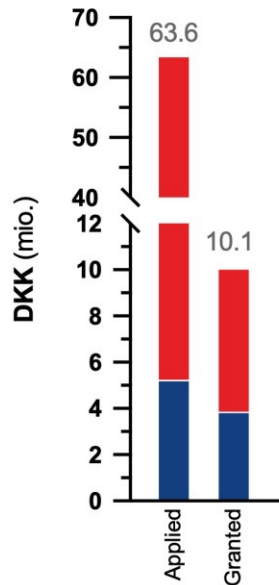
According to OUH/SDU goals, the field-weighted citation impact should be above 1.0. This has persistently been achieved.

# Funding

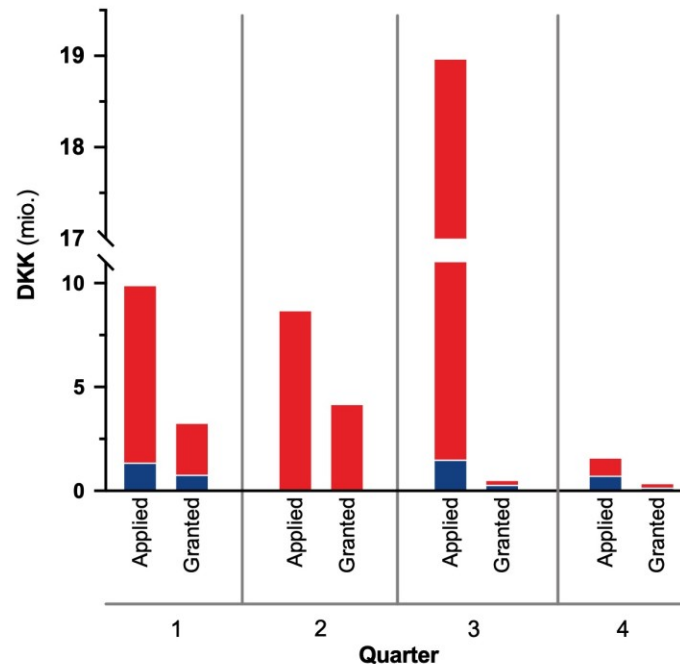
**GRANTED FUNDS**  
(2016–2019)



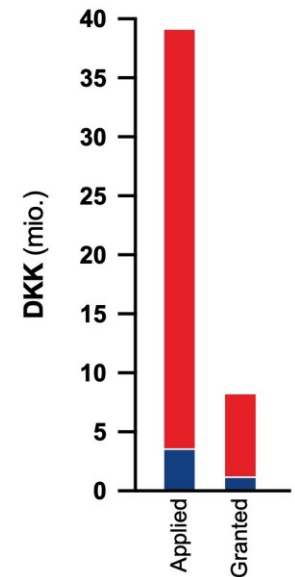
**APPLIED FOR AND GRANTED FUNDS**  
(2020)



**FUNDING**  
(Quarterly, 2021)



**TOTAL FUNDING**  
(2021)



In 2021, we increased our research funding, particularly the external funding. Our rate of success (granted/applied) was 21%, and external funding constituted 85% of our total funding

# Completed PhD study

## Comorbidity and survival in chronic lymphocytic leukemia



**PhD:** Emelie Hamotal Curovic Rotbain

Chronic lymphocytic leukemia (CLL) is a cancer of the blood, lymph nodes, spleen, and bone marrow with a median age at diagnosis of 72 years. There are several types of treatment for CLL, including chemotherapy, immunotherapy, and targeted agents, and the choice of treatment depends on age, presence of comorbidities, prognostic factors, patient preferences, and previous treatment. The thesis included four register-based studies of different aspects of treatment, survival, use of the healthcare system, and comorbidity for patients with CLL.

The findings illustrated that over a third of all patients with CLL had one or more comorbidities at diagnosis of CLL, and all comorbid conditions were associated with shorter survival. Furthermore, patients with CLL had increased use of the healthcare system after diagnosis, and patients with CLL with comorbid conditions had higher healthcare utilization than patients with CLL without comorbidities. The newly developed CLL comorbidity index was associated with survival and treatment outcomes in patients both at diagnosis and at first treatment and can be used as a quick and easy method to quantify comorbidity. Finally, the results showed that CLL patients receiving intensive chemoimmunotherapy in a real-world setting had a long overall survival and that immunoglobulin variable heavy chain mutational status was an important prognostic factor.



# Completed PhD study

Development of clinically applied next generation bioinformatics – driven by the genomic heterogeneity of mantle cell lymphomas for evidence-based diagnostics, disease tracking and follow-up

**PhD:** Marcus Høy Hansen

The PhD project of Marcus Høy Hansen aimed to investigate and implement novel quality measures for the improved detection of somatic mutations or structural variants from whole-exome sequencing (WES) and targeted sequencing. The motivation was to leverage the clinical applicability of next-generation sequencing, using mantle cell lymphoma as a versatile model for hematologic B-cell malignancies. While recurrent mutations contribute to the oncogenesis of MCL, such as ATM mutations and lesions involving tumor suppressor TP53 or the NOTCH1 pathway, the pronounced heterogeneity and small overlap between cases are striking.

This diversity called for a specialized strategy aiming at systematic and high-resolution patient profiling to overcome the inherent noise of WES, while maximizing the informational output. It showed that false-positive coding somatic mutations from purified diagnosis-relapsed paired MCL-patient samples were efficiently decreased an order of magnitude by intersecting DNA mutations with RNA. Furthermore, the standard deviation of heterozygous variant allele frequencies provided an effective quality measure. Developed methods for detecting acquired copy-number alterations showed that the genomic juxtaposition of variant allele frequencies to the relative depth of sequencing coverage provided efficient means for resolving otherwise neglected copy-neutral loss-of-heterozygosity. Finally, mathematical considerations underlying detection of minute residual disease by clonal rearrangements of immunoglobulin genes were proposed.

# Completed PhD study

## Impact of Molecular Heterogeneity in B Cell Malignancies



**PhD:** Simone Valentin Hansen

In study I, it was observed that inhibition of LILRA4, a gene found to be overexpressed in half of patients with mantle cell lymphoma (MCL) compared to healthy individuals, resulted in >two-fold downregulation of MIF, which is a pro-inflammatory cytokine, suggesting a possible immune regulatory role in MCL.

In study II, the transcriptome of CD19+ bone marrow (BM) cells from eight MCL patients was analyzed at the single-cell level, demonstrating a striking heterogeneity across patients. Although restricted light chain protein expression was expected, 11% of SOX11+ malignant cells co-expressed  $\kappa$  and  $\lambda$  transcripts. In a patient with the more aggressive blastoid variant, SOX11 was co-expressed with the early lymphocyte marker, SOX4 and the precursor lymphoblastic marker, FAT1, suggesting a potential prognostic role. The expression of markers, such as SOX4, IgG, IgA, and CD27, associated with various B cell differentiation stages may suggest that the patients carry B cells of different stages.

In study III, a thematic literature review investigated the evidence of an immature disorder or early and progressive clonal expansion leading to MCL. Evidence included reports of concurrent myeloid and lymphoid malignancies in the same patient, and studies demonstrating loss of genetic aberrations in patients between diagnosis and relapse. Yet, the evidence is fragmented in the current literature, and further investigation is needed.





# Ongoing PhD study

Monitoring circulating tumor DNA in aggressive large B-cell lymphoma  
– a tool for personalized medicine

**PhD student:** MD Gayaththri Vimalathas

Aggressive large B-cell lymphoma is the most frequent type of lymphoma with an annual incidence of approximately 450 cases in Denmark. The disease is deadly, but with immuno-chemotherapy, 60-65% can be cured. Unfortunately, 30-40% of the patients will relapse or are primary refractory. When treatment is completed, the patients undergo an end-of-treatment imaging scan and enroll in a monitoring program consisting of regular clinical examinations and imaging scans. It can be difficult to determine, if activity seen on imaging scans is caused by lymphoma activity or benign conditions. Further, it is not always possible to obtain tissue biopsies for diagnostic clarification. Clinicians therefore need a more sensitive and easily accessible method that allows for longitudinal monitoring to detect residual disease and thus identify patients at risk of relapse earlier. The aim of this PhD project is to evaluate the potential utility of circulating tumor DNA in aggressive large B-cell lymphoma as a novel molecular biomarker of minimal residual disease using Next Generation Sequencing in a real-life, clinically feasible set-up. The perspectives of our project are to obtain greater diagnostic accuracy, more timely therapeutic intervention in case of residual disease or relapse, and ultimately improved patient survival.

**Supervisors:** MD, PhD, Associate Professor Thomas Stauffer Larsen, Department of Hematology, OUH; Professor Charlotte Guldberg Nyvold Hematology-Pathology Research Laboratory, Department of Hematology, OUH; MD Michael Boe Møller, Department of Clinical Pathology, OUH; Head of Innovation, Clinical Associate Professor, Thomas Kielsgaard Kristensen, Department of Clinical Innovation, OUH.

# Ongoing PhD study

## Prognostication in multiple myeloma



**PhD student:** MD Louise Redder

It can be difficult to predict how things will develop, when a patient is diagnosed with multiple myeloma. Many prognostic models have tried, but the models are not tested in the general myeloma population and are therefore not used in clinical work. The purpose of this PhD project is to verify which model can provide the most accurate prognosis for patients with multiple myeloma.

Using data from the Danish Myeloma Register and the National Patient Register, we will validate proposed prognostic models in the Danish myeloma population. Towards the end of the project, we will examine whether quality of life can be used to determine the prognosis. Identifying the most precise prognostic model will provide the best basis for selecting patients' treatment.

**Supervisors:** Professor Niels Abildgaard, Department of Hematology, OUH; Professor Henrik Frederiksen, Department of Hematology, OUH; MD, PhD, Associate Professor Lene Kongsgaard Nielsen, Department of Hematology, OUH; Biostatistician, Associate Professor Sören Möller, OPEN, OUH.



# Ongoing PhD study

The role of mesenchymal stromal cell  
and bone marrow stromal dysfunction in multiple myeloma

**PhD student:** MD Mette Bøegh Levring

Many patients with multiple myeloma suffer from the debilitating complication of lytic bone disease, causing fractures, pain, and immobilization; all affecting patients' quality of life. Research shows that the cause of lytic bone disease is interaction between the malignant plasma cells and the stromal cells in the bone marrow. In this 3-year PhD-project, we investigate the bone marrow stroma of patients with multiple myeloma. We will focus on the bone forming osteoblasts and their precursor cells, mesenchymal stromal cells. We will examine the cells with both functional cell cultures and genetic transcription to characterize the cells in great detail. We will compare the characteristics of stromal cells from different stages of multiple myeloma and from healthy donors. Our mission is to understand how stromal cells are involved in the development of lytic bone disease. A better understanding of this will facilitate development of new treatment for bone disease, improving quality of life for many patients with MM.

**Supervisors:** Professor Niels Abildgaard, Department of Hematology, OUH; Professor Charlotte Guldberg Nyvold, Hematology-Pathology Research Laboratory, Department of Hematology, OUH; Professor Moustapha Kassem, Laboratory of Molecular Endocrinology, Department of Endocrinology, OUH; MD, PhD Ida Bruun Kristensen, Department of Hematology, OUH.

# Ongoing PhD study

Treatment and Monitoring of the Bone Disease in Multiple Myeloma Patients



**PhD student:** MD Michael Tveden Gundesen

Bone disease in multiple myeloma (MM) leads to severe pain and suffering. Though great improvements have been obtained in the treatment of MM, healing the bone disease remains a clinical challenge. This project aims to evaluate the bone-healing potential of ixazomib and to determine the best method for monitoring the bone disease by evaluating the effect of different imaging modalities.

The bone-healing potential of ixazomib is tested in an explorative study of 30 patients with MM associated bone disease receiving ixazomib. Patients are followed for 2 years of treatment and evaluated by NaF-CT scans.

In another study, we follow 267 patients receiving treatment with zometa for two to four years. Zometa is a well-proven protective agent for bone disease in MM, but the treatment is not without side effects, and the optimal treatment period is unknown. The hope is that we will be able to determine the optimal treatment period to secure an optimal treatment effect with fewest possible side effects. This study is conducted in collaboration with centers of the Nordic Myeloma Study Group.

**Supervisors:** MD, PhD Thomas Lund, Department of Hematology, OUH; Professor Niels Abildgaard, Department of Hematology, OUH; Clinical director of Oncoradiology Jon Thor Asmussen, Department of Radiology, OUH; MD Anne Lerberg Nielsen, Department of Nuclear Medicine, OUH.



# Ongoing PhD study

On adverse outcomes in immune thrombocytopenia  
– a population-based cohort study

**PhD student:** MD Nikolaj Mannering

Immune thrombocytopenia (ITP) is an acquired autoimmune disease characterized by a low number of circulating platelets in the bloodstream. Patients suffer from bleedings, treatment toxicity, reduced quality of life and shortened life expectancy. It is believed that disease complications and side effects from treatment contribute equally to complications and excess mortality. However, these observations are based on a very small number of patients and frequencies. Impact of complications from disease and treatment are not well understood.

Using data from Danish health registries, our study therefore aims at providing up-to-date knowledge on possible and yet unexplored complications and late effects to ITP. We have constructed a large population-based cohort comprising >5,000 patients with ITP and >200,000 age-sex matched comparisons from the Danish population. The patients were diagnosed during the period 1980-2016 and have complete follow-up.

During this period, the treatment options for ITP have changed radically. We will use our data to provide updated mortality and adverse health outcome effects, focusing particularly on temporal variation. Our dataset is unprecedented in this field of research.

We aim at conveying results to clinicians in order to optimize treatment, follow-up and to improve outlook for patients with ITP.

**Supervisors:** Professor Henrik Frederiksen, Department of Hematology, OUH; MD, PhD Dennis Lund Hansen, Department of Hematology, OUH; Professor Anton Pottegård, Department of Public Health, University of Southern Denmark.

# Ongoing PhD study

Drug resistance in patients with chronic lymphocytic leukemia



**PhD student:** MSc Sólja Remisdóttir Veyhe

Chronic lymphocytic leukemia is the most common type of leukemia in adults with about 450 new cases in Denmark annually. Although promising results have been obtained with the targeted treatments, ibrutinib and venetoclax, some patients still experience poor treatment response. The aim of the project is to provide novel and valuable information on the molecular pathways and kinetics involved in resistance to these drugs. The hope is that this will enable us to predict who will benefit from the treatment, before treatment start. Further, it might enable early detection of the development of resistance during treatment.

Thus, the project has the potential to influence the clinical course of each individual patient, both before and during treatment.

**Supervisors:** Professor Charlotte Guldberg Nyvold, Hematology-Pathology Research Laboratory, Department of Hematology, OUH; Professor Henrik Frederiksen, Department of Hematology, OUH; MD, PhD Karen Juul-Jensen, Department of Hematology, OUH; Professor Karen Dybkær, Department of Clinical Medicine, Aalborg University Hospital.

# Peer-reviewed publications in 2021

**Evans syndrome in adults : an observational multicenter study.** / Fattizzo, Bruno; Michel, Marc; Giannotta, Juri Alessandro; Hansen, Dennis Lund; Arguello, Maria; Sutto, Emanuele; Bianchetti, Nicola; Patriarca, Andrea; Cantoni, Silvia; Mingot-Castellano, Maria Eva; McDonald, Vickie; Capecci, Marco; Zaninoni, Anna; Consonni, Dario; Vos, Josephine Mathilde; Vianelli, Nicola; Chen, Frederick; Glenthøj, Andreas; Frederiksen, Henrik; Gonzalez-Lopez, Tomas Jose; Barcellini, Wilma.

I: Blood Advances, Bind 5, Nr. 24, 28.12.2021, s. 5468-5478.

**Assessment of atherosclerosis in multiple myeloma and smoldering myeloma patients using 18F- sodium fluoride PET/CT.** /

Arani, Leila S.; Zirakchian Zadeh, Mahdi; Saboury, Babak; Revheim, Mona Elisabeth; Øestergaard, Brian; Borja, Austin J.; Samadi Samarin, Davoud; Mehdizadeh Seraj, Siavash; Kalbush, Eman; Ayubcha, Cyrus; Morris, Michael A.; Werner, Tom J.; Abildgaard, Niels; Høilund-Carlsen, Poul F.; Alavi, Abass.

I: Journal of Nuclear Cardiology, Bind 28, Nr. 6, 12.2021, s. 3044-3054.

**COVID-19 severity and mortality in patients with CLL : an update of the international ERIC and Campus CLL study.** /

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