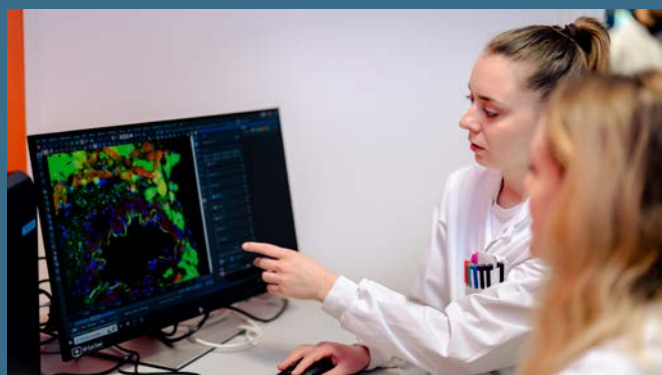


Translational Research Centre

Formerly known as Forskerparken - Glostrup

→ **LI** Translationelt
Forskningscenter
Medicinsk Bibliotek



**Translational Research Centre,
Annual Report of 2023**

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Editorial Team:

Kristian Agmund Haanes

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INTRODUKTION - DANSK

Det forgangne år har budt på store ændringer for Glostrup Forskerpark. Forskerparken blev oprettet i 2007, hvor nogle gamle værkstedsbygninger og vaskeri blev ombygget til at huse fuldt moderne forskningsfaciliteter inklusive dyrestald. Etableringen blev iværksat for midler, som Københavns Amt fik i forbindelse med salget af NESA aktier, og den daværende vicedirektør for Glostrup Hospital, Morten Brinkløv, var den bærende kraft i etableringen af Forskerparken. Dette var yderst visionært og skulle give Glostrup Hospitals kliniske forskere mulighed for at udføre forskning på højt niveau i umiddelbar nærhed af hospitalet.

Forskerparken har siden oprettelsen været ledet af Lars Edvinsson, som sammen med Jes Olesen i 2021 fik den prestigefyldte Brain Prize fra Lundbeck-fonden. Et generationsskifte har imidlertid været under opsejling de seneste par år, og 2023 blev året, hvor stafetten blev givet videre til undertegnede efter Lars Edvinssons kompetente ledelse. Der foreligger nu et stort ansvar med at føre arven videre samt gennemføre en fornyelse af Forskerparken, således at den fortsat kan rumme verdensklasse forskning i rummet mellem den basale og kliniske forskning.

I 2023 har forskerne i Forskerparken endnu engang gjort sig positivt bemærket og opnået flotte resultater både nationalt og internationalt. Det har givet sig udtryk i flotte 130 videnskabelige artikler, 3 PhD forsvar samt flotte priser til flere af Forskerparkens forskere (se

venligst senere i denne årsberetning for detaljer). Det tegner lyst for fremtiden.

I ønsket om at knytte Forskerparken tættere til de kliniske forskningsmiljøer for at opnå størst mulig synergi mellem forskningsmiljøerne, vil de kommende år blive brugt på at identificere og videreudvikle translationelle forskningsprojekter med henblik på en yderligere styrkelse af den translationelle forskning på Rigshospitalet. Som startskud til dette initiativ skiftede Forskerpark Glostrup derfor navn pr. 1. marts 2024 til Translationelt Forskningscenter, Rigshospitalet (TRACE). Et navneskifte alene ændrer naturligvis ingenting, men alle forskere i TRACE har i det forgangne år arbejdet tæt sammen på flere tiltag, der skal styrke den translationelle forskning, og denne årsberetning rummer flere detaljer om dette.

Året har således budt på ændringer, men det er kun starten, idet vi vil arbejde målrettet på, at samarbejdet med de kliniske afdelinger og integrationen i hospitalet yderligere styrkes over de kommende år for at udnytte det fulde potentiale af TRACE med en placering midt i Rigshospitalets højt profilerede og anerkendte kliniske forskningsmiljø, så det til fulde understøtter Rigshospitalets overordnede vision om at være til gavn for den enkelte patient og det samlede sundhedsvæsen.

Niklas Rye Jørgensen

Niklas Rye Jørgensen
Head of TRACE

INTRODUCTION - ENGLISH

The past year has brought significant changes for Glostrup Research Park. The research park was established in 2007, when some old workshop and laundry buildings were converted into fully modern research facilities, including an animal facility. The establishment was initiated with funds that Copenhagen County received from the sale of NESA shares, and the then Deputy Director of Glostrup Hospital, Morten Brinkløv, was the driving force behind the creation of the research park; "Glostrup Forskerpark". This was extremely visionary and aimed to provide Glostrup Hospital's clinical researchers the opportunity to conduct high-level research in close proximity to the hospital.

Since its establishment, the research park has been led by Lars Edvinsson, who, along with Jes Olesen, received the prestigious Brain Prize from the Lundbeck Foundation in 2021. However, a generational transition has been underway over the past few years, and 2023 marked the year when the baton was passed to me after Lars Edvinsson's competent leadership. There is now a great responsibility to carry on the legacy and renew the research park so that it can continue to accommodate world-class research in the space between basic and clinical research.

In 2023, the researchers at the research park have once again made a positive impact and achieved impressive results both nationally and internationally. This has resulted in an impressive 130 scientific articles, 3 PhD defenses, and several

awards for the research park's researchers (please see later in this annual report for details). The future looks bright.

In the desire to tie the research park more closely to the clinical research environments to achieve the greatest possible synergy, the coming years will be spent identifying and further developing translational research projects with the aim of further strengthening translational research at Rigshospitalet. As a kickoff to this initiative, the Glostrup Research Park was renamed the Translational Research Centre, Rigshospitalet (TRACE) on March 1, 2024. A name change alone naturally changes nothing, but all researchers in TRACE have over the past year worked closely together on several initiatives to strengthen translational research, and this annual report contains more details about this.

Thus, the year has brought changes, but this is only the beginning, as we will work purposefully to further strengthen collaboration with the clinical departments and integration into the hospital over the coming years to fully exploit the potential of TRACE, with its location in the midst of Rigshospitalet's highly profiled and recognized clinical research environment, to fully support Rigshospitalet's overarching vision of benefiting the individual patient and the entire healthcare system.

Niklas Rye Jørgensen



Head of TRACE

STRATEGY

Every organization needs a strategy. Right? But how does one devise a strategy for a research organization populated by several research teams with distinct research themes and aims?

One way is to build the strategy around a common ambition following the principles of 'sensemaking' and 'enacted strategizing' as derived from Karl Weick's ideas on strategic development. Weick introduced the concept of enacted strategizing as an alternative to the traditional view of deliberate and planned strategies. Enacted strategizing emphasizes the idea that strategies emerge and evolve through ongoing interactions and improvisations within organizations (which is also why Weick insists on using verbs rather than nouns). This view challenges the notion of strategy as a predetermined plan and highlights the importance of flexibility, adaptation, and learning in strategy formulation and implementation. In science, this enables the organization to quickly adapt and to seize opportunities as they arise without losing sight of their strategic direction.



Authored by professor, pharmacist, PhD Lasse Kristoffer Bak

At TRACE, we began this process in June 2023 with a seminar session at our annual Summer Symposium for all the research teams and TRACE staff members. Here, we worked in groups to produce input for a joint ambition. Based on this input, we drafted a preliminary ambition that was discussed among the TRACE research teams and staff, and the feedback provided was incorporated into our final ambition statement.

The future challenge, for the research teams as well as the TRACE staff, is to work out strategic activities founded in our new, joint ambition. The goal is that the sum of all these activities, large and small, will become the TRACE enacted strategizing.



Professor and pharmacist Lasse Kristoffer Bak.

Our ambition

At TRACE, we do world-leading translational research that transforms basic science into clinical solutions for improved patient care and enhanced public health. We do this through international collaborations with both public and private sector partners, by housing state-of-the-art research facilities, by nurturing an attractive research environment, and by engaging with health care professionals and policy makers.

We currently focus on areas such as stroke, headaches, migraine, sensory biology, ophthalmology, bone diseases, and multiple sclerosis but welcome any group dedicated to translational research that shares our values.

We value the strength of teamwork and have a collaborative and trustful working environment extending to all employees and students.

We empower young researchers and have a vibrant research training community that thrives on trustful supervision and mentorship, curiosity, creativity, and intellectual rigor.

We engage with the local and global community via public outreach, social media and news outlets, and involve all employees and students.



ECONOMY OVERVIEW - 2023

Financial Summary - actual Expenses (t. DKK)

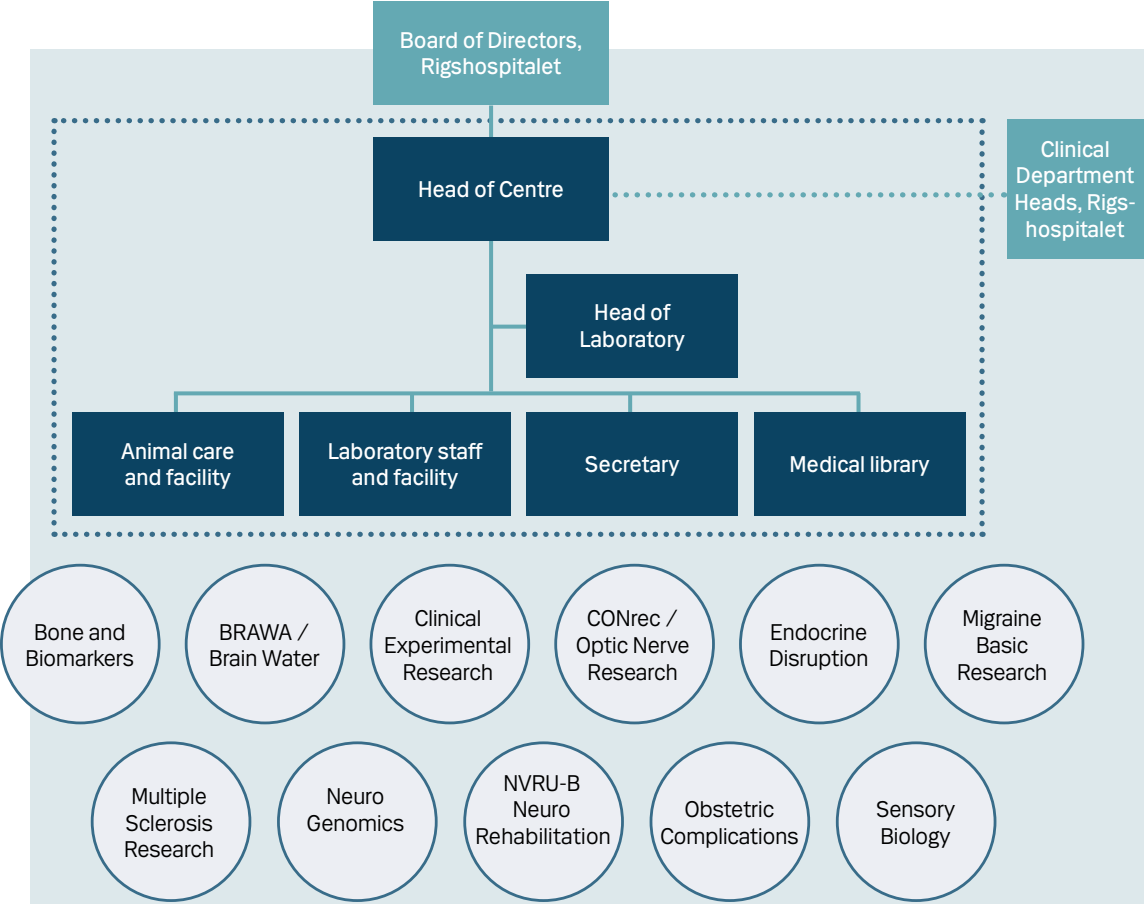
Category	Actual (t. DKK)
Centre Budget	6,770
Personnel	5,497
Operations	1,209
Net Result	64



The financial status for 2023 is healthy, with actual expenses well managed within the yearly budget, resulting in a small net surplus of 64 t. DKK.



HOW ARE WE ORGANIZED?



The diagram illustrates the organizational structure of TRACE within the dotted line. These components form the core operational framework of the centre.

Outside the dotted line are various research units that organizationally belong to other departments. These research units interact with the centre as part of their collaborative efforts. The central leadership communicates with the clinical department heads and other stakeholders to coordinate these interactions and ensure alignment with the centre objectives in support of Rigshospitalet's vision and strategy.

WHO ARE WE?

As we conclude the year 2023, this section provides an overview of our current staff and their contributions.

ADMINISTRATION

Niklas Rye Jørgensen, Head of Centre. Niklas is focused on reinforcing the integration of clinical and basic research with focus on strategic development. In addition to being head of TRACE, he is head of Section of Clinical Biochemistry, Rigshospitalet Glostrup and professor of clinical biochemistry at the Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen.



Niklas Rye
Jørgensen

Kristian Agmund Haanes, Head of Laboratory and Deputy Head of Centre, is the daily manager of TRACE with particular focus on effective execution and implementation of new initiatives. In addition to his administrative tasks at TRACE, Kristian is heading his own research group at the site (Sensory Biology) and is associate professor at the Department of Biology at Faculty of Science, University of Copenhagen.



Kristian Agmund
Haanes

Hanne Aggergaard Nielsen, Secretary, is the secretary of the centre handling administrative duties that support both office and research activities. Tasks involve coordinating meetings, ordering lab supplies, keeping track of equipment, and providing administrative support, all essential for maintaining an efficient and effective research environment.



Hanne Aggergaard
Nielsen

The Medical Library at Rigshospitalet Glostrup supports all scientists at Rigshospitalet with comprehensive services, including managing PURE registrations, sourcing hard-to-find references, and maintaining a collection of relevant literature.

THE MEDICAL LIBRARY

Karine Korsgaard, Librarian, Karine is the superuser for the hospital's PURE registration system. She also assists with literature searches, sourcing hard-to-find references, and provides guidance to scientists.



Karine Korsgaard

Lene Madsen, Office Clerk/Librarian, Lene manages library tasks and supports PURE registration duties. In addition, Lene oversees the budget and finances of TRACE, including invoicing and payments, ensuring efficient financial operations.



Lene Madsen

The Animal Facility at TRACE maintains high standards of animal welfare and supports scientific research, ensuring their living conditions meet regulatory standards. All animal caretakers maintain the animal facility and ensures the well-being of the animals by providing daily care.

THE ANIMAL FACILITY

Sara Stefansen, Animal Technician, who started in 2023, is the full-time animal technician. Sara's dedication to animal welfare is evident in her attention to the needs of the animals and her role in training new staff on best practices. She is conducting routine health checks and providing enrichment to enhance the quality of life for the animals. Sara also performs administrative duties related to TRACE and assists scientists with their experiments when time allows.



Sara Stefansen

Tanja Hegner, Animal Technician, shows her commitment to animal welfare through her attentive routines and support for the animals. She ensures the animals well-being by maintaining clean and safe living environments and by closely monitoring their daily health and behaviour. Tanja assists scientists with their experiments when time allows.



Tanja Hegner

The veterinary students at the University of Copenhagen are dedicated to animal care during weekends and holidays, contributing to the well-being of the animals and supporting the facility's operations.

Bjarke Skovgaard Hansen, Veterinary Student, is a master's student in veterinary science at the University of Copenhagen, sharing a commitment to animal welfare.



Bjarke Skovgaard
Hansen

Malene Tærstøl Jepsen, Veterinary Student is a master's student in veterinary science at the University of Copenhagen, sharing a commitment to animal welfare.



Malene
Tærstøl Jepsen



THE MEDICAL LIBRARY

The Medical Library at Rigshospitalet, Glostrup is located at the Translational Research Centre. Our primary goal is to assist employees at Rigshospitalet Glostrup in finding the health knowledge they need.

One of our main purposes is to support employees in seeking information on health-related topics. With our expert competences, we help our users develop thorough searches for relevant knowledge. The quality of these searches is crucial, and we assist in navigating smoothly through the process of creating a database and exploring search techniques.

Another significant part of our work is registering research articles affiliated with Rigshospitalet. Rigshospitalet publishes approximately 3,500 research articles each year. The purpose of this registration is to highlight and provide an overview of the research carried out at Rigshospitalet. The tool used for registration is a web-based IT system (PURE).

In 2023, the registration process was centralized. Previously, registration took place within the hospital departments, but as of 2023, the Medical Library is responsible for this task. This centralization ensures an always updated portal.

The PURE web portal can be accessed at the web address: <https://research.regionh.dk/en/>. The data from PURE can be used for branding research groups, departments, and Rigshospitalet as leading entities. The data shows all research performed, both nationally and internationally. Potential collaborators can also find relevant researchers for future cooperation opportunities.

The Medical Library at Rigshospitalet, Glostrup also has a book collection consisting of approximately 1,500 books, including nursing literature and medical handbooks.

THE ANIMAL FACILITY

Animal welfare is important to us, and we strive to provide the highest standard for the animals in our facility. We aim to ensure that the animals are housed in a way that will contribute to their physiological and behavioral needs, and that they are provided with an environment that is as calm as possible for the animals to breed and participate in our studies.

The animal facility houses mice and rats in open conventional type III and type IV cages, and we prioritize the welfare of animals by focusing on species-specific needs. We offer our rodents different enrichment in the cages to stimulate their natural behaviour, and all of our animals are given peanuts, corn, sunflower seeds, and hay bricks as a supplement to their normal diet. This is to stimulate foraging and gnawing behavior.

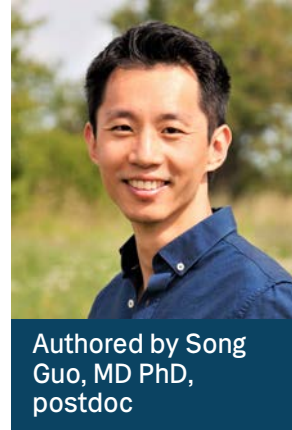
We have a variety of enrichments for our animals, such as four different nesting materials for our mice, different types of shelters, a chew stick, a hammock, a cardboard tunnel in the lid, hemp rope, a handle tube, and bedding. Our animals are only handled by cupping or with tunnels to minimize stress and with water and a normal diet are available ad libitum.

Our rats have a shelter, different types of tunnels, a chew stick, two different nesting materials, hemp rope, and bedding. Every week we also offer our rats scented enrichment such as hemp rope, cocoons, happi mats, etc., to stimulate their senses.



TRANSLATIONAL RESEARCH – WHAT IS IT?

The vision and purpose of health science is to make new discoveries that eventually benefit the individual patient and the overall healthcare system. However, in recent decades it seems that enormous investments in basic and clinical research are not yielding the expected benefits. Causes could be that the complexity of modern science is at such a high level that novel groundbreaking discoveries are more difficult to achieve. Another cause could be due to the widening gap between basic and clinical research. Over the past 30 years, the ecosystems of basic and clinical research have diverged, and the abyss left behind is sometimes labelled the “Valley of Death”. There is no question that we do excel in basic research in Denmark and that basic science is the foundation for clinical research, but what we should be asking is, have we neglected the mandate to apply that knowledge.



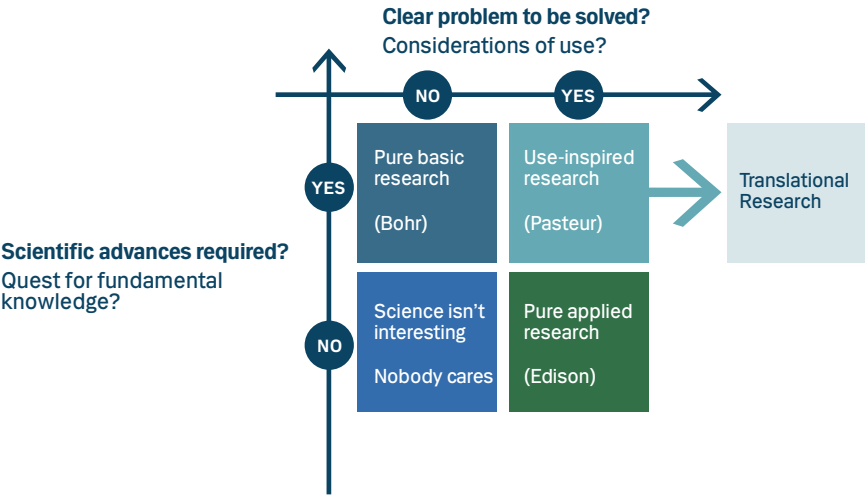
Authored by Song
Guo, MD PhD,
postdoc

The aim of translational research is to translate basic science discoveries more quickly and efficiently into clinical practice to benefit patients. I believe one of the characteristics of successful contemporary science is teamwork. Only through collaboration between clinical, basic, and pharmaceutical sciences working together on clear scientific questions can we provide better care and therapies for patients. The COVID vaccine is a great example of such success.

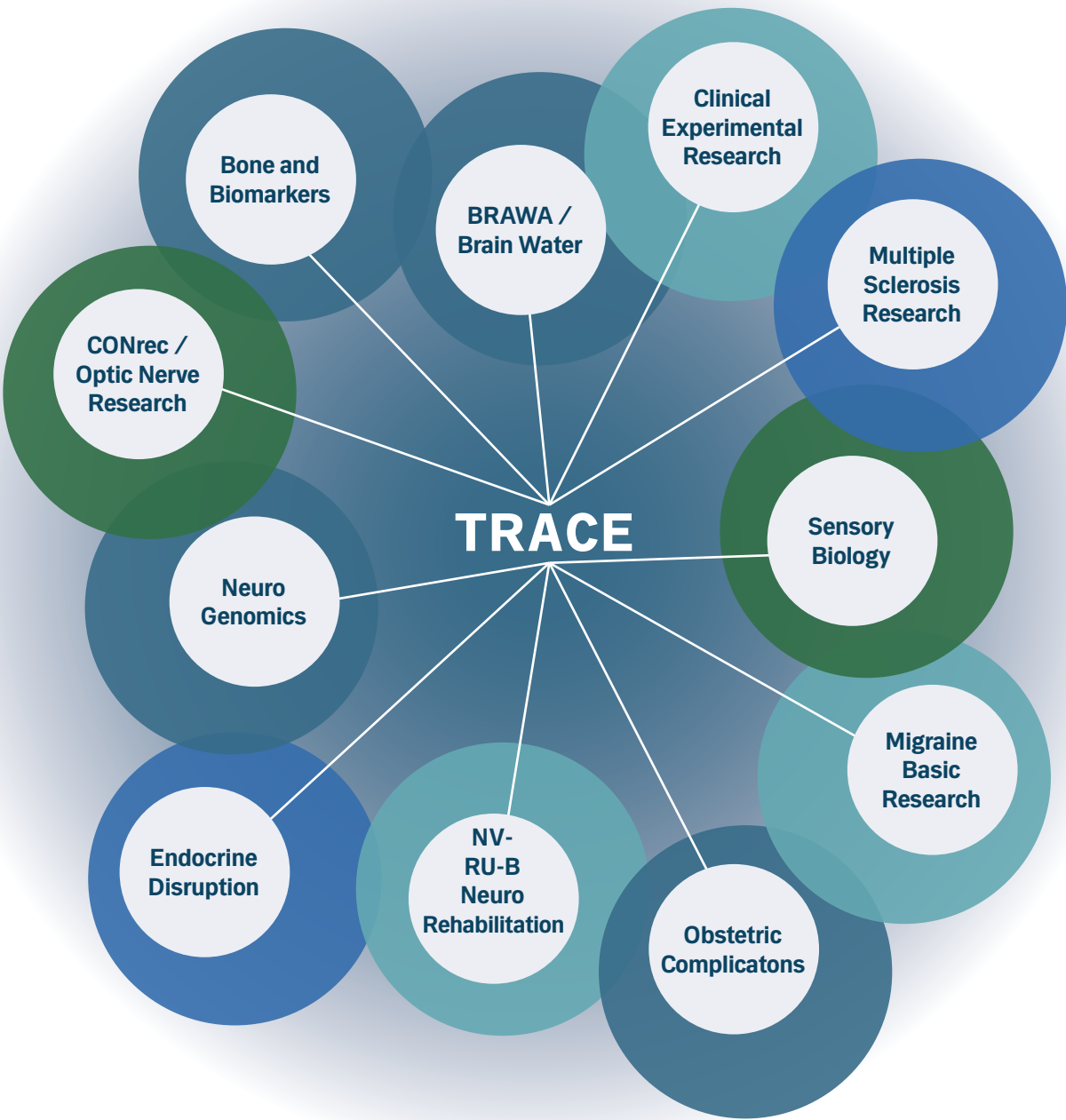
I am a medical doctor who have conducted clinical research for over 10 years, before I took the step crossing over to basic research. The reason for taking this step is because of a very interesting collaboration between Panum Institute, Danish Headache Center and Lundbeck in a post-doctoral programme called BRIDGE. The recent breakthroughs in headache medicine and research are the result of translational work and collaboration, taking ideas from bedside to bench and back. Animal experiments are necessary to understand the different mechanistic components of the migraine attack. Afterwards, these mechanistic findings from basic research will hopefully be translated to humans and tested in clinical experiments and trials in the development of novel migraine therapies.

The facilities at TRACE, close to The Danish Headache Center, is the optimal site for enabling a bidirectional translation of research findings between humans and animals. TRACE offers a unique environment where researchers from different scientific fields can meet each other and share their ideas and knowledge for the benefit of innovative research projects. My recent translational project investigating the mechanisms of PACAP38 in migraine has contributed with knowledge in understanding anti-PACAP38 therapies, which has shown efficacy in phase II trials and is now entering phase III. My time at TRACE has been an exceptional opportunity to develop and educate myself in becoming a more complete translational researcher. I can only recommend others doing the same.

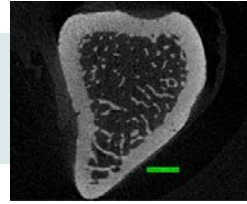
PASTEUR’S QUADRANT



RESEARCH UNITS AT TRACE



BONE AND BIOMARKERS



Principal Investigator – Niklas Rye Jørgensen



Professor

(Department of Clinical Medicine,
Faculty of Health and Medical Sciences,
University of Copenhagen)

Chief physician

(Department of Clinical Biochemistry)

Principal Investigator – Lasse Kristoffer Bak



Professor

(Department of Drug Design and
Pharmacology, Faculty of Health and Medical
Sciences University of Copenhagen)

Pharmacist

(Department of Clinical Biochemistry)

The research is focused on two major areas. The first investigates the pathophysiological mechanisms of metabolic bone diseases with special emphasis on bone disease in relation to other chronic diseases including neurological diseases, immobilization, cancer, diabetes and medicine-induced bone loss. There is a strong focus on the development and evaluation of novel biomarkers for bone disease. The approach used includes both basic laboratory studies, animal models as well as clinical studies and epidemiological/register-based studies enriched with clinical data. Thus, a true translational approach is applied. Current projects focus on the mechanisms for developing bone destruction in multiple myeloma, iatrogenic bone loss associated with treatment of other chronic diseases and finally the clinical use of bone turnover markers for monitoring anti-osteoporotic treatment and for monitoring treatment pause in osteoporosis patients.

The second area of research is on therapeutic drug monitoring. (TDM) and pharmacokinetic models where we focus on developing new models for prediction of clinical outcome based on clinical data and measurements of blood concentrations of different drugs for a more personalized approach to dosing of patients. TDM includes both new models for predicting efficacy of already established drug analyses but also exploration of new analyses of medicines where TDM has not previously been used.

Ankita Agrawal – Senior scientist



Exploring the relevance of extracellular adenine nucleotides and ionotropic purinergic receptor 7 (P2X7) in multiple myeloma that attacks the bone marrow.

Michael Schønemann Rand – 1st year PhD



The research investigates the effectiveness of bone turnover marker monitoring of oral bisphosphonate therapy in patients with osteoporosis in regard to increasing medication adherence and bone mineral density and reducing risk of fracture.

Morten Christian Melchior Nissen – Research Assistant



The research investigates the clinical usefulness of monitoring of osteoporosis patients during treatment pause.

Susan Herrmann – Chemist, Department of Clinical Biochemistry

The research focuses on

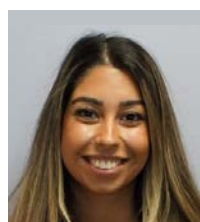
- a) Purinergic signaling in health and disease, and
- b) The Role of neuropeptides in the Regulation of Bone Metabolism

Tanja Hegner – Animal Technician

Assists researchers by preparing equipment and materials, handling animals, recording data, and ensuring all procedures adhere to established protocols during experiments.

Eva Risborg Høyer – Stud. Pharm, master project

Molecular and pharmacological characterization of P2X7 receptor in myeloma cell lines

Melisa Demir – Stud. Pharm, master project

Molecular and pharmacological characterization of P2X7 receptor in myeloma cell lines

Lærke Charlotte Beuschau – Stud. Pharm, master project



Measurement of cortisol/cortisone ratio as supplement to the currently used THF + allo-TFH/THE ratio in the diagnosis of Syndrome of Apparent Mineralocorticoid Excess (SAME).

Co-supervised students: PhD students: Sabina Hauge (Niklas), Gowthami Gunapalasingham (Niklas), Sofie Norlin Mølgaard (Niklas), Lin Yang (Lasse).

Publication Highlights in 2023

Expression of the Purinergic P2X7 Receptor in Murine MOPC315.

BM Myeloma Cells. Høyer ER, Demir M, Bak LK, Jørgensen NR, Agrawal A. Receptors. 2023;2(3):191-203. doi:<https://www.mdpi.com/2813-2564/2/3/13>.

New Emerging Biomarkers for Bone Disease: Sclerostin and Dickkopf-1

(DKK1). Dincel AS, Jørgensen NR. Calcif Tissue Int. 2023;112(2):243-57. doi:10.1007/s00223-022-01020-9.

Academic engagement

Grant committee: Evaluation committee in Region H for research funding

Scientific committees: Scientific advisory board: P2X receptors as therapeutic targets (PRESTO), EU funded Action on Cooperation in Science and Technology, Management Committee and Science Communication Coordinator of PRESTO. International Society of Bone Morphometry (ISBM) Early Career Investigators Committee. Danish Society for Clinical Biochemistry: Committee for the specialist training program in clinical biochemistry. National working group on therapeutic drug monitoring. Committee on advancement of research, Danish Society for Clinical Academics. International Osteoporosis Foundation: Scientific Advisory Committee. International Federation for Clinical Chemistry: Committee for Bone Metabolism. ESCEO Working Group on Bone Turnover Markers in the diagnosis and management of osteoporosis.

Editorial work: Editorial board for Neurochemical Research, Frontiers in Endocrinology, Current Opinion in Pharmacology (associate editor)

BRAWA / BRAIN WATER



Principal scientist – Connor Stanley James Westgate



Senior Scientist

Danish Headache Center,
Department of Neurology
Rigshospitalet-Glostrup.

Our team's research investigates the biology and pathophysiology of cerebral hydrodynamics and intracranial pressure using the disease idiopathic intracranial hypertension (IIH) as a disease model. Intracranial pressure physiology is poorly understood, so focusing on a model disease enables us to investigate unknown biology while being driven by clinical need. We particularly focus on understanding the role of endocrine and metabolic dysfunction of intracranial pressure, while investigating the clinical sequelae of raised pressure, namely headache and ocular outcome. Here we wish to elucidate the mechanisms underlying raised intracranial pressure and the process that underly neuroretinal degeneration in raised intracranial pressure.

We also perform biochemical phenotyping of IIH patients with an aim of changing clinical practice through prognostic and diagnostic markers, as well understanding the underlying pathophysiology of IIH. These findings directly inform our animal research ensuring truly translational research. Our ultimate aim to understand the biology of intracranial pressure to enable us to develop targeted therapies that can alleviate raised pressure and its detrimental clinical sequelae for the benefit of patients.

**Rigmor Højland Jensen – Professor, Overlæge, Dr.med.,
Director for Danish Headache Center**



Leader of the translational CSF-research group and focus mainly on the clinical human aspects of IIH, secondary causes of increased intracranial hypertension and of spontaneous intracranial hypotension.

Sajedeh Eftekhari – Senior scientist PhD



until October 2023 and was funded by the Lundbeck foundation and Candys Foundation. Sajedeh Eftekhari had led the IIH group for more than 5 years and pioneered the many projects related to the continuous ICP-recording in rats. Sajedeh was also the mentor for Connor Westgate, Ida Israelsen and four Master students.

Ida Israelsen – former PhD student



and employed until October 2023 and was funded by the Lundbeck Foundation. Submitted her PhD thesis entitled 'The mechanisms underlying intracranial pressure regulation in the context of risk factors associated with Idiopathic Intracranial Hypertension' using an animal model in autumn 2023.

Christina Kamp-Jensen – cand Pharm, 1st year PhD



Funding by Lundbeck Foundation and Rigshospitalets Research Foundation. The research investigates the distribution of sex hormones and their role in CSF-production. Moreover, Christina is investigating the steroid hormone profile in IIH patients with a view towards diagnostic and prognostic factors.

Tanja Lylloff – Pharma student

Funding by Rigshospitalet The research investigates the effects of the rodent estrus cycle on steroid hormones in headache relevant tissues.

Nadja Skadkær Hansen – MD, 2nd year PhD student

Funding by Novo Nordic Foundation. The clinical research investigates treatment effects of GLP1-agonism on weight loss and intracranial pressure in patients with new-onset idiopathic intracranial hypertension, along with metabolic parameters, visual outcomes, headache burden and quality of life.

Louise Norgil Donslund – Cand Pharm

Former Master student. Louise defended her master thesis in the summer of 2023, where her study focused on investigating the endocrine disrupting properties of acetazolamide and topiramate.

Publication Highlights in 2023

Effects of caffeine on intracranial pressure and pain perception in freely moving rats.

Israelsen IME, Westgate CSJ, Kamp-Jensen C, Jensen RH, Eftekhari S. Headache. 2023 Oct;63(9):1220-1231. doi: 10.1111/head.14634.

Glucocorticoids modify intracranial pressure in freely moving rats. Westgate CSJ, Israelsen IME, Kamp-Jensen C, Jensen RH, Eftekhari S. Fluids Barriers CNS. 2023 May 25;20(1):35. doi: 10.1186/s12987-023-00439-y.

Other Group members

Johanne Korsbæk, MD, PhD, Post Doc, Danish Headache Center, Dagmar Beier, MD, Professor, Odense University Hospital, Vlasta Vukovic. MD, Senior Registrar, Danish Headache Center, Katrine Svart, Stud med, Danish Headache Center.

Academic engagement 2023

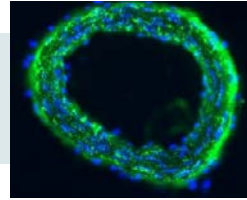
Scientific advisory board: Rigmor Hoejland Jensen is serving in the Advisory Board for Lundbeck Pharma.

Other committees: Rigmor Hoejland Jensen is serving as Director in Lifting The Global Burden (WHO-organisation).

Funding

Thanks to the Lundbeck foundation, Candys Foundation, Rigshospitalets Research foundation and Migræne fonden af 1988.

CLINICAL EXPERIMENTAL RESEARCH



Principal Investigator – Lars Edvinsson MD, PhD



Professor in Internal Medicine

Faculty of Medicine, University of Lund

Director

Experimental Vascular Research
Laboratory, Biomedical Center,
University of Lund

Our team started 1996 and has focused ever since on discoveries of perivascular nerves regulating autonomic functions related to control of cerebral blood flow in health and disease. We have written major books in the field of Cerebral Blood Flow and Metabolism. During the last two decades we have focused on receptor regulation and discovered the upregulation of contractile receptors as an important disease modifier in the brain circulation, with role in stroke damage development. This has resulted in an ongoing Phase IB/IIA trial at the neurosurgery clinic at Rigshospitalet. It is projected to end at Q4 2024. If positive, it may pave the way for novel therapies.

The second line of research has focused on identification of sensory neurotransmitters in the trigeminovascular system. Of note we discovered the calcitonin gene related peptide (CGRP) in the trigeminal system 1984 and paved the way for current understanding and migraine therapy with monoclonal antibodies and gepants. These drugs are now in clinical practice worldwide. Lars Edvinsson received the Lundbeck Brain Prize 2021 from the hands of the Danish King Fredrik. Ongoing work focus on questions related to hormonal regulation of the sensory system.

Anja Holm Senior – Researcher, Associate Professor



Center for RNA Medicine, Department of Clinical Medicine, Aalborg University, Funding: Lundbeck foundation. The research focuses on exploring the role of sex hormones on the CGRP system in both RAMP1 dependent and -independent manners. Additionally, novel RNA-targeted migraine therapeutics are being designed and developed as part of this research.

Jesper Peter Bömers – PhD student



The research focuses on molecular interventions for aneurysmal subarachnoid hemorrhage in a rodent model, aiming to discover potential treatments which could pave the way for improved clinical outcomes.

M Emelie Pitkänen Fungrbrant – MD, 1st year PhD



Funding by Rigshospitalet. The research investigates the role of MEK1/2 and PKC in treatment of experimental subarachnoid haemorrhage using behaviour methods and in vivo MRI T7 in collaboration with the MR centre at Hvidovre hospital.

Kine Stamp-Larsen – project student



Center for RNA Medicine, Department of Clinical Medicine, Aalborg University. The research focuses on establishing an in vitro migraine model. By stimulating cells expressing the CGRP encoded gene CALCA with different concentrations of female sex hormones and analyzing the levels of genes involved in the CGRP-system on both RNA and protein levels.

Sofia Setareh Abtahi – Master student



Department of Pharmacology, University of Copenhagen. The research focuses on identifying new potential targets for treating menstrual migraine. These targets could be tested experimentally in relevant migraine models to assess their efficacy.

Co-supervised students

Spyridoula Kazantzi PhD Student (Sensory Biology), characterization of signalling pathways that are activated in arteries following in a model mimicking stroke, utilizing myograph techniques. Philip V. Reducha, PhD Student (Sensory Biology), changes of RNA levels following inflammation.

Publication Highlights in 2023

Progesterone distribution in the trigeminal system and its role to modulate sensory neurotransmission: influence of sex. Maddahi A, Warfvinge K, Holm A, Edvinsson JCA, Reducha PV, Kazantzi S, et al. J Headache Pain. 2023;24(1):154. doi:10.1186/s10194-023-01687-x.

Heterogeneous vasomotor responses in segments from Göttingen Minipigs coronary, cerebral, and mesenteric artery: A comparative study. Sams A, Haanes KA, Holm A, Kazantzi S, Mikkelsen LF, Edvinsson L, et al. Vascul Pharmacol. 2023;153:107231. doi:10.1016/j.vph.2023.107231.

Editor: The Journal of Headache and Pain

Grant committee: Tegger foundation

Scientific advisory board: SHS board

Other committees: ERC Neuroscience board, Brussels, Belgium.

CONREC / OPTIC NERVE RESEARCH

Principal Investigator – Steffen Hamann



Clinical Research Associate Professor

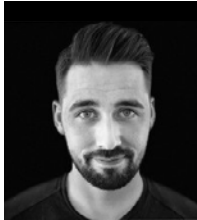
Department of Ophthalmology,
Copenhagen University Hospital,
and Department of Clinical Medicine,
University of Copenhagen

Our research group has two major focus points. The first centers around optic neuropathies, where axonal compression, inflammation and loss of blood supply potentially lead to loss of vision. In particular, we want to understand the underlying pathobiology of increased intracranial pressure states, ischemic optic neuropathies, and optic disc drusen. In this focus point we perform clinical studies and patient trials on patients with optic neuropathies, and translational research, where we in rodent models investigate the effect that raised intracranial pressure or other equivalents to human disease have on the retina and optic nerve. We also perform basic studies focusing on osteoclast activity on histological specimen of optic disc drusen in order to ultimately develop a treatment for this disease based on a decalcification principle.

Our second major focus point is oculomics – the study of the eye as a biomarker for systemic disease – with a particular focus on brain disease. Here we employ advanced artificial intelligence-based, multimodal deep phenotyping of the retina and optic nerve as a proxy for early and accurate diagnosis of neurologic disease, often detectable even before the onset of symptoms. Informed by the results from these, mainly clinical studies, our goal in the near future is to set up a translational arm, using OCT-based deep phenotyping of the retina and optic nerve looking for signatures of brain disease in animal models.

Group members currently involved in translational research:

Snorre Malm Hagen, PhD student, MD



Research focusing on optic nerve and retinal signatures of raised intracranial pressure in rodent models. Will defended his PhD thesis in 2024.

Josephine Mejdahl Bentin, MD



Former masters student. Performed basic studies on the effect of osteoclasts targeting the calcified property of optic disc drusen in histology specimen.

Publication Highlights in 2023

Retinal vessel dynamics analysis as a surrogate marker for raised intracranial pressure in patients with suspected idiopathic intracranial hypertension. Hagen SM, Wibroe EA, Korsbæk JJ, Andersen MS, Nielsen AB, Nortvig MJ, et al. Cephalalgia. 2023;43(3):3331024221147494. doi:10.1177/03331024221147494.

Discriminating Between Papilledema and Optic Disc Drusen Using 3D Structural Analysis of the Optic Nerve Head. Girard MJA, Panda S, Tun TA, Wibroe EA, Najjar RP, Aung T, et al. Neurology. 2023;100(2):e192-e202. doi:10.1212/wnl.0000000000201350.

Other Group members

Lasse Malmqvist, MD, PhD, Alvilda Steensberg, MD, PhD Student, Elisabeth Wibroe, MD, PhD Student, Michael Stormly Hansen MD, PhD Student, Lea Lykkebirk, MD, PhD Student, Sanja Cejvanovic, MD, PhD Student, Marius Mårtensson, Medical Student, Michaela Graven Nielsen, MD, Junior Scientist, Christopher Maximillian Behrens, MD, Junior Scientist, Morten Jørgensen, MD, Junior Scientist, Andreas Worm Bendtsen, MD, Junior Scientist

Academic engagement 2023

Editor: Steffen Hamann is Associate Editor on Neuro-Ophthalmology (Taylor & Francis)

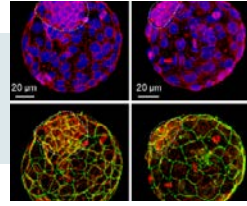
Consortia: Steffen Hamann is the founder and chair of the international Optic Disc Drusen Studies (ODDS) Consortium and leader of the neuro-ophthalmology workgroup in the EU supported European strategical reference network for rare eye diseases ERN-EYE.

Other committees: As of July 1, 2024, Steffen Hamann is leading the International Relations Committee of NANOS (North American Neuro-Ophthalmology Society) Funding.

Thanks to the VELUX Foundation, Rigshospitalet Research Foundation, Synoptik Foundation, and Øjenforeningen.



ENDOCRINE DISRUPTION



Principal Investigator – David M Kristensen



Senior researcher
(Copenhagen University
Hospital)

Professor (Molecular
Physiology, Department of
Science and Environment)

Our team's research focus on understanding how the environment impacts human development and adult homeostasis. We are doing this by using clinical studies in combination with animal models, cellular assays, and modelling. The central aims of this work have been in a translational manner to understand disease mechanisms and create better treatments for patients by: (i) identifying new drug targets; (ii) understanding off target effects of drugs already in the clinic; and (iii) understanding how ubiquitous xenobiotics can drive recent increases in prevalence of adverse health outcomes within reproduction, metabolism, and neurobiology.

Brian Skriver Nielsen Post Doc,



Funding by the Miljøstyrelsen

The research focuses on understanding disrupting effects of everyday pharmaceuticals on early development. Moreover, Brian is leading several projects involving effects on metabolism and brain development.

Emira Hackic Scientific Assistant,



Funding by the Lundbeck foundation.

The research focuses on investigating the xenobiotic compounds effect on migraine signalling.

Publication Highlights in 2023

Xenobiotic Exposure and Migraine-Associated Signaling: A Multimethod Experimental Study Exploring Cellular Assays in Combination with Ex Vivo and In Vivo Mouse Models. Rasmussen RH, Christensen SL, Calloe K, Nielsen BS, Rehfeld A, Taylor-Clark TE, et al. Environ Health Perspect. 2023;131(11):117003. doi:10.1289/ehp12413.



MIGRAINE BASIC RESEARCH

Principal Investigator – Jes Olesen



Professor

Department of Neurology,
Danish Headache Center,
Copenhagen University Hospital
– Rigshospitalet, Glostrup

Principal Investigator – Sarah Louise T. Christensen



Senior scientist,

Department of Neurology, Danish Headache Center

Instructor

Department of anaesthesia, Critical care, and Pain Medicine Beth
Israel Deaconess Medical Center – Harvard Medical School

External Associate Professor

Department of Clinical Medicine,
Copenhagen University Hospital

The focus of our research is to understand migraine pain mechanisms and identify potential therapeutic targets. This is done via development and validation of animal models of migraine based on findings in human migraine provocation studies. The animal models are applied to identify relevant behavioural endpoints in rodents, decipher molecular signalling pathways involved in migraine pain, and identify contributions from different cell types of the trigeminovascular system. Furthermore, we use ex vivo assays to study neuropeptide release and arterial dynamics in isolated tissue from the trigeminovascular system.

Academic engagement 2023

Editor for journals: Pharmaceuticals, special edition: guest editors Sarah Louise Tangsgaard Christensen and Jes Olesen.

Karina Obelitz Ryom – Post Doc



Funding by Candys Foundation
The research focuses on exploring the contribution of large conductance potassium channels in the generation of migraine pain primarily by use of in vivo mouse models.

Song Guo – Postdoc (end date 31.12.2023)



Funding by the BRIDGE translational Excellence Programme

Project focussing on mechanisms of PACAP38 induced migraine pain by use of in vivo mouse models and wire myography.

Rikke Holm Rasmussen – 3rd year PhD



Funding by Foreningen til støtte af forskning ved Dansk Hovedpine Center

The research investigates migraine signalling pathways with focus on how xenobiotics may activate these pathways and contribute to migraine pathophysiology.

Inger Jansen-Olesen – Senior Scientist (end date 31.09.2023)



Funding by Candys Foundation.

Co-supervision and research focusing of vascular signal transduction and its contributions to migraine pathophysiology.

Charlotte Ernstsén – PhD student and postdoc (end date 31.09.2023)

Funding by Candys foundation
The research investigated migraine treatment targets and their signalling pathways.

Amalie Clement – Postdoc (end date 31.10.2023)

Funding by Foreningen til støtte af forskning ved Dansk Hovedpine Center.

Research investigating applicability of different behavioural readouts to detect migraine-relevant pain in mouse models.

Cecilie Luna Christiansen Master student (end date 31.11.2023)

Research project validating the hotplate test as readout in migraine mouse models. Both in terms of stability towards repeated testing and ability to detect altered sensory thresholds.

Publication Highlights in 2023

Xenobiotic Exposure and Migraine-Associated Signaling: A Multimethod Experimental Study Exploring Cellular Assays in Combination with Ex Vivo and In Vivo Mouse Models. Rasmussen RH, Christensen SL, Calloe K, Nielsen BS, Rehfeld A, Taylor-Clark TE, et al. Environ Health Perspect. 2023;131(11):117003. doi:10.1289/ehp12413

PACAP signaling is not involved in GTN- and levromakalim-induced hypersensitivity in mouse models of migraine. Guo S, Ernstsén C, Hay-Schmidt A, Kristensen DM, Ashina M, Olesen J, et al. J Headache Pain. 2022;23(1):155. doi:10.1186/s10194-022-01523-8

MULTIPLE SCLEROSIS RESEARCH

Principal investigator – Jette Lautrup Frederiksen



MD, DMSc. Professor
at Department of Neurology,
Rigshospitalet and University
of Copenhagen

Principal investigator – Gunnar Houen



MSc, PhD, DSc. Research associate
at Department of Neurology,
Rigshospitalet and professor
at Department of Biochemistry
and Molecular Biology, SDU

The research group focuses on the immunology of multiple sclerosis (MS) and related disorders, including optic neuritis, myelin oligodendrocyte glycoprotein-associated disease (MOGAD) and neuromyelitis optica (NMO). This translational research focuses on the interplay of predisposing genetic factors and environmental factors examining patients from our clinical research group at Department of Neurology. Especially the role of Epstein-Barr Virus as a major and necessary driver of the central nervous system inflammation in MS has been investigated. Based on this, we are now focusing on the interplay of EBV with the immune system in relation to disease etiology, diagnosis, treatment and prognosis.

Nicole Hartwig Trier – Post. Doc.

Funding by Rigshospitalet.
The research focuses on the role of Epstein-Barr Virus and other viruses in MS and MOGAD.

Kirsten Beth Hansen – Laboratory technician.

The research focuses on the role of Epstein-Barr Virus and other viruses in MS and MOGAD.

Nadia Zivlaei – MSc student

University of Copenhagen
The research focuses on the role of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS CoV-2), Epstein-Barr Virus and other viruses in MS.

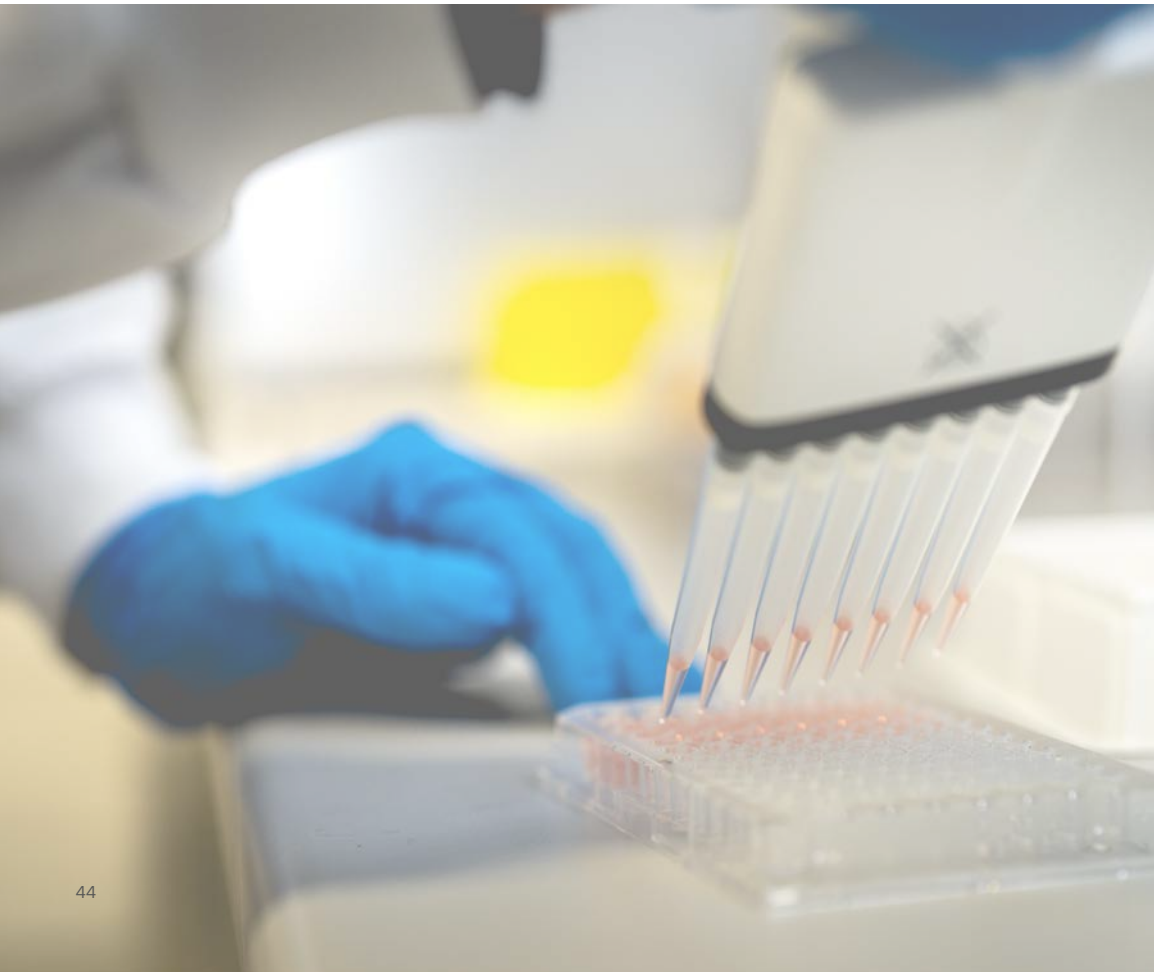
Daut Can Asani – MSc student

University of Roskilde
The research focuses on antibody structure and the role of Epstein-Barr Virus and other viruses in MS.

Publication Highlights in 2023

Antibody Cross-Reactivity in Auto-Immune Diseases. Trier NH, Houen G. *Int J Mol Sci.* 2023;24(17). doi:10.3390/ijms241713609

Antibodies to expanded virus antigen panels show elevated diagnostic sensitivities in multiple sclerosis and optic neuritis. Gåsland H, Trier NH, Kyllensbech C, Draborg AH, Slibinskas R, Ciplys E, et al. *Immunol Lett.* 2023;254:54-64. doi:10.1016/j.imlet.2023.02.003.



NEURO GENOMICS

**Principal Investigator – Associate Professor Thomas F Hansen MSc PhD****Senior Researcher**

Rigshospitalet, Copenhagen University Hospital:
Danish Headache Center
Danish Multiple Sclerosis Center
Translational Research Centre

Associate Professor

Novo Nordisk Foundation Research Center for Protein
Research, Copenhagen University

The NeuroGenomic Group specializes in genetics and genomics research, dedicated to unraveling the complexities of the human genome and its role in neurological disorders. Utilizing a systems biology approach, the group strives to understand the disease mechanisms underlying neurological conditions. The research is further enhanced by a commitment to translational approaches, with the ultimate aim of advancing precision medicine in the field of neurology. Based at the Translational Research Centre, the team collaborates closely with the Danish Multiple Sclerosis Center (DMSC), the Danish Headache Center (DHC), and the Novo Nordisk Center for Protein Research at Copenhagen University.

Lisette Kogelman – Associate Professor MSc, PhD

The research focuses on whole genome sequencing of familial migraine and twins with migraine, exploring genetic comorbidity and disease trajectories in neurological disorders.

Isa Amalie Olofsson – MD, PhD, BRIDGE Post Doc



The research focuses on identifying genetic variants associated with individuals who have never experienced a headache.

Mona Ameri Chalmer – MD, PhD, Part-Time Post Doc



The research focuses on a clinical and genetic approach to migraine sex differences and menstrual migraine, including mapping migraine onto the omics atlas of the menstruation cycle.

Tanya Ramdal Techlo – MSc, PhD-Student



The research focuses on the use of whole exome sequencing and whole genome sequencing from families to find the causative genetic factors of migraine and epilepsy.

Olafur B. Davidsson – MSc, PhD, Biostatistician



The research focuses on migraine, including triptan consumption from 1994 to 2019, and the correlations between migraine, preeclampsia risk, and childhood cancer. It aims to develop predictive models for triptan efficacy, requiring further genetic studies on migraine.

Ragnar Kristjánsson – MSc, PhD



The research focuses on employing advanced approaches in human genetics to elucidate disease etiology and progression and to identify novel causative variants.

Publication Highlights in 2023

Rare variants with large effects provide functional insights into the pathology of migraine subtypes, with and without aura. Björnsdóttir G, Chalmer MA, Stefánsdóttir L, Skúladóttir AT, Einarsson G, Andrésdóttir M, et al. *Nat Genet.* 2023;55(11):1843-53. doi:10.1038/s41588-023-01538-0.

Cluster Headache Genomewide Association Study and Meta-Analysis Identifies Eight Loci and Implicates Smoking as Causal Risk Factor. Winsvold BS, Harder AVE, Ran C, Chalmer MA, Dalmaso MC, Ferkingstad E, et al. *Ann Neurol.* 2023;94(4):713-26. doi:10.1002/ana.26743.

Consortia

- Danish Blood Donor Study [DBDS]: Steering Member
- Danish Blood Donor Study Genomic Consortium [DBDS-GC]: Co-PI
- Copenhagen Hospital Biobank [CHB-degen, CHB-brain]: Protocol member on neurological disorders
- International Headache Genetics Consortium [IHGC]: Deputy Chair
- Collaboration on Cluster Headache Genetics [CCG]: PI

Current Funding

Independent Research Counsel: The cyclome (DFF Project 2), in collaboration with SSI (Prof. Mette Nyegaard) and Hvidovre Hospital (Prof. Henriette S Nielsen).

BRIDGE Post Doc, Isa Olofsson, in collaboration with Copenhagen University (Prof Eva Hoffman) and deCODE Genetics (Gyda Björnsdóttir).

Candy's Foundation, PI Jes Olesen.

NVRU-B / BASIC NEUROVASCULAR AND NEUROREHABILITATION RESEARCH

Principal Investigator – Christina Kruuse



Clinical Professor,
Department of Brain and Spinal Cord
Injury Copenhagen University Hospital,
and Department of Clinical Medicine,
University of Copenhagen

Our translational research group NVRU addresses basic mechanisms of neuronal and neurovascular signaling in health and neurological diseases. We focus on stroke, traumatic brain- and spinal cord injury. We work from bench to bedside and back, aligning findings in preclinical studies to implementable treatments in neurovascular disease and improving neurorecovery after brain and spinal cord injury. We specialize in repurposing drugs for use in neurovascular disease or neuronal injury for ease of applicability in the clinical practice.

NVRU-B, established in TRACE in 2023, is a part of the clinical NVRU group allocated to Dept of Brain and Spinal Cord Injury, Rigshospitalet, formerly at Dept of Neurology Herlev Gentofte Hospital.

The current pre-clinical projects focus on vascular and neuroinflammatory effects of treatment modifying cellular cyclic nucleotide signaling regulated by phosphodiesterases (PDE) in an animal stroke model and blood from humans. Pre-existing or induced neuroinflammation may be a key component involved in both detrimental and restorative mechanisms in stroke, and modifying the response may improve recovery. The animal stroke models are currently done in collaboration with Professor Kate Lambertsen, Neurobiology Research Unit, Odense SDU, but will be further evolved and established at TRACE. We further benefit from the close interaction with other key groups at TRACE on cellular signalling analysis.

Group members currently involved in translational research:

Nina Steen Vindegaard Sørensen – Post doc, MD



The overall research focus is post-stroke immunological alterations and the immune system as treatment target in neurorehabilitation after stroke - in this specific project investigations of phosphodiesterase in a stroke model.

Publication Highlights in 2023

Patient-tailored transcranial direct current stimulation to improve stroke rehabilitation: study protocol of a randomized sham-controlled trial. Kolmos M, Madsen MJ, Liu ML, Karabanov A, Johansen KL, Thielscher A, et al. *Trials*. 2023;24(1):216. doi:10.1186/s13063-023-07234-y.

Testing the cognitive effects of tadalafil. Neuropsychological secondary outcomes from the PASTIS trial. Pauls MM, Fish J, Binnie LR, Benjamin P, Betteridge S, Clarke B, et al. *Cereb Circ Cogn Behav*. 2023;5:100187. doi:10.1016/j.cccb.2023.100187.

Funding

Læge Sofus Carl Emil Friis og hustru Olga Doris Friis' Legat.



OBSTETRIC COMPLICATIONS



Principal Investigator – Line Rode



**Senior researcher
PhD, MD**

Our research group is part of an interdisciplinary network that includes the Department of Obstetrics, the Center of Fetal Medicine, and the Department of Clinical Biochemistry at Rigshospitalet. The core of our research is prediction and prevention of common obstetric complications. It is centered on developing and testing screening algorithms that incorporate biochemical markers to identify pregnant women at increased risk of complications such as preeclampsia, preterm birth, and intra-uterine growth restriction. The overall aim of the research is to support the possibility of offering pregnant women individualized antenatal care based on each woman's risk profile, with a societal cost-effectiveness benefit. We focus on prediction during the first trimester of pregnancy, allowing targeted preventive treatments to contribute to reaching the best possible short-term and long-term outcome for mother and child. The research is based on large prospective cohort studies, clinical randomized trials, and epidemiological studies, forming the basis for a wide range of national and international collaborations that bridge clinical biochemistry and fetal medicine/obstetrics. Our international collaborations include researcher from UK, Sweden, Austria, and Australia. As part of our work, we perform analysis of biomarkers on automatized equipment (B·R·A·H·M·S KRYPTOR compact PLUS).

Mille Kirk (previously Taagaard) – Midwife and MSc in Human Biology



Funding by Rigshospitalet's Research Fund, Introductory scholarship 2023-2024.

Mille's research is focused on assessing first-trimester biomarkers associated with spontaneous preterm birth and identifying maternal risk factors related to the condition. The aim is to combine these factors in a first-trimester prediction model for spontaneous preterm birth.

Supervision of PhD students

Co-supervisor for midwife Nina Nathan. UCPH, ongoing. Main supervisor: Professor Hanne K Hegaard. Project title: Labour dystocia and augmentation – predictors and prevention.

Co-supervisor for MD Iben Riishede Christiansen. UCPH. Defended 2023. Main supervisor: Associate professor Charlotte K Ekelund. Project title: Screening for preeclampsia in the first trimester of the pregnancy.

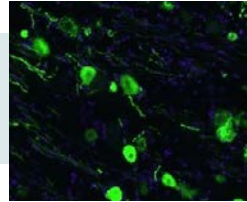
Publication Highlights in 2023

Pre-eclampsia screening in Denmark (PRESIDE): national validation study.

Riishede I, Rode L, Sperling L, Overgaard M, Ravn JD, Sandager P, et al. Ultrasound Obstet Gynecol. 2023;61(6):682-90. doi:10.1002/uog.26183.

Paracetamol use prior to and in early pregnancy: Prevalence and patterns among women with and without chronic medical diseases. Taagaard M, Rode L, de Wolff MG, Damm P, Hagen CP, Fisher MB, et al. Br J Clin Pharmacol. 2023;89(8):2582-91. doi:10.1111/bcp.15732.

SENSORY BIOLOGY



Principal Investigator – Kristian A. Haanes



Senior researcher and Associate Professor

Department of Biology,
Copenhagen University Hospital

Our team's research investigates the physiological roles of sensory nerves, focusing on neurons within the trigeminal ganglion that play a key role in pain transmission, crucial for understanding migraines and other primary headaches. We study these neurons' mechanisms for transmitting signals, adapting to changes, and protecting against damage, with a focus on the pathophysiology of migraine and related sensory disturbances. Additionally, our work includes examining the blood vessels these nerves innervate to find ways to improve resistance to ischemic injuries, such as those caused by strokes. Our examination of the trigeminovascular system seeks to understand its influence on neurovascular innervation and sensory dysfunctions, with an emphasis on pain processing. The research encompasses the system's role in supplying blood to cerebral arteries and the dura mater, providing insights into stroke, glaucoma, and migraine. An important part of our study is Calcitonin Gene-Related Peptide (CGRP), for its vasodilatory effects and its potential in treating ischemic conditions.

Karin Maria Löfgren Nordahl – Post Doc,



Funding by the Lundbeck foundation.
The research focuses on exploring the therapeutic implications of neuropeptides in the treatment of glaucoma and elucidating their role in the pathophysiology of cluster headaches.

Philip Victor Reducha – 3rd year PhD

Funding by the Lundbeck foundation
The research focuses on investigating the roles of inflammation, neuropeptide release, and transient receptor potential (TRP) channels in the pathophysiology of migraine.

Spyridoula Kazantzi – 2nd year PhD

Funding by Rigshospitalet.
The research investigates the role of arterial cellular differentiation in cardiovascular disease and arteriosclerosis, utilizing myograph techniques and arterial contraction measurements.

Jens Bjelke Kristensen -2nd Year PhD

Funding: Innovation Foundation Industrial PhD - Gubra.
The research explores the connection between migraine and cardiovascular diseases, integrating the roles of neuropeptides and peptide antagonists in the underlying mechanisms.

Mette Nyholm Jensen – 1st year PhD

Funding by the Lundbeck foundation.
The research investigates the role of neuropeptides and neural pathways in migraine pathophysiology, with an additional focus on the influence of sex hormones.

Sofia Lyng Wæver – Student assistant, BSc student



Funding by the Lundbeck foundation.
The research investigates neuropeptide expression with mouse models and immunohistochemistry.

Isabella Mai Christiansen – Research assistant



Funding by the Lundbeck foundation.
The research focused in directional CGRP release in the trigeminal vascular system.

Jesper Peter Bömers – Post Doc



by the Lundbeck foundation.
Research focuses on inflammation as a factor in migraine, with modulation of signaling pathways. Further the link between subarachnoid haemorrhage and the use of CGRP antibodies was investigated.

Co-supervised students

PhD student M Emelie Pitkänen Funghrant, MD (KEFO), PhD student Christina Kamp-Jensen (IIH), and Master student Tanja Lylloff (IIH).

Publication Highlights in 2023

Intraocular Adeno-Associated Virus-Mediated Transgene Endothelin-1 Delivery to the Rat Eye Induces Functional Changes Indicative of Retinal Ischemia-A Potential Chronic Glaucoma Model. Nordahl KML, Fedulov V, Holm A, Haanes KA. Cells. 2023;12(15). doi:10.3390/cells12151987.

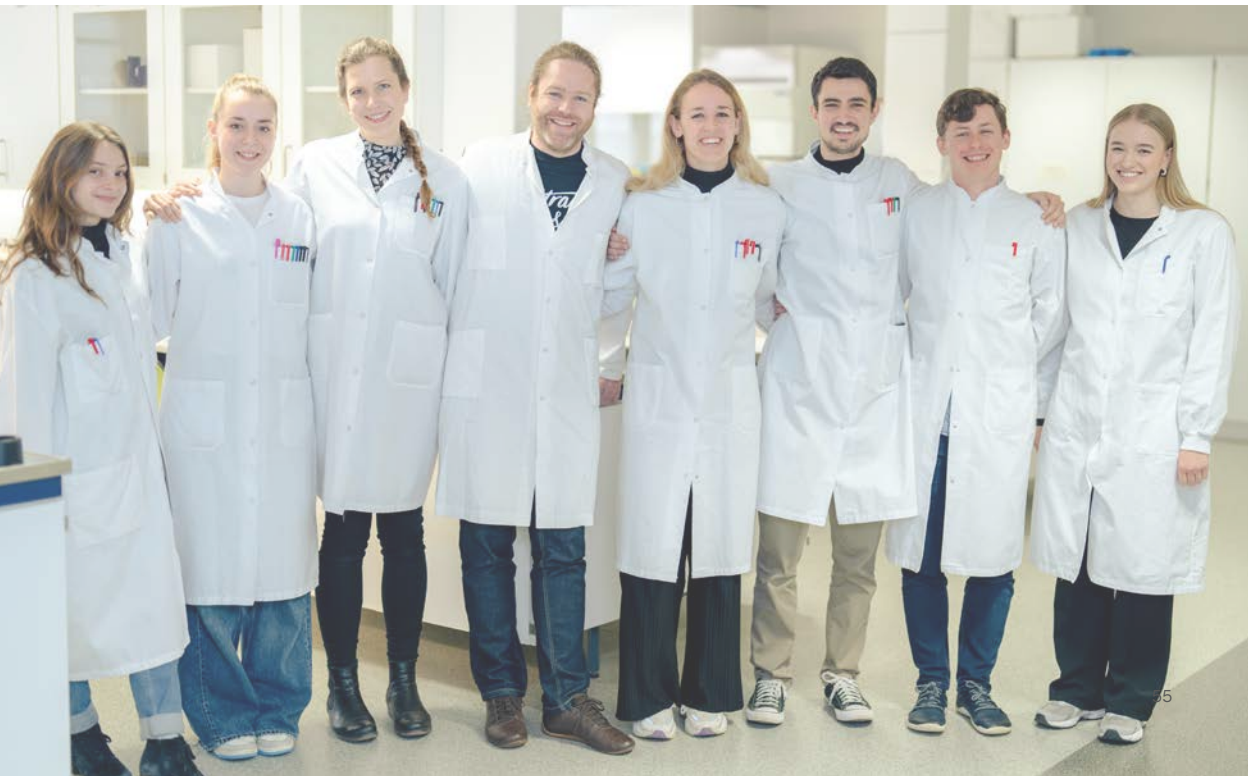
Rodent behavior following a dural inflammation model with anti-CGRP migraine medication treatment. Reducha PV, Bømers JP, Edvinsson L, Haanes KA. Front Neurol. 2023;14:1082176. doi:10.3389/fneur.2023.1082176.

Editorial work

Editor for Journal of Headache and Pain.

Funding

Thanks to the Lundbeck foundation and Innovation foundation for funding.



PhDs DEFENDED 2023

INVESTIGATIONS OF MIGRAINE TREATMENT TARGETS USING ANIMAL MODELS

Charlotte Ernstsén

Defended 20th of June, 2023



The PhD thesis describes a series of mixed methodology used with the intent of answering some quite challenging questions in migraine headache pain research. The thesis sought to examine whether experimental models in mice could help identify novel molecular targets for new therapies for migraine treatments. By looking at targets from different angles using a combination of in vivo and ex vivo techniques as well as genetic modification in mice, the thesis has made a distinct contribution to understanding migraine and pain.



This research used known migraine triggers (nitroglycerin, CGRP, and PACAP-38) to study migraine relevant signalling in mice. The mice's touch sensitivity, measured with von Frey filaments, could be induced with these known triggers and indicated migraine-like pain. Anti-migraine drugs like sumatriptan and the CGRP receptor antagonist olcegepant were then tested to assess if they could block this touch sensitivity. The studies showed the combining sumatriptan and olcegepant did not enhance the effect compared to using either drug alone in the nitroglycerin-induced migraine model. This suggests more evidence is needed before combining these drugs in clinical practice, despite the approval of new drugs (gepants) in Europe. Nitroglycerin-induced touch sensitivity in mice could also be blocked by peripheral injections of olcegepant and an anti-CGRP antibody, but not by central injections of these treatments. This indicates that future migraine treatments should focus on targeting CGRP in the body. Finally, the peptide PACAP-38 was found to act independently of CGRP in the mice and causes blood vessel dilation differently than nitroglycerin. This suggests PACAP-38 might be crucial for patients who do not respond to CGRP-targeting treatments, an especially important finding amidst the emergence of clinical trials using PACAP-targeting treatments.

All at Copenhagen University Hospital – Rigshospitalet, Copenhagen, Denmark:

Main supervisor

Prof. David M. Kristensen, PhD
Department of Neurology,

Primary Co-Supervisor

Sarah L. Christensen, DVM, PhD
Department of Neurology

Co-Supervisor

Professor Jes Olesen, MD, PhD
Department of Neurology,

Assessment Committee

Professor Klas Abelson, PhD Head of
Section Department of Experimental
Medicine, University of Copenhagen,
Denmark (Chairperson)

Clinical Professor Flemming W. Bach,
MD, PhD Department of Clinical
Medicine, Aarhus University Hospital,
Denmark

Lecturer Milena De Felice, PhD School
of Clinical Dentistry, University of
Sheffield, UK



ADVANCED APPROACHES IN HUMAN GENETICS TO ELUCIDATE DISEASE ETIOLOGY AND PROGRESSION AND IDENTIFY NOVEL CAUSATIVE VARIANTS

Ragnar P. Kristjánsson

Defended 15th of August



Ragnar Kristjánsson's research focuses on employing advanced approaches in human genetics to elucidate disease etiology and progression and to identify novel causative variants. As a PhD student, he utilizes cutting-edge genomic techniques and data analysis to uncover the genetic basis of neurological disorders. His work involves comprehensive genome-wide association studies (GWAS) and the integration of multi-omics data to understand the genetic architecture of these diseases. This research aims to contribute to the development of more effective diagnostic and therapeutic strategies for neurological conditions by identifying specific genetic factors that influence disease risk and progression.

All at Copenhagen University Hospital – Rigshospitalet, Copenhagen, Denmark:

Main supervisor

Associate Professor Thomas Folkmann Hansen
Danish headache center

Co-Supervisors

Kari Stefansson,
deCODE genetics

Patrick Sulem,
deCODE genetics
Assessment Committee:

Associate Professor Simon Rasmussen,
NNF Center for Protein Research (CPR),
University of Copenhagen, Denmark
(Chairperson)

Professor Bjarni Jóhann Vilhjálmsson,
(Opponent, Aarhus University, Denmark)

Professor Wesley Thompson (Opponent,
UC San Diego, United States

ASPECTS OF AN EXPERIMENTAL MODEL OF SUBARACHNOID HAEMORRHAGE

Jesper Peter Bømers, MD

Defended 8th of September, 2023

Aneurysmal subarachnoid hemorrhage (SAH) affects around 500 individuals annually in Denmark, leading to significant mortality and diverse sequelae. Advances in diagnostics and treatment have reduced mortality, though cognitive deficits and depression often persist among survivors, impacting their quality of life. Delayed cerebral ischemia (DCI), affecting about one-third of patients, was once attributed to vasospasm but is now understood as a multifactorial event initiated by early brain injury (EBI).

This thesis investigated the relevance of a rat model of SAH, confirming its suitability for simulating clinical conditions and examining interventions targeting the MAPK/ERK/1/2 pathway and a PKC inhibitor. These treatments improved vascular contractility, reduced intracranial pressure, and enhanced sensorimotor functions, indicating potential for clinical application. Additionally, significant mitochondrial dysfunction was observed in the hippocampus following SAH, suggesting that mitochondrial health should be a focus in DCI research. Overall, the findings support the continued use of the rat model for SAH research and highlight the importance of targeting mitochondrial function in future studies.



All at Copenhagen University Hospital – Rigshospitalet, Copenhagen, Denmark:

Main supervisor

Prof. Tiit Illimar Mathiesen, MD, PhD
Department of Neurosurgery

Assessment Committee:

Clinical Associate Professor Louisa M Christensen, MD, PhD (Chairperson)

Co-Supervisors

Prof. Lars Edvinsson, MD, PhD
Clinical Experimental Research, TRACE

Professor Robert Loch Macdonald, MD, PhD (Opponent, Department of surgery, University of Toronto)

Associate Professor Kristian Agmund Haanes, PhD
Sensory Biology, TRACE

Professor Nikolaus Plesnila, MD, PhD (Opponent, Institute for Stroke and Dementia Research (ISD) University Hospital, LMU Munich)

Michael K Karlsson, MD, PhD
Department of Neurosurgery

Prof. Kirsten Møller, MD, PhD
Department of Neuroanaesthesiology



TEACHING

Scientists at TRACE engage extensively in teaching activities at both national and international higher educational institutions. Their expertise spans various disciplines, including pharmacology, biochemistry, neuroendocrine and environmental health, cell biology, physiology, headache, and neuroscience, as well as health sciences. These teaching activities involve a wide range of programs, courses, and seminars aimed at different academic levels and professional groups. The following list details the specific teaching contributions made by TRACE scientists:

- Pharmacology and Biochemistry
- RNA Medicine – From Bench to Bedside: PhD Course, Aalborg University
- Designing and Evaluating Pharmacological Research: MSc program in Medicine with Industrial Specialization, Aalborg University
- Principles of Pharmacology: MSc program in Pharmaceutical Sciences, University of Copenhagen
- Organ-related Pharmacology: BSc program in Pharmacy, University of Copenhagen
- Courses in Clinical Biochemistry: BSc and MD programs, University of Copenhagen
- Pharmacology and Medicinal Chemistry: Continuous education program for biomedical laboratory scientists and laboratory technicians, University College Copenhagen
- Neuroendocrine and Environmental Health
- Info meeting on environmental pollutants, Danish Parliament (Christiansborg), Denmark
- Society for Pediatric and Perinatal Epidemiologic Research, USA
- Cell Biology and Physiology

- Advanced Cell Biology, Human Anatomy, Human Biology and Evolution: Roskilde University (Master and Bachelor courses)
- Cellular and Integrative Physiology, Advanced Topics in Physiology: Master courses, Copenhagen University
- Human Physiology (Menneskets Fysiologi): Bachelor courses, Copenhagen University
- Headache and Neuroscience
- Master of Headache Disorder: Faculty of Health, Copenhagen University
- Master of Neuroscience (Sensory Systems Module): Faculty of Health, Copenhagen University
- Headaches: PhD course, Neuroscience Academy Denmark, Copenhagen University
- Master of Headache Disorders: Faculty of Health, Copenhagen University
- Summer School in Neuroscience: PhD course, University of Southern Denmark
- National Meeting for Association of Young Neurologists, Neurosurgeons, and Neurophysiologists
- Lectures on Stroke and Migraine: Monthly lectures for physicians and researchers within universities and healthcare, Lund University
- Health Sciences
- Master of Health Science, Integrated Course in the Life Cycle: Faculty of Health, Copenhagen University

PRIZES AND RECOGNITIONS

Work Anniversary

TRACE Secretary Hanne Aggergaard – 25 Years

We are pleased to recognize Hanne Aggergaard Nielsen on her 25th anniversary with TRACE. From the inception of Forskerparken, now known as TRACE, Hanne has played a crucial role in shaping the center into what it is today.

Hanne has been a key person in supporting both our office and research activities. Her efforts have ensured the seamless operation of our daily functions and contributed significantly to our research environment. Hanne has made countless personal connections and influenced many people, always making the day better with her caring presence. She is known for always having a fresh pot of coffee ready, creating a welcoming space where people can come by and enjoy a cup.

Throughout the past 25 years, Hanne has been a constant presence, contributing to the growth and success of TRACE. Her work has helped establish a collaborative and productive atmosphere, making a lasting impact on our organization.



Thank you, Hanne, for your invaluable contributions over the years.

Lundbeck Foundation's Talent Prize 2023

Awarded to: Connar Stanley James Westgate

Affiliations: Danish Headache Center, Rigshospitalet and TRACE

Connar Stanley James Westgate has been honored with the Lundbeck Foundation's Talent Prize 2023 for his groundbreaking research on idiopathic intracranial hypertension (IIH), a rare headache disorder. This prestigious award recognizes his contributions to understanding the complex biological mechanisms underlying IIH.

Connar's research focuses on mapping the physical symptoms and biological underpinnings of IIH, particularly the disorder's characteristic increased fluid pressure in the brain. His work aims to uncover the biochemical changes associated with IIH by examining hormone and protein levels in blood, urine, and lipid samples from women affected by the disorder. His findings demonstrate that obesity in women with IIH is due to abnormal metabolism, challenging the notion that these patients can simply control their weight through dieting.

Additionally, Connar's research explores the broader implications of increased brain fluid pressure, using IIH as a model to understand similar conditions caused by other medical issues, such as stroke or brain tumors. His innovative approach offers potential for improved diagnostics and treatment of IIH and related disorders. Connar's work provides valuable validation for patients, highlighting that their weight issues are a consequence of their disorder rather than personal failure.



AMERICAN HEADACHE SOCIETY: FRONTIERS IN HEADACHE RESEARCH SCHOLARSHIP AWARD

Awarded to: Sarah Louise Tangsgaard Christensen

Affiliation: Basic Migraine Research

Research Topic: In vivo two-photon imaging of meningeal blood vessels and sensory afferents in a mouse model of levcromakalim induced migraine.

DANISH HEADACHE SOCIETY: BEST RESEARCH RESULTS

Awarded to: Rikke Holm Rasmussen

Affiliation: Basic Migraine Research

Research Topic: The study identifies that a NO-feed forward mechanism initiated by endothelial nitric oxide synthase is driving mechanical hypersensitivity in the mouse model of levcromakalim induced migraine. This research adds important knowledge to our understanding of migraine pain generation.

PAUL DUDLEY WHITE INTERNATIONAL SCHOLAR AWARD

Awarded to: Spyridoula Kazantzi, Lars Edvinsson and Kristian A. Haanes

Affiliations: Sensory Biology and KEFO

Spyridoula Kazantzi was selected as a Paul Dudley White International Scholar for an abstract submitted to the Basic Cardiovascular Sciences Scientific Sessions 2023. This award recognizes the primary author of the highest ranked abstract submitted from Denmark, reflecting Dr. White's vision for global excellence in cardiovascular science and medicine.

PAUL DUDLEY WHITE INTERNATIONAL SCHOLAR AWARD

Awarded to: Jesper Bömers, Tiit Mathiesen, Lars Edvinsson and Kristian A. Haanes

Affiliations: Department of Neurosurgery, KEFO and Sensory Biology

Jesper Bömers received the American Heart Association 2023 Paul Dudley White International Scholar Award for his abstract "Temporal Change Of Brain Mitochondrial Function In A Rodent Model Of Subarachnoid Hemorrhage." This award is presented to the primary author of the highest ranked abstract submitted from each country to the American Heart Association's International Stroke Conference 2023. Jesper Bömers and co-authors was acknowledged during the conference in Dallas, TX, USA, February 7-10, 2023.

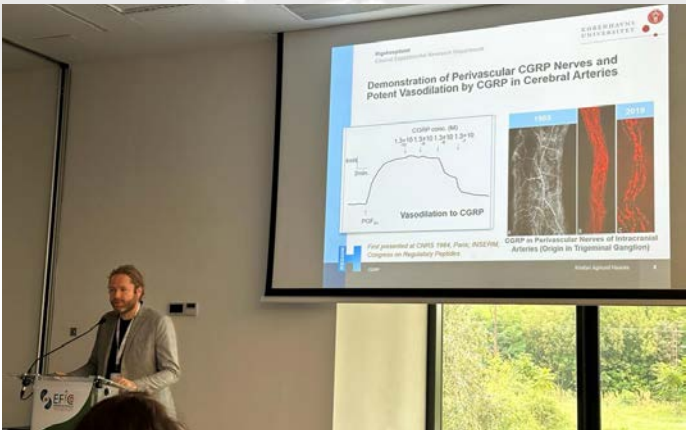
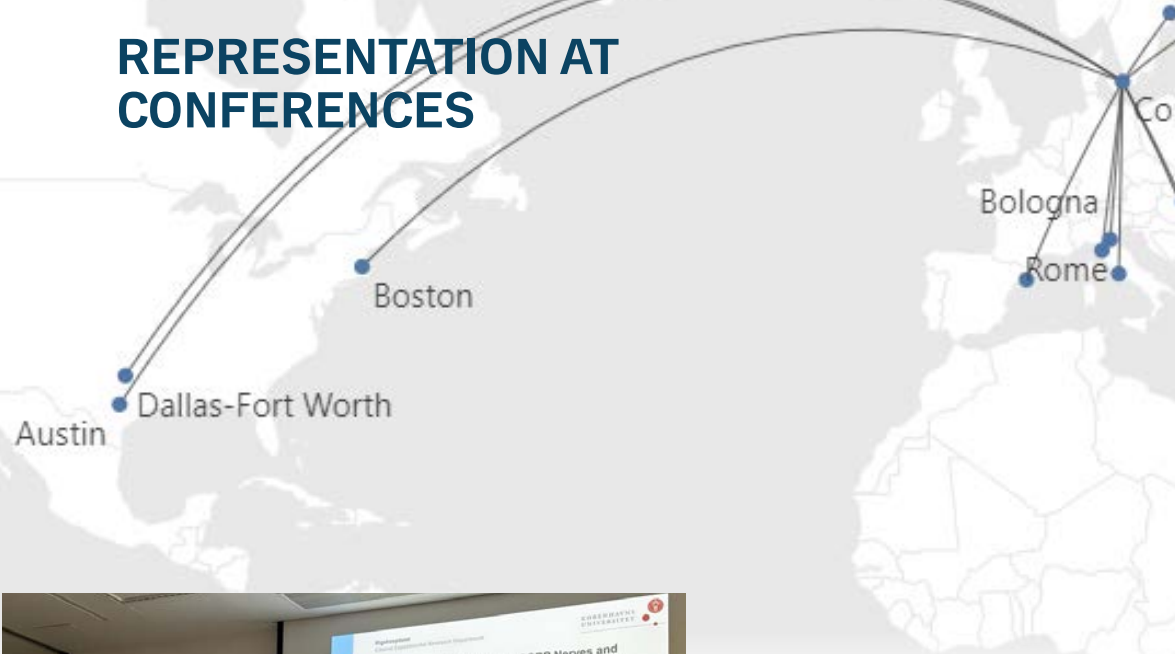
EUROPEAN ACADEMY OF NEUROLOGY

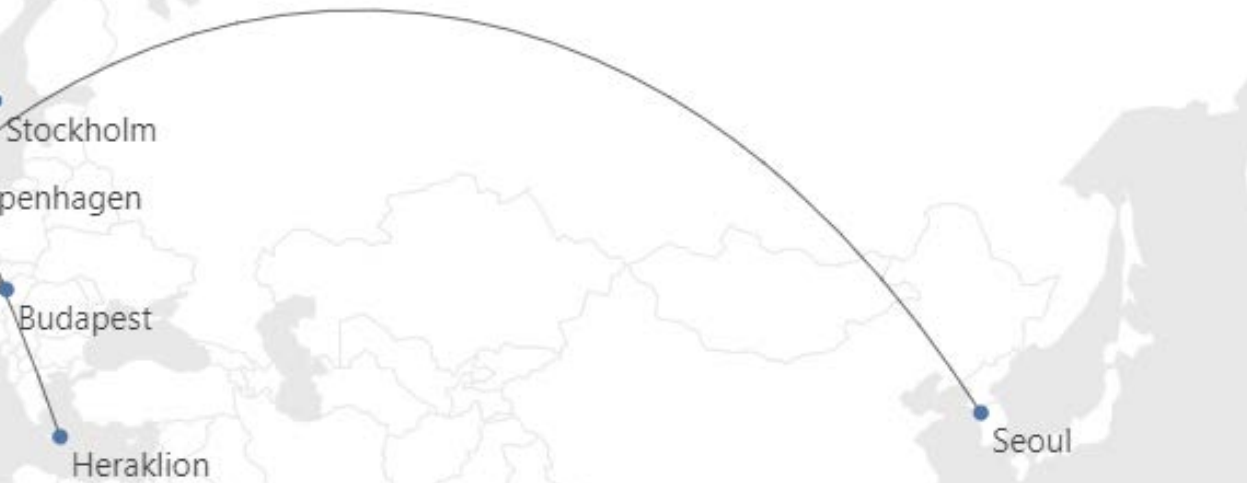
Honorary Member: Jes Olesen

Affiliation: Basic Migraine Research



REPRESENTATION AT CONFERENCES





- Basic Cardiovascular Sciences Scientific Sessions 2023, Boston, USA
- Cerebral Vascular Biology (CVB), Upsala, Sweden
- Danish Headache Society Meeting 2023
- European Academy of Neurology Meeting, Budapest, Hungary
- European Headache Congress (EHC), Barcelona, Spain
- FMF World Congress 2023, Crete, Greece
- International Headache Congress (IHC) 2023, Seoul, Korea
- International Stroke Conference (ISC) 2023, Dallas, USA
- P2X Receptors as Therapeutic Targets (PRESTO), EU funded Action. Feb 2023, Ferrara, Italy
- Preclinical and Clinical Aspects of P2X Receptors as a Common Route in Different Diseases, PRESTO. Sep 2023, Pisa, Italy
- WordLab 2023, Rome, May 2023
- 14th Congress of the European Pain Federation EFIC, Budapest, Hungary
- American Headache Society 65th Annual Scientific Meeting, Austin, USA
- Annual Meeting of the Danish Society of Neurologists 2023

HIGHLIGHTS OF INTERNAL COLLABORATION PROJECTS

BONE METABOLISM AND RNA DRUG DEVELOPMENT COLLABORATION

Obesity's impact on bone health remains controversial. Senior researchers Ankita Agrawal from "Bone and Biomarkers" and Anja Holm from "Clinical Experimental Research" have combined their expertise to address this issue. Ankita, with extensive experience in bone metabolism, and Anja, specializing in RNA drug development, have created a synergistic approach.

Anja's team investigated the effects of a novel anti-obesity drug in a high-fat diet model, while Ankita examined the drug's impact on bone structure and strength. Their findings indicate that the drug prevented weight gain in mice and improved bone health compared to untreated mice.

In another project, Ankita's approach of suppressing purinergic receptors to mitigate bone destruction in multiple myeloma is complemented by Anja's development and screening of multiple RNA drug candidates. This collaboration allows for a comparative analysis of permanent versus transient gene silencing.

These collaborations aim to provide insights into the relationship between obesity and bone health and offer potential strategies for mitigating bone destruction in multiple myeloma. The ongoing work seeks to develop effective treatments while minimizing adverse effects for patients.

BIOLOGICAL SEX, THE ESTRUS CYCLE, AND MIGRAINE

Menstrual migraine and the female predisposition to migraine and other headache disorders are poorly understood, highlighting the disparity of knowledge between male and female biology in health and disease. In a collaboration, Connor Westgate from the BRAWA, Kristian A. Haanes from the Sensory Biology, and Bjarne Styris have from the Department of Pharmacy at KU have sought to understand this underlying biology. Their combined expertise in steroid biochemistry, neurobiology, and analytical chemistry has led to a clinically meaningful master project.

Tanja Lylloff, a master student from the Department of Pharmacy, has been conducting experiments to address this knowledge gap. Tanja has split her time between TRACE and Pharma. She collected serum, CSF, trigeminal ganglia, and pituitary glands from male and female rats, covering all stages of the rodent estrus cycle. The tissue samples were analyzed using LC-MS/MS to measure steroid hormones, revealing unique biological insights. The trigeminal ganglion appears to regulate its steroid hormone levels locally, independently of circulating steroid levels. Additionally, the male trigeminal ganglion differs hormonally from the female trigeminal ganglion, suggesting that current strategies investigating serum steroids in menstrual migraine may be inappropriate.

Based on these findings, the study will continue with Mette and Connor performing pain threshold experiments in female rats, considering the estrus cycle. This ongoing research aims to elucidate the biology underpinning menstrual migraine and the female predisposition to headache.



SCIENTIFIC AND SOCIAL EVENTS IN TRACE

In 2023 several scientific and social events occurred in TRACE. These included a line of social clubs with the purpose of bringing scientists in TRACE closer together in an informal setting. Also, the first Glostrup Summer Symposium was held with a whole day of scientific content followed by a social gathering.

GLOSTRUP SUMMER SYMPOSIUM

The first Glostrup Summer Symposium was held on June 8th, 2023. More than 30 scientists, staff, and collaborators participated in the event. The day program included presentations from group leaders of the research groups. Additionally, the overall plan and the intended future development of TRACE were presented by the head of the center. A group session focused on formulating an ambition statement with the intention of collecting input from all related personnel. After the interesting and highly intriguing presentations of high scientific level, the event continued in Inger and Jes Olesen's beautiful home and garden north of Copenhagen. Several team-building and social activities took place, including blind-folded soccer, croquet, shooting, and a music quiz. This was a wonderful day with many social interactions creating and catalyzing collaboration and interpersonal relations. The symposium is planned to be an annually recurring event for the researchers and staff at TRACE but open to interested collaborators, clinicians, and other colleagues with an interest in science.





SOCIAL CLUB 2023

Social club was revived in 2023, where we had an initial social meeting in June and where we got social after the summer holiday.

September – A trip into Glostrup

Social club officially kicked off with a visit into Glostrup, organized by Rikke and Ankita, where we visited Café Dem. Here we enjoyed some Turkish food, while Spyridoula shared some Greek witchcraft, reading tea leaves. The evening ended up in a dodgy bodega in Glostrup, I will let you imagine what happened there.

October – Spooky spectacular

Emilie and Philip put their collective film nerd powers to the test and decorated the meeting room in a spooky get up with skeletons, pumpkins and even a mist-generator. They also provided a decadent supply of sweets as well as prepared the nerdiest film quiz, where no one got over 50%.

November – Efterårs hygge

Mette and Spyridoula brought the cozy autumn feel into our meeting room, decorating it with autumnal leaves and preparing a gorgeous array of food, complemented with a set of very compromising games and challenges for the participants to avoid embarrassment with.

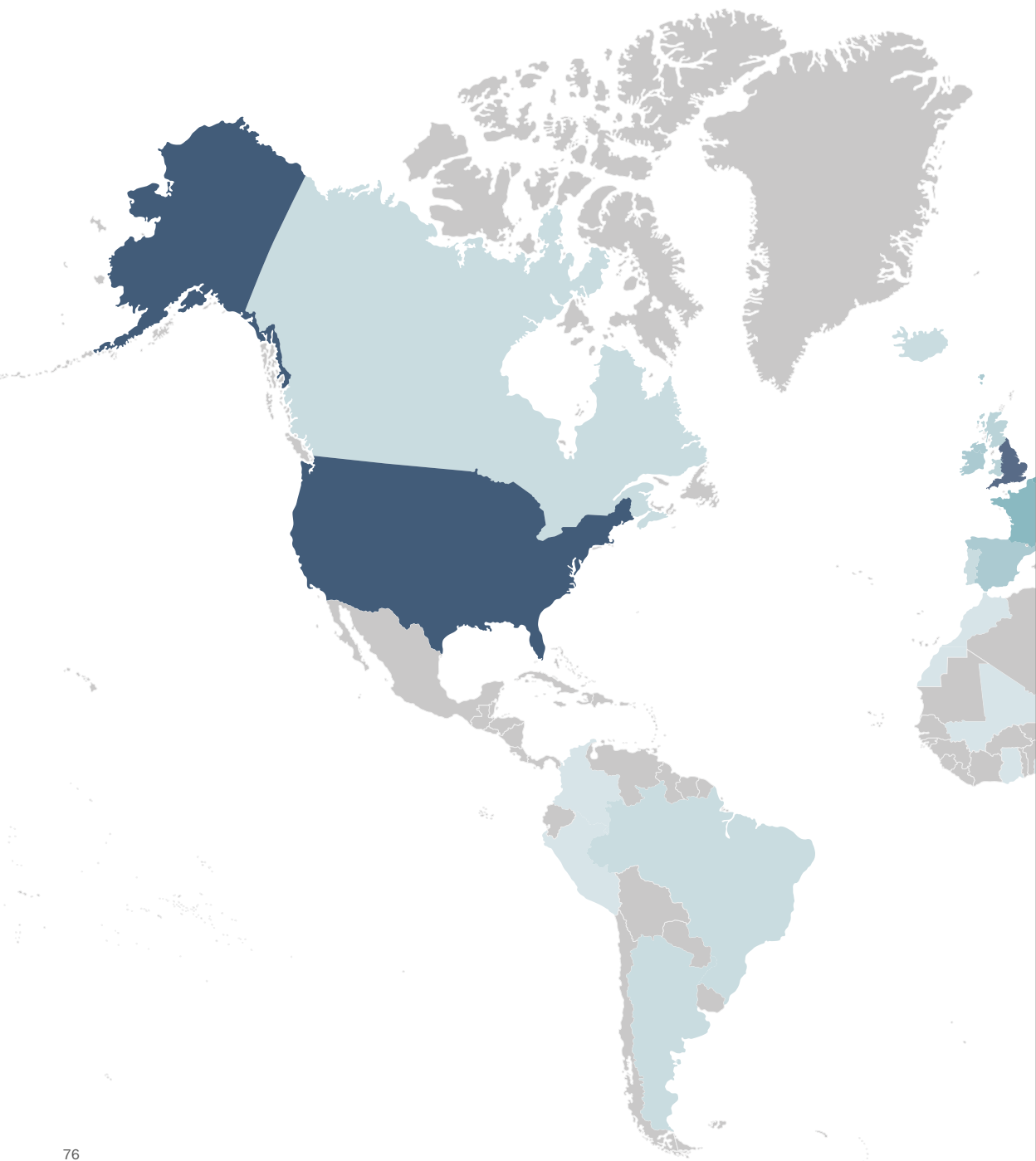
December – Christmas decoration

To cap the year of social club of, a dedicated few decorated the then Forskerpark with Christmas decorations coupled with warm gløgg, all the sweets things one would expect from Christmas with festive music thrown in, plus some of Rikke's excellent baking.





TRACE INTERNATIONAL COLLABORATIONS



130

Journal articles

15

Reviews

5

Editorials

4

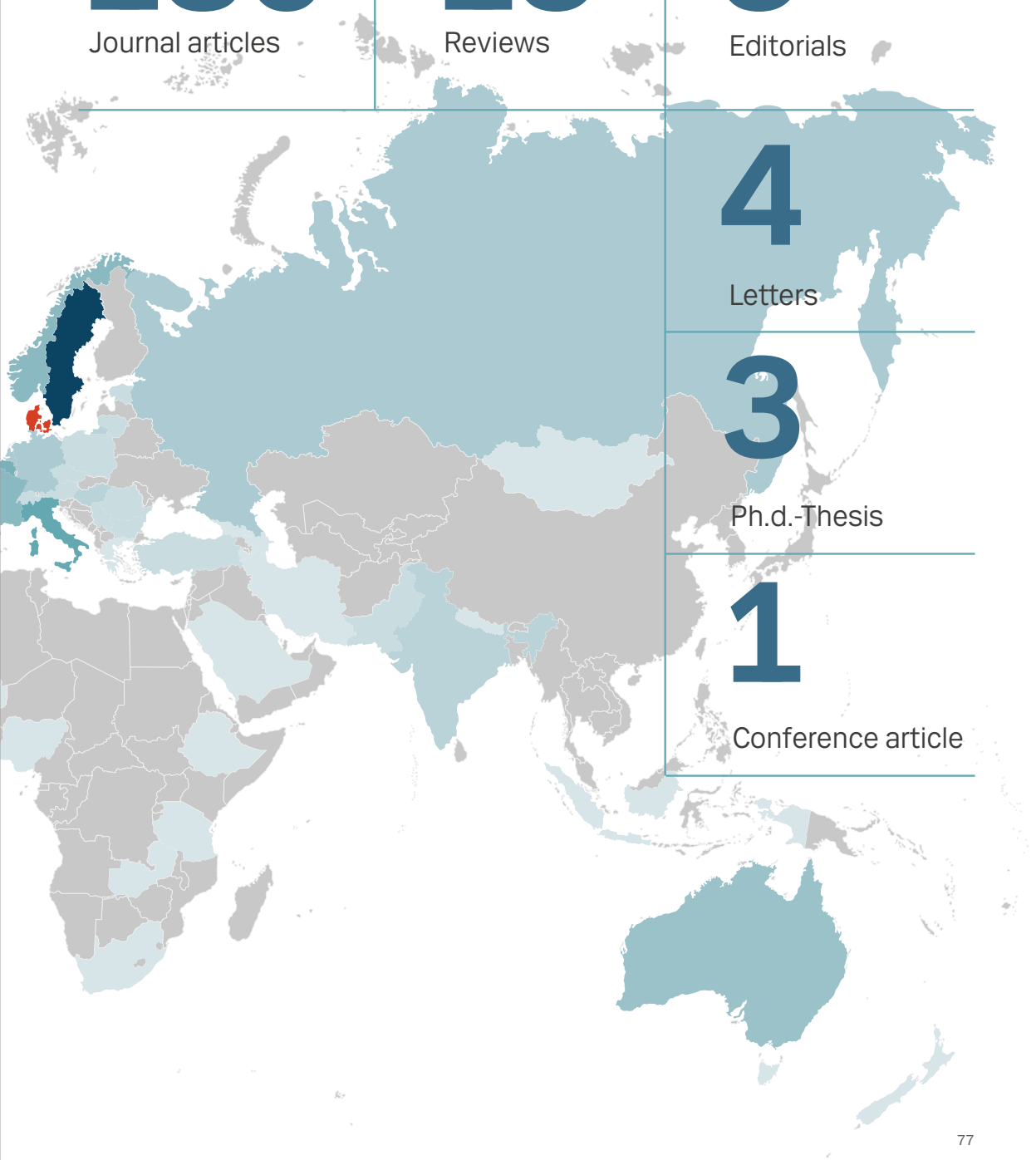
Letters

3

Ph.d.-Thesis

1

Conference article



PUBLICATIONS

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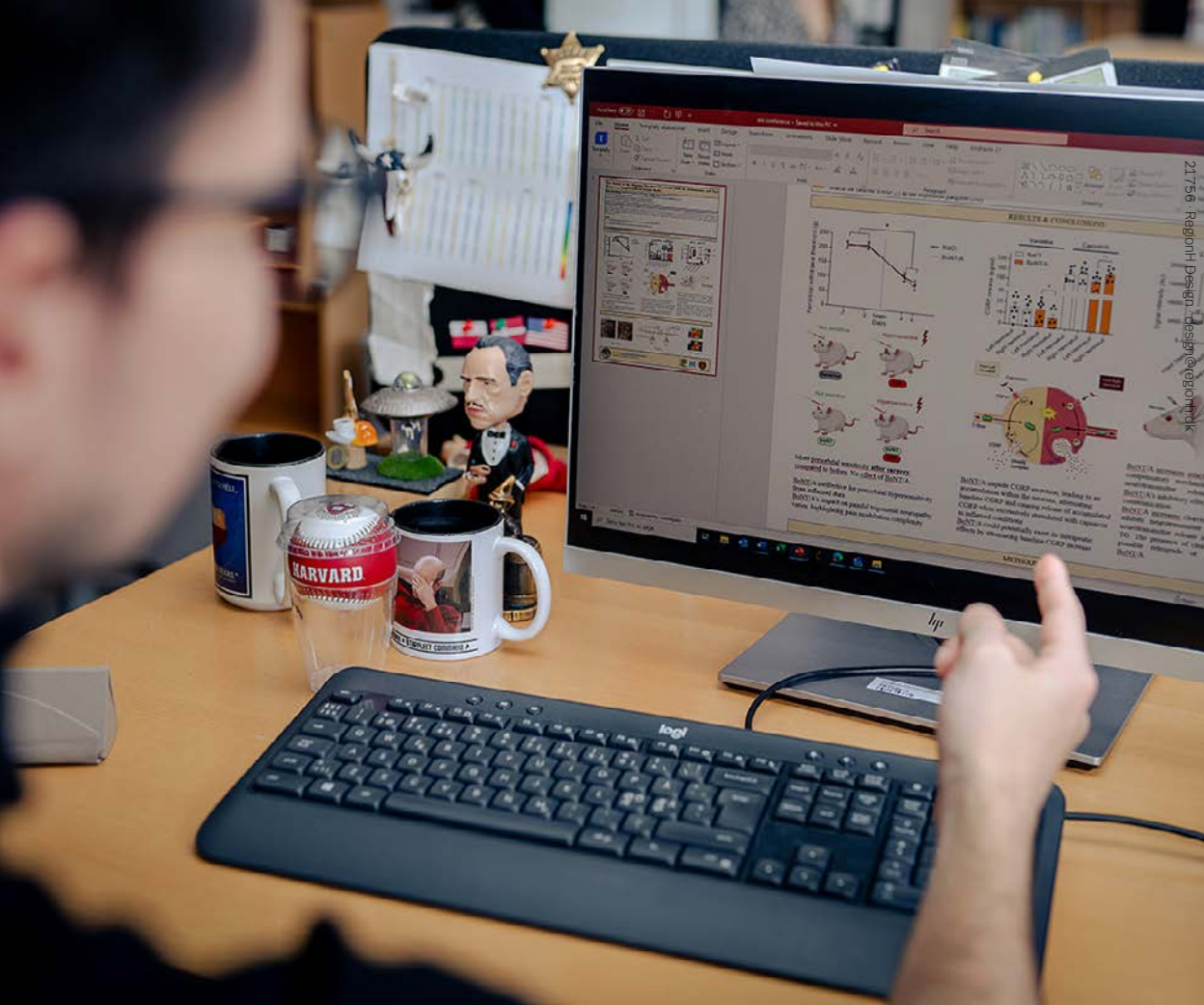
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