## UNIVERSITY OF COPENHAGEN NOVO NORDISK FOUNDATION CENTER FOR PROTEIN RESEARCH



# Annual Report 2020

Novo Nordisk Foundation Center for Protein Research



### COLOPHON

#### ABOUT

Novo Nordisk Foundation Center for Protein Research (CPR) was founded in 2007 at the Faculty of Health and Medical Sciences, University of Copenhagen, to promote basic and applied discovery research on human proteins of medical relevance.

The establishment, growth and continuation of the center has been possible thanks to unprecedented and repeated financial support by the Novo Nordisk Foundation as well as through significant contributions from the University of Copenhagen.

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Editor in Chief	Executive Director Dr. Jiri Lukas
Editors	Nanna Rønbjerg Christoffersen, Research Coordinator, CPR Marianne Bom, journalist   publicer.dk
Design and Layout	Kiberg & Gormsen   kiberg-gormsen.dk
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# Becoming a world-leading protein explorer

The ambition of Novo Nordisk Foundation Center for Protein Research (CPR) is to be a world-leader in exploring how proteins drive fundamental biological processes in humans. The research can ultimately lead to new ways to diagnose, prevent and treat diseases.

CPR has a unique strategy to tackle the challenge of how proteins drive fundamental biological processes in humans by interdisciplinary research and the development of new technologies. The center combines three different approaches to reach its goal to become a world-leading protein explorer:

- Develop and combine under one roof the broadest possible spectrum of state-of-the-art protein technologies combined with high-end computation and big data management
- Perform highly effective technology-driven and mechanism-oriented protein research
- Translate basic discoveries to health care.

#### CPR STAFF

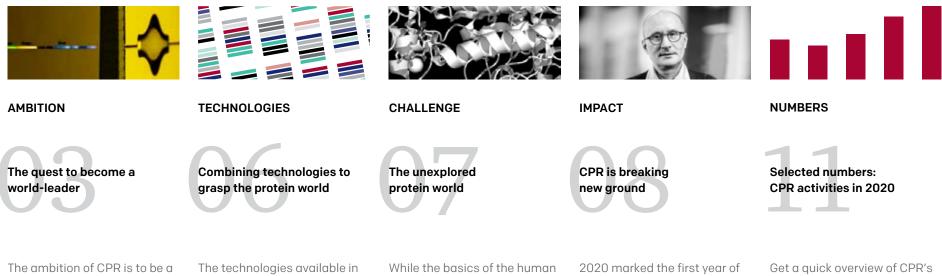
At the end of 2020, CPR employed 222 staff members from 39 different countries compared to 190 at the end of 2019. CPR employees fall into three main categories: scientific personnel, research support and administrative support, of which scientific personnel constitute 70%.



#### CONTENTS



## Annual Report 2020



The ambition of CPR is to be a world-leader in exploring how proteins drive fundamental biological processes in humans. The research can lead to new ways to diagnose, prevent and treat diseases. The technologies available in CPR span the entire spectrum from mapping all protein variants in a cell to visualising how individual proteins assemble in functional networks that drive fundamental physiological processes.

While the basics of the human genome, the DNA, was roughly mapped in 2001, the expression of the DNA in proteins - the human proteome - is still widely unexplored. Take a look into how proteins are made in a cell.

2020 marked the first year of CPR's new five-year budget of 700 million DKK granted by the Novo Nordisk Foundation in 2019. The new funding period allows CPR to expand at many levels, including the addition of a completely new and very important area of biomedicine driven by proteins and their modifications. Get a quick overview of CPR's research output, financial turnover, educational activities and outreach events.

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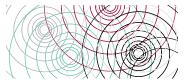
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therapy



SYNERGIES



HIGHLIGHTS

Mapping internal and external collaborations

A graphic overview of how CPR

research programs comple-

ment each other and a map

of CPR's network of external

collaborators.



**PROGRAMS AND** 

**TECHNOLOGIES** 

The five CPR research programs, their technologies and the landmark results accomplished by the research groups in 2020.

CPR has a clear governance structure tailor-made to maximize efficient governance internally and foster interactions with the Faculty of Health and Medical Sciences at the University of Copenhagen and other research organisations.

GOVERNANCE

**Organisation and** 

leadership

CPR researchers published 152 articles including 130 primary research articles and 11 review articles in 2020. Find the full reference list here.



PUBLICATIONS



### TECHNOLOGIES



# Combining technologies to grasp the protein world

The technologies available in CPR span the entire spectrum from mapping all protein variants in a cell to visualising how individual proteins assemble in functional networks that drive fundamental physiological processes. This allows for a highly collaborative and interdisciplinary research environment where the different research areas cross-fertilise and bring together different approaches to explore and understand proteins. From January 2020, CPR's technology portfolio was expanded with functional genomics, due to the arrival of Research Director Anja Groth and the Protein Memory Program.

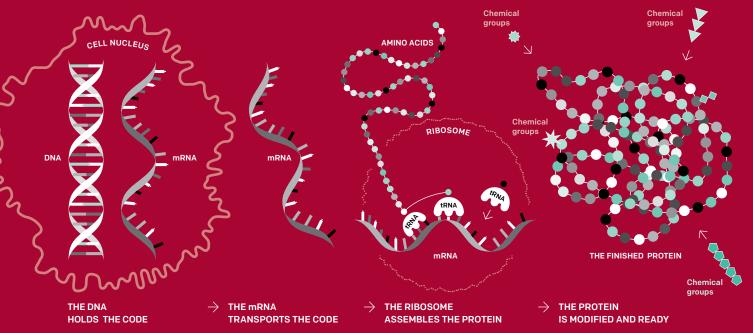
Technology	Mass spectrometry	Big data management and analysis	Protein imaging	Cryo-electron microscopy and x-ray crystallography	Functional genomics Explores genome organization and function.	
	Analyses all protein variants in a sample.	Predicts how proteins interact and cooperate.	Investigates protein function in living cells.	Deciphers the structure of individual proteins and protein complexes.		
	University         Univers					
What the technology can do?	Reveals the identity and amounts of proteins and their modifica- tions in a biological sample by measuring the mass-to-charge ratio of ions.	Indicates how proteins function and vary across the population by generating and analysing molecular interaction networks in health and disease.	Tests the function of selected proteins /protein networks in live cells by light microscopy and image analysis. Visualises how proteins move around over time, how they inter- act and the effects on the cell.	Studies molecules and molecu- lar interactions by the use of biophysical instruments. The structure and biophysical features of a protein reveal how it moves, how it interacts with other molecules, and more.	Uses DNA sequencing to un- derstand genome function and how proteins provide epigenetic information, which is passed on to daughter cells to maintain cell identity and fate in next cell generation.	
How the technologies interrelate at CPR	Mass spectrometry produces a list of proteins present in the sample for further processing by big data analysis.	Big data analysis integrates data sets collected from proteomics and other omics technologies, health data and more - and supports hypothesis generation for further testing in the laboratory.	Microscopy is used to investi- gate and functionally comple- ment the results from mass spectrometry and big data analysis.	Protein characterization and structural studies contributes to the understanding of a protein's function, thus complementing all other protein technologies at CPR.	In a cross-disciplinary approach functional genomics is com- bined with CPR technological strongholds such as proteomics structural biology, and big data analysis to reveal protein func- tion in genome regulation.	

### CHALLENGE

# $\supset$ The quest to understand the human proteome

While the basics of the human genome, the DNA, was roughly mapped in 2001, the expression of the DNA in proteins – the human proteome – is still widely unexplored. With potentially millions of different protein variants in the human body, it is a huge challenge to find the key players relevant for disease diagnosis, prevention and treatment. Novo Nordisk Foundation Center for Protein Research has taken up this challenge to lead the way for new treatments in the clinical world.

#### HOW PROTEINS ARE MADE IN A CELL



DNA is composed of a series of four alternating bases that define our genetic sequence. It contains around 20.000 genes that code for the expression of an unknown number - potentially more than a million - of protein variants, which regulate most functions in the human body.

The production of a specific protein begins when the DNA of a gene is copied into an mRNA molecule - a messenger RNA - which contains the code for the protein. The mRNA transports the protein code from the cell nucleus into the cytoplasm of the cell. It brings the code to the ribosome, the 'protein assembly line'. The ribosome translates the code brought to it by the mRNA. Every sequence of three bases carries a signal for tRNAs – transfer-RNAs - to bring a specific amino acid to the ribosome and place it in an exact spot in the chain of acids that builds the protein like pearls on a string. Proteins are made out of a total of 20 different amino acids. In the final stage, the chain of amino acids is cut, folded and brought to a three dimensional shape. A variety of chemical groups are added by enzymes (other proteins) providing the new protein with its final distinctive structure, function and activity. These 'post-translational modifications' (PTMs) dramatically diversify the protein pool in the human body that contains potentially millions of different protein variants.

#### WHAT PROTEINS DO

Proteins run the human body in myriad ways. If you look into a medium-sized cell of a human, you find billions of proteins at work. All proteins perform a job of importance for human life and health. Sometimes errors occur and cause illness. In fact, most diseases manifest at the level of proteins, and most drugs target proteins or are proteins themselves.

Proteins take care of many different functions in the body.

They are:

 enzymes – or socalled biological catalysts - that speed up chemical processes – such as the addition of post-translation modifications to new proteins.

 receptors that bind to specific ligands in their environment and forward this signal to other molecules – such as the receptors in the nose that bind to odor molecules and convey this information to the brain.

- transporters that take molecules from one place to another – such as hemoglobin bringing oxygen from the lungs to the muscles.
- structure builders that hold together cells and tissue as a scaffold – such as collagen holding together the cells of the skin.
- hormones that travel the bloodstream to stimulate specific cells or tissues – such as insulin from the pancreas that promotes glucose uptake in liver, muscle and fat.
- antibodies that detect pathogenic bacteria and viruses in our body as part of the immune system.
- contractile proteins that allow biological structures to contract- such as myosin and actin that make up the majority of muscle tissue.
- storage that serves as biological reserves - such as ferritin that stores iron inside the cell.

# Sharing research and technology

It is CPR's ambition to share knowledge and technology with the surrounding community. With our research, we push the current limit of knowledge and technological development within protein research and we want the results to be put to practical use for other researchers, health personnel and the pharmaceutical industry.

The key to success for Novo Nordisk Foundation Center for Protein Research (CPR) is to collect the best minds and the best protein technology under one roof. We see it as our prime task to identify where we can break new ground within protein research relevant for preventing disease, and we are fortunate to continue this thanks to funding: 2020 marked the first year of CPR's new five-year budget of 700 million DKK granted by the Novo Nordisk Foundation in 2019.

In 2020, we expanded CPR with a new research program by recruiting Anja Groth, a world leader in epigenetics and a highly innovative researcher. Anja Groth successfully launched the Protein Memory Program (p. 29) and moved her research group to CPR at the very onset of the COVID-19 pandemic. Her research is at the crossroad between basic research – uncovering how cell identity is copied and transmitted to daughter cells, a field we know surprisingly little about – and applied research – because this knowledge is of major biomedical importance and can lead to new avenues to sustain health across a lifespan and prevent disease.

At CPR, we are strong advocates for the societal value of basic research in its own right. This year, Matthias

Mann and an international team sequenced the full protein profile of 100 organisms ranging from viruses and bacteria to plants, animals and humans. The mapping more than doubled the number of experimentally verified proteins known (p. 23). This data is made freely accessible and constitutes a rich source of information about proteins that will aid researchers across the world in a wide variety of topics – from understanding evolution to the development of new drugs.

We are proud that as a natural extension of our passion for basic research, CPR continues to be very successful in fostering translational medical research. An excellent example is The Danish Disease Trajectory Browser, which is an online tool to explore temporal disease progression (trajectories) in 7.2 million Danish patients over a period of 25 years. The tool, developed by Søren Brunak and his team (p. 30), is extremely user-friendly for a very broad biomedical community; it requires no bioinformatics or medical informatics skills but simply uses statistical summary data from patients to visualize how often patients with one disease get a specific other disease at a later point. The trajectory browser is part of a plan to develop several resources that can help Danish health personnel improve disease management of individual patients along the course each patient will take.

CPR's long-term ambition has been to facilitate access to technologies that are traditional bottlenecks in protein research. In addition to our tangible success in the areas of bioinformatics tools and cryoelectron microscopy, the year 2020 has witnessed another major addition to this portfolio by launching the new Proteomics Research Infrastructure (PRI) at the University of Copenhagen, Faculty of Health and Medical Sciences. PRI is headed by Michael Wierer, a renowned expert in mass spectrometry. It will leverage CPR's world-leading research in mass spectrometry-driven proteomics by providing access to an advanced facility to a wider scientific community.

I hope you enjoy reading about CPR's research highlights in our 2020 Annual Report.

Executive Director and Group Leader Novo Nordisk Foundation Center for Protein Research

#### CPR'S VISION

...is to become a world-leader in exploring how protein modifications and their functional networks drive fundamental biological processes that underlie health and disease.

#### CPR'S MISSION

...is to integrate innovative protein technologies, big data analytics and mechanismbased research to:

- Advance understanding of disease-related protein networks
- Train future leaders in academia and industrial biomedicine
- Become an unmatched global partner in protein science.

"We are proud that as a natural extension of our passion for basic research, CPR continues to be very successful in fostering translational medical research. An excellent example is The Danish Disease Trajectory Browser, a tool for exploring almost 25 years of data from the Danish National Patient Register." Jiri Lukas

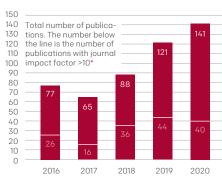




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# Selected numbers: CPR activities in 2020

#### No. of publications

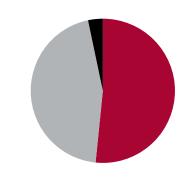


\* The journal impact factor (Web of Science) is an indicator calculated annually for peer-reviewed journals. The impact factor of a journal indicates the average yearly number of citations received per article published in that journal during the two preceding years.

#### **RESEARCH OUTPUT**

In 2020, CPR researchers published 141 articles: 131 primary research articles reporting on original research and 10 review articles. Commentary and book chapters are not included in the diagram.

More than one in four of the articles (28%) were published in journals with a journal impact factor above 10. Annual funding and distribution



- NNF center grant 117.3 million DKK
- Competitive research grants 102.5 million DKK
- University of Copenhagen funds 7.5 million DKK
- ••• Total 227.3 million DKK

#### FUNDING

In 2020, the total turnover of CPR was 227.3 million DKK.

- Close to half was attracted as competitive grants, supplementing the Novo Nordisk Foundation center grant of 117.3 million DKK.
- The competitive research grants (102.5 million DKK) stem from: 63% Danish private grants, 22% EU grants, 11% Danish public grants, and 4% other international grants.

#### No. of courses No. of attendees

Outside Faculty of Health and Medical Sciences in DK and abroad	5 • 121	2 • 50	1•30	4 • 70
Faculty of Health and Medical Sciences at UCPH*	10 • 224	12 • <b>39</b> 5	2 • 24	4 • 64
CPR organized and co-organized	2 • <b>70</b>	2 • 77	3 • 69	3 • <b>190</b>
	Under graduates	PhD students	Post- docs	

Total 17 • 415 16 • 522 6 • 123 11 • 324

\* Excluding CPR organized courses \*\* Mixed audience covers undergraduate students, PhD students, postdocs and academic staff.

#### TEACHING ACTIVITIES

Approximately 1,384 persons attended 50 courses taught by CPR researchers in 2020. CPR's educational activities draw on the research excellence and unique opportunities associated with being a university-based research center. One example is CPR's contribution to the Faculty initiative 'BRIDGE – Translational Excellence Programme'. CPR offers three annual couses in this postgraduate program that aims to give a deeper understanding of the scientific underpinnings of complex diseases, the ability to translate insights between the basic and clinical sciences, and training to manage the essential collaboration between disciplines.

#### No. of outreach events



events in 2020

#### OUTREACH

CPR researchers want to share the knowledge on protein research. In 2020, they participated in 95 outreach events:

- 76 press and media interactions
- 10 broadcast e.g. TV/radio/podcast
- 5 talks one of them at a symposium organized by the Royal Danish Academy of Sciences and Letters at the occasion of HM The Queen's 80th birthday
- **3** activities for high school students
- 1 website on epigenetics targeted to future students and the public.

## New programme focuses on cellular memory

In January 2020, internationally renowned Professor Anja Groth established a new research programme at the Novo Nordisk Foundation Center for Protein Research (CPR) dedicated to research in epigenetic cellular memory.

The cells in a human body divide constantly throughout life. In the process of one cell developing into two daughter cells, proteins help carry information between generations, so that a skin cell actually becomes two skin cells, and a liver stays a liver when cells divide. The cellular identity is maintained via so-called epigenetics mechanisms that assert their function "upon" (in Greek: epi) the genetic inheritance encoded in DNA.

The new CPR "**Protein Memory Program**" will specifically investigate how information in proteins and their modifications contribute to maintenance of cellular identity and epigenetic memory. This is a field in rapid development, as discussed in a review article from the Anja Groth group published in Nature Cell Biology in 2020.

"Research in cellular memory is important because it helps us understand how organisms are built at the most detailed molecular level. It is also important because it helps us comprehend how diseases arise and develop, when loss of cellular memory allow cells to acquire unwanted properties such as unrestricted cell division and growth as what we see in cancer," says Research Director and Professor Anja Groth. At CPR, she heads a group of 15 researchers, many of whom were part of her team at the Biotech Research & Innovation Center (BRIC) in Copenhagen, where the group was located before moving to CPR.

"I have been incredibly happy to be at BRIC where I had the opportunity to build and develop my group. By moving to CPR, we will be able to further develop our research area. At CPR, we can expand the programme by recruiting younger groups within complementary research areas and here we have a unique opportunity to integrate CPR strongholds in protein networks, protein signaling and protein structure with our expertise in cellular memory. This type of synergy is really what we need in order to make true breakthroughs," says Anja Groth.

For a description of the "**Protein Memory Program**" go to page 29.



#### ANJA GROTH

is a highly innovative researcher known for developing novel technologies and pioneering the field of epigenetic cell memory, which in 2018 led her to cofound the spin-out Ankrin Therapeutics based on her discoveries in genome and epigenome maintenance. She has received numerous grants and awards in Denmark and abroad, including HM Queen Margrethe II's Science award, the Elite Research Prize, two ERC grants and the Heirloom Award for Women Scientist Leaders. She is elected member of the European Molecular Biology Organization and the Royal Danish Academy of Sciences and Letters.

The Groth Group moved their laboratory into newly renovated facilities at CPR in March 2020. Group members Nazaret Reverón-Gómez, Matthew Todd and Kathryn Jane Wattam (background) are seen in the photo.

HIGHLIGHTS

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p 14

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Associate Professor Nicholas Taylor meeting with group members. Left to right: Rooshanie Nadia Ejaz, Leyre Marin Arraiza, Monica Santiveri Saez and Claudia Kielkopf. Monica Santiveri first-authored the article published in Cell (p. 14).

## Tiny protein motor fuels bacterial movement

The ability to move is key for some bacteria to efficiently spread infections. But how do they actually move? Research at Novo Nordisk Foundation Center for Protein Research (CPR) has provided fundamental insight into the mechanism that powers bacterial movement.

A lot of bacteria strains such as salmonella and E. coli propel themselves forward by rotating threads, known as flagella, which for some years have been known to be driven by the flagellar rotary motor. But for long it remained a mystery how the fixed part of the motor, the stator unit situated in the cell wall, actually powers the movement of flagella.

#### MYSTERY SOLVED

In 2020, researchers at CPR solved the mystery when they revealed that the stator unit itself is in fact also a rotary motor. This tiny motor powers the large motor, which makes the threads rotate, causing the bacteria to move.

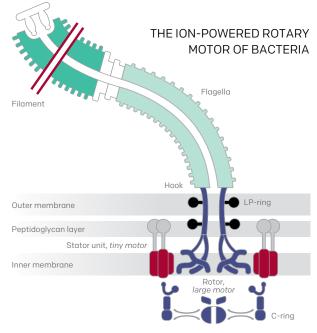
"Now we know the actual composition, structure and function of the stator unit and this paves the way for therapeutic purposes. Since we now know what makes bacteria move, we may also be able to inhibit this movement and stop bacteria from spreading. So our next step will be to find out if it is possible to inhibit the stator units using chemical compounds, which could have antibiotic effects," says Associate Professor and Group Leader Nicholas Taylor.

#### HOW BACTERIA CHANGE DIRECTION

The researchers determined the structure of the stator unit complex by using cryo-electron microscopy. Working with this technology, they were able to elucidate the stator unit's architecture, see how it is activated, and provide a detailed model for how this tiny motor powers the rotation of the flagellar motor.

"Furthermore, our model shows how the stator unit can power rotation of the bacterial flagellar motor in both directions, which is crucial for the bacteria to change their swimming direction. Without direction change, bacteria would only be able to swim straight in one direction," says Nicholas Taylor.

The study was carried out by researchers in the Taylor Group in collaboration with researchers from Humboldt-Universität zu Berlin and Harvard University. It was published in Cell.



The ion-powered rotary motor consists of a rotor surrounded by a ring of stator protein complexes that power its rotation. The motor is bidirectional: chemotactic signaling can cause a conformational change in the rotor, known as "switching", which results in a change of the rotational direction of the motor.

## Speed-regulating proteins secure safe DNA replication

Researchers at Novo Nordisk Foundation Center for Protein Research (CPR) have found a long wanted answer to a puzzling question: How do molecular motors driving duplication of DNA avoid speeding and DNA damage? The answer lies in the so-called MCM proteins and their 'babysitters'.

Every time a cell divides in a human body, several thousands of proteins have to work together at a safe pace to assemble identical copies of the cell's DNA, a process known as DNA replication. In this process, there is risk of DNA damage causing diseases such as cancer. This can occur, if the proteins assembled into molecular motors called 'replisomes' move along DNA too fast, leading to their collision. In other words the DNA replication needs speed control.

In 2020, researchers at CPR identified the proteins behind the speed control. They are the minichromosome maintenance (MCM) proteins that are bound to DNA in great excess. Until the CPR results were published in Nature, researchers around the world had noticed the many MCM proteins in the cells, but did not understand why they are so many.

#### THE 'MCM PARADOX' SOLVED

"We can see the MCM proteins in the microscope, but for decades scientists did not know what the vast majority of them actually do. From an evolutionary standpoint, it did not make sense to maintain a huge surplus of proteins only as back up, with no other important function. We have now solved this "MCM

#### paradox" by finding that all the MCM proteins in our cells actually have a defined function," says first author Hana Sedláčková, postdoc at CPR.

It was alreadyknown that MCM proteins are an essential component of the replicative helicase that forms the core of the molecular motor of genome replication. The news revealed by CPR research is how MCM proteins actually ensure DNA replication at the right pace. Using cutting edge technology, the researchers found that MCM proteins exist in two protein forms in the cellular environment – parental and nascent MCMs, which differ in their age but also in the engagement in the DNA replication process.

The parental MCM proteins are recycled from previous rounds of DNA replication and they are preferentially used as active replicative helicases. The nascent MCM proteins are newly synthesised that remain inactive and function as 'speed bumps', which are essential to set the physiological speed of replication and allow error-free DNA copying.

Using 4D imaging, the researchers monitored the life cycle of MCM proteins and observed how the nascent

MCMs are produced in the mother cells and how their daughters inherit them.These findings also explain how safe life continuation is secured – the cell's memory of speed control is passed on through cell generations from mother cells to their daughters.

#### MOLECULAR BABYSITTERS

The researchers also found that the function of nascent MCM depends on another protein, the MCM binding protein (MCMBP). They dubbed MCMBP a 'molecular babysitter', since the job of this protein is to escort the newly born MCM proteins to the DNA where they do their speed regulating work. The 4D imaging showed that in the absence of MCMBP, DNA replication takes place at a higher speed, leading to DNA damage.

This new knowledge may be of relevance to the development of a new strategy for cancer treatment. The researchers are currently testing the idea that genetic or pharmacological removal of MCMBP and the resulting high speed of DNA replication, can be tolerated by normal cells but will be lethal to cancer cells.

The studies were performed in collaboration with researchers from the Choudhary Group at CPR.

## HIGHLIGHTS

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## Youngest part of the team became first author in Nature

"Even as a student you feel part of the team," says Hana Sedláčková who joined the Copenhagen Bioscience PhD Programme at CPR in 2016, and crowned her PhD with a paper in Nature.

#### "Now it's done."

That thought came to the mind of Hana Sedláčková when she learned that Nature had accepted her work for publication in July 2020. She was first author of the article in the prestigious scientific journal and still a PhD student, which is a combination rarely seen. Most often, the researchers achieving this chill of recognition present much longer CVs.

Thereby, Hana Sedláčková fulfilled the ambition that was sowed in her mind during the first few weeks as a pre-doctoral researcher at CPR in 2016.

"When I started at CPR, I was working with a very talented postdoc, Kumar Somyajit, who showed me in a microscope how the MCM proteins look in the cell. It had been a longstanding question among researchers why cells generate so many MCM proteins when only a small portion is used to generate replicative helicase during the process of DNA replication. For several decades, scientists did not know the role of the vast majority of MCM proteins, and collectively called this enigma the MCM paradox. I looked at the MCM proteins in the microscope and thought: 'This is so strange. How come that scientists didn't solve this enigma before?'," says Hana Sedláčková, who decided that solving the MCM paradox should be her focus during the upcoming four years as a researcher and PhD student.

"Other young researchers might have been scared to take on this ambitious project, but for me it was simply interesting to find out: What is the role of huge amount of MCMs during DNA replication?" says Hana Sedláčková.

#### SUCCESS THROUGH CURIOSITY AND GUIDANCE

She solved the paradox thanks to her own curiosity and drive, and, she adds, even more thanks to an extremely stimulating scientific environment at CPR and an intense interdisciplinary knowledge exchange in the Copenhagen Bioscience PhD Pogramme. Here, PhD students and researchers from four Novo Nordisk Foundation Research Centers and other research institutions get together for regular seminars and meetings.

"So many colleagues have been guiding me so well to develop technical skills but also conceptual and importantly critical thinking, for instance by saying: "Look Hana, there is a new imaging technology, which might help you to solve your research question." And this valuable feedback from my colleagues I always appreciated a lot and many of these suggestions were included in our final story published in Nature," says Hana Sedláčková, now a postdoc at CPR.

Hana Sedláčková graduated from Masaryk University in Brno in the Czech Republic, where she began work in the lab already as a high school student. As a talented scholar, she participated successfully in several national and international competitions and in 2016, she experienced the positive dilemma having to choose between two prestigious PhD positions abroad.

#### ATTRACTED BY THE OPEN CULTURE

"Copenhagen won that competition. I already knew the city and the university since I visited Ian Hickson's Iab in the Department of Cellular and Molecular Medicine for a month during my masters. Now, I was looking for at Iab to dive deeply into cell biology, and the number one was Jiri Lukas' group and the Bioscience PhD Programme It looked amazing - an opportunity to really deal with fundamental questions in cell biology, to freely develop new ideas and to participate in the networking among centers. That is why I decided to come," says Hana Sedláčková.

### HIGHLIGHTS

# Youngest part of the team became first author in Nature



It made her want to come back that she during her first visit was pleased by the lifestyle in Copenhagen and the flat hierarchy at the university. She recommends other talented young researchers to follow in her footsteps.

"Copenhagen is a beautiful city. It is so nice how you can transport by bike to the lab. And most importantly, the science is done at a top level internationally. I really like the collaborative way of working here. I can go from CPR to another building and talk openly about my project also with other scientists outside of CPR. In some other academic cultures, one can meet a more secretive atmosphere and a steep hierarchy. Here it's flat. Even as a student you are an equal member of the research team."

THE COPENHAGEN BIOSCIENCE PHD PROGRAMME is designed for international talents to come to Denmark and start their research careers at a Novo Nordisk Foundation Research Center. The four-year program recruits up to 16 international students annually. It is divided into a pre-doctoral year followed by three years of PhD training at one of the four Novo Nordisk Foundation Research Centers embedded at the University of Copenhagen or the Technical University of Denmark. The four centers are part of the Copenhagen Bioscience Cluster, a Novo Nordisk Foundation initiative.

### HIGHLIGHTS

# 2020Brief Highlights

#### NEW DIRECTOR OF THE PROTEIN SIGNALING PROGRAM

Starting January 2020, Niels Mailand, in addition to being group leader, became new Research Director of the Protein Signaling program, previously headed by Jiri Lukas. The advancement was unanimously supported by CPR's Scientific Advisory Board.

#### NEW CENTER FOR HEALTH DATA SCIENCE

A new Center for Health Data Science (HeaDS) opened in 2020 at the Faculty of Health and Medical Science at University of Copenhagen with the aim to strengthen data science across the faculty and support the biomedical community with access to cutting-edge bioinformatics. CPR Research Director Søren Brunak helped conceptualise HeaDS with Dean Ulla Wewer and is part of the steering group as are fellow CPR Group Leaders Lars Juhl Jensen and Simon Rasmussen. CPR alumni Tugce Karaderi and Alberto Santos have established their own research groups at HeaDS, which is led by Professor Anders Krogh.

#### EXTERNAL FUNDING

CPR had a high success rate with Independent Research Fund Denmark in 2020, with four group leaders receiving a total of 12.5 million DKK. Research Director Matthias Mann attracted 6.2 million DKK from EU Horizon2020 as part of the ISLET consortium (Advancing Innovative Stem Cell-Based Therapy for Diabetes in Europe). The Mann Group was also awarded 1.1 million DKK from the Chan Zuckerberg Foundation for participation in the Human Cell Atlas project. PhD student Ann Schirin Mirsanaye received 146,000 DKK from various contributors for the Sustainable Research Symposium in 2020 on behalf of 'CPR Goes Green'.

#### SCIENTIFIC PRIZES

CPR leaders received several prestigious prizes in 2020. CPR Executive Director Jiri Lukas received the Anders Jahre Award for Medical Research for many years of outstanding research on cell cycle regulation and genome integrity in cancer. Jiri Lukas share the award with long-time colleague Jiri Bartek from the Danish Cancer Society Research Center. CPR's new Research Director Anja Groth received HM Queen Margrethe II's Science Award. CPR Deputy Director Jesper V. Olsen received the KFJ Prize awarded by Kirsten and Freddy Johansen's Foundation. Julien Duxin and Nicholas Taylor were elected for the EMBO Young Investigator Program, and will receive financial and practical support for a period of four years. Associate Professor Nicolai Wewer Albrechtsen was elected into the Young Academy, a scientific academy for young talented researchers as part of the Royal Danish Academy of Sciences and Letters.

#### ALUMNI OVERVIEW

An important part of CPR's mission is to train future leaders in academia and industrial biomedicine. On average, our young researchers train with us for a fouryear period as a PhD student or a postdoctoral fellow (postdoc) before moving on to the next step of their career outside CPR. Since the centre's establishment in 2009, CPR alumni have established 21 academic research groups. In 2020, four PhD students defended their thesis and received their PhD degree. Four PhDs, ten postdocs, one assistant professor and one associate professor left CPR for new positions. The alumni have moved on to new careers within academia and industry in Denmark and abroad. Two PhD students ventured into entrepreneurship by establishing their own consulting firms.

Researchers leaving CPF	R in 2020	$\rightarrow$	To these sectors		$\rightarrow$	In these regions	
PhD	4		Academia	9		Denmark	12
Postdoc	10		Industry	5		EU	3
Assistant Professor	1		Entrepreneurship	2		Outside EU	2
Associate Professor	1						
Total	16			16			16

Ricardo García Martín from Montoya Group at work in the laboratory.

HIGHLIGHTS

FOUNDATION CEN

## HIGHLIGHTS

The researchers performed an in-depth study of the proteins of 100 taxonomically diverse organisms by the use of an advanced proteomics workflow. Photo shows the facilities in Copenhagen.

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# The proteome landscape of the kingdoms of life

In the largest mapping of proteins ever conducted across different organisms, a cross-disciplinary team of researchers from Research Director and Professor Matthias Mann's labs have analysed and compared the proteins of 100 organisms.

Proteins perform the vast majority of functions in all biological domains but their large-scale investigation has lagged behind due to technological challenges. Apart from human samples, only a limited number of organisms have so far had their entire sets of proteins – their proteomes – mapped, and there are few comparisons of the proteomes across species.

A study from Novo Nordisk Foundation Center for Protein Research (CPR) published in Nature in 2020 takes a big leap forward by analysing and comparing the proteins of 100 organisms including animal, plant, bacteria, archaea (an ancient type of single-celled microorganisms) and viruses. For comparison, a number of extensively studied model organisms were included – for example brewer's yeast, *Escherichia coli (E. coli)* bacteria and *Drosophila melanogaster* (fruit fly), which are widely used to research biological phenomena and human disease.

#### THE DARK PROTEOME

The study shows that the different life forms have remarkable similarities, for example a high fraction of the total proteome in all the analysed species dedicated to maintaining protein homeostasis and folding. Likewise, a high fraction is involved in supplying energy resources to the cell.

Contrary to expectation, even well-studied model organisms still contributed many previously unknown proteins. The study also showed a large number of highly expressed proteins without a known function. Exploration of this 'dark proteome' is attractive as these proteins may indicate essential but unique features in the evolutionary development of these organisms, and they may be useful for the biotechnology industry.

#### A VALUABLE RESOURCE FOR THE RESEARCH COMMUNITY

The study greatly increases the number of experimentally verified proteins, especially in bacteria and archaea. The current Swiss-Prot database (version 2019\_03), which inventories all proteins that have been experimentally verified, holds 559,634 proteins from all species. An additional 803,686 proteins from the new study more than double the number of proteins with experimental evidence, providing a valuable resource for the research community. The study was carried out by a cross-disciplinary team of researchers from Research Director and Professor Matthias Mann's labs in Copenhagen and Munich at the Max Planck Institute for Biochemistry. The team was able to infer common and specialized biological functions of the identified proteins and to compare them to close and distant relatives from all taxonomic levels. These analyses were enabled by advanced software called the 'clinical knowledge graph' developed in Professor Mann's lab in Copenhagen. The data can be interactively explored at: www.proteomesoflife.org.

# Studies on extracts of African frog eggs may improve future chemotherapy

One protein seems to play a key role when cancer cells avoid the impact of chemotherapy and continue to spread, research at Novo Nordisk Foundation Center for Protein Research (CPR) has revealed.

A successful collaboration between four research groups across several programmes at CPR has uncovered that one specific protein named RFWD3 is likely to play a key role when cancer cells manage to repair their DNA and continue cell division although the DNA was purposely damaged by chemotherapy. The consequence is reduced effect of the treatment.

"We found strong evidence that the protein RFWD3 is responsible for orchestrating the repair of different DNA lesions induced by chemotherapy. If we can inhibit this protein in patients subjected to chemotherapy, we could potentially block cells from fixing DNA lesions. This may lead to more effective treatment in the future," says Associate Professor and Group Leader Julien Duxin who led the research project.

#### THE AFRICAN CLAWED FROG

The research uncovered that RFWD3 seems to recruit key factors needed in DNA repair and signaling in cells that obtain DNA lesions, such as cancer cells. The group did their studies on egg extracts from the African clawed frog, containing the same repair factors as human cells. The researchers removed the

#### JOINED EFFORTS OF FOUR CPR RESEARCH GROUPS

The description of the role of the RFWD3 protein in DNA repair, published in Molecular Cell in 2020, is the culmination of three years of research in the Duxin Group. The RFWD3 protein was identified in proteomics-based screening studies performed in collaboration with the Nielsen Group, which also helped describe the protein interaction network of RFWD3. The Rasmussen Group analysed data from deep sequencing of DNA repair products that helped evaluate error free repair across DNA lesions. The Mailand Group helped verify the function of RFWD3 in human cells.

RFWD3 protein and observed that the absence of the protein resulted in a profound defect in recruitment of the components needed to repair and tolerate the damage. This led to the conclusion that this specific protein is an essential coordinator of DNA repair and DNA damage bypass.

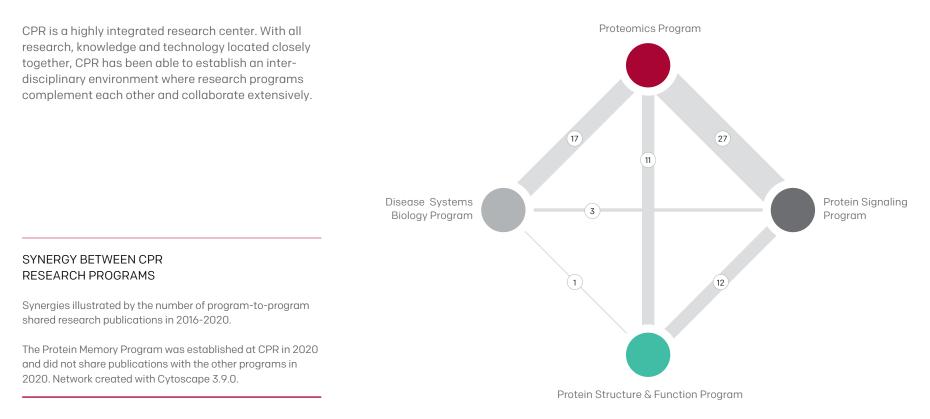
"Since the 1950s, doctors have treated cancer patients with different types of extremely toxic agents, which have been approved in the clinic because they are effective at killing cancer cells. But the truth is that we still don't know how sometimes cells repair the damage caused by the treatment. It is a huge knowledge gap, which we are trying to fill in with our fundamental research," says Julien Duxin.

## HIGHLIGHTS

The Duxin Group focuses on understanding the basic principles of DNA replication and DNA repair by the use of egg extracts from the African clawed frog, *Xenopus laevis*. The extraction process destroys the egg cells, leaving a solution that contains all the molecules needed to recapitulate the processes that take place during cell division and DNA repair. When DNA is added to the solution, it is assembled into a nucleus and is then efficiently replicated. This makes cell-free frog egg extracts a powerful technology to study DNA replication and DNA repair mechanisms. Photo shows a vial of purified frog eggs.

# Internal and external synergy

Collaboration and exchange of ideas is high priority at the Novo Nordisk Foundation Center for Protein Research (CPR), since an open-minded and curious attitude among researchers increases the chance of generating frontier research. This applies to CPR internally as well as in collaboration with hospitals, universities and the biomedical industry in Denmark and abroad.



### SYNERGIES

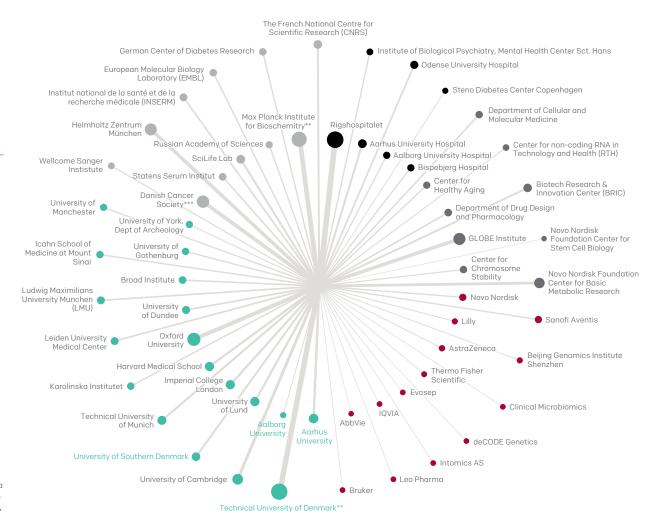
# Internal and external synergy

Novo Nordisk Foundation Center for Protein Research (CPR) actively interacts with the Faculty of Health and Medical Sciences at University of Copenhagen, hospitals in the region and scientific partners from around the world. The global reach of CPR is evident in the large number of collaborations that the center has established around the world.

## SYNERGY BETWEEN CPR AND EXTERNAL COLLABORATORS

Synergies illustrated by the number of published collaborations with external partners in 2018-2020. The 60 most frequent partners across five different categories are shown. The number of collaborations is represented by the thickness of lines (2-53). Network created with Cytoscape 3.9.0.

- Corporation
- Hospital
- Research Institution
- University
- Faculty of Health and Medical Sciences, University of Copenhagen
- 40 of 53 collaborations with Max Planck Institute of Biochemistry (MPI) are related to Matthias Mann's appointment as Director of Department of Proteomics and Signal Transduction, MPI.
- \*\* 36 of 51 collaborations with Technical University of Denmark (DTU) are related to Søren Brunak's appointment as Professor of Bioinformatics, Department of Health Technology, DTU.
- \*\*\* 13 of 34 collaborations with Danish Cancer Society (DCS) are related to Elena Papaleo's appointment as Group Leader of Computional Biology Lab at DCS.



# Research programs and technologies in 2020

The research groups at the Novo Nordisk Foundation Center for Protein Research (CPR) are organized into five programs. Each program is dedicated to run a technological platform that provides state-of-the-art research resources and interdisciplinary support to fellow researchers in the center.



### RESEARCH PROGRAMS



## Protein Memory Program

The program investigates how proteins control cellular identity via epigenetic mechanisms that govern the expression of the genetic information encoded in DNA. Understanding how cell identity is copied to new cells is essential for healthy life and understanding diseases.

#### THE GROTH GROUP

... Elucidates how chromatin organization is copied and epigenetic information passed on during cell division to maintain genome function. The program develops innovative genomics and proteomics technologies to understand chromatin replication and epigenome maintenance.

#### 2020 landmark

**66** We have successfully initiated a new multi-disciplinary research program at CPR aiming to break new ground in understanding proteinbased mechanisms underlying cellular memory. We have published a seminal review paper on epigenetic cell memory and a proteomics based mathematic model for propagation of chromatin states. **99** 

- Professor, Research Director and Group Leader Anja Groth

#### PLATFORM RUN BY THE PROTEOMICS PROGRAM

The Genomics Platform provides high-throughput DNA and RNA sequencing and covers applications from classical genomics to singlecell transcriptomics. The platform offers support from project planning to downstream analyses to all researchers at CPR.

Professor Anja Groth Research Director and Group Leader



# Disease Systems Biology Program

The program is leading in developing innovative tools to analyze and interpret big biomedical data effectively to better understand disease development and improve treatment options. The program combines multi-omics molecular network biology data and clinical data from the healthcare sector.

Professor Søren Brunak Research Director and Group Leader

#### THE BRUNAK GROUP

... combines molecular and clinical data in novel ways in order to understand disease progression patterns in multi-morbidity patients. Understanding diseases in a lifelong perspective gives valuable insights for more precise treatment.

#### 2020 landmark

**K** We presented an online tool to explore disease progression in 7.2 million patients spanning 25 years. The tool displays summary statistics that can help divide patients into subgroups, which early in their disease potentially could benefit from different treatments such that later complications may be avoided or reduced. Relations between diseases are complex and are also influenced by the genes they share. **33** 

- Research Director, Professor and Group Leader Søren Brunak

#### THE JENSEN GROUP

... develops state-of-the-art tools for generation and analysis of molecular interaction networks from proteomics data and text mining. The tools are made freely available to the scientific community.

#### 2020 landmark

**II** a collaborative study between the Jensen and Brunak groups and Odense University Hospital, we analysed registry data for alcoholic liver disease patients to identify upstream diagnoses that can help with earlier diagnosis of alcoholic liver disease and downstream diagnoses to understand its progression to liver failure. **!!** 

- Professor and Group Leader Lars Juhl Jensen

#### THE RASMUSSEN GROUP

... focuses on computational analysis of variation in the human proteome, genome and microbiome. By developing deep learning algorithms for omics data, they aim to increase the understanding of human diseases for more precise diagnostics and treatments.

#### 2020 landmark

**11** A main achievement of the group this year has been developing our deep learning frameworks for analysis of large scale genomics, metagenomics, proteomics and registry data. Furthermore, we reconstructed more than 400 ancient Viking genomes in a massive effort to understand the evolution of human genomes. **55** 

- Associate Professor and Group Leader Simon Rasmussen

## PLATFORM RUN BY THE DISEASE SYSTEMS BIOLOGY PROGRAM

The Big Data Management Platform provides a shared, scalable computational infrastructure to handle the vast amounts of data produced by the various technology platforms at CPR, such as raw mass spectrometry and imaging data.

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## Protein Signaling Program

The program uses cutting-edge methodologies to illuminate how proteins communicate and work together to protect cellular DNA from harmful changes. This enables a detailed molecular understanding of diseases and paves the way for improved treatment of patients.

Professor Niels Mailand Research Directo and Group Leader

#### THE MAILAND GROUP

... seeks to obtain detailed molecular insights into the signaling processes promoting cellular stress management to protect against genetic changes, which underlie many diseases. This knowledge provides opportunities for development of new and improved treatment strategies.

#### 2020 landmark

**11** We discovered how patient-associated mutations in the FAM111 proteases drive rare hereditary human disorders via a gain-of-function mechanism that undermines cell fitness and survival. We also used genome-scale CRISPR screening to unravel essential functions of cellular signaling processes. **33** 

 Research Director, Professor, and Group Leader
 Niels Mailand

#### THE DUXIN GROUP

... uses protein extracts from frog eggs to study fundamental mechanisms of DNA repair and DNA replication. They primarily focus on how cells repair DNA lesions known as DNA-protein crosslinks, which can cause cancer and accelerated aging if left unrepaired.

#### 2020 landmark

**11** We have found strong evidence that the protein RFWD3 orchestrates the repair of different DNA lesions induced by chemotherapy. If we can inhibit this protein, we could potentially block cells from tolerating DNA lesions, which could lead to more effective chemotherapy in the future. **33** 

- Associate Professor and Group Leader Julien Duxin

#### THE LUKAS GROUP

... explores how proteins that guard the integrity of the human genome assemble into functional pathways, how they organize themselves in the cell nucleus, and how they communicate with the external environment and cellular metabolism to shield DNA against heritable and disease-predisposing mutations.

#### 2020 landmark

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 Professor, Executive Director and Group Leader Jiri Lukas

#### THE NILSSON GROUP

... investigates essential enzymes called protein phosphatases that control a vast number of signalling processes in the cell. Understanding how protein phosphatases function and select their target proteins may advance rational drug design for a range of human diseases.

#### 2020 landmark

**66** We performed a global mapping of substrates (targets) of the protein phophatase PP2A and explained how this important regulator of cellular function recognises its substrates. This allowed us to uncover a new mechanism by which PP2A suppress cancer growth. **99** 

- Professor and Group Leader Jakob Nilsson



#### PLATFORM RUN BY THE PROTEIN SIGNALING PROGRAM

The Protein Imaging Platform provides cutting-edge technology and support to all researchers at CPR that use microscopy to investigate the behavior of proteins in the cell, such as protein localization, activity and interactions, either as a snapshot or over time.



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## Protein Structure and Function Program

The program visualizes the 3D structure of individual proteins and their assemblies to understand key biological processes. Understanding how these molecules function improves the understanding of biological mechanisms and disease development and facilitates drug development.

Professor Guillermo Montoya Research Director and Group Leader

# NOVO NORDISK FOUNDATION CENTER FOR PROTEIN Ó 20

#### THE MONTOYA GROUP

... visualizes the functional details of protein complexes involved in cell cycle progression and genome editing and integrity. Deciphering the mechanisms behind these important processes provides the basis for understanding disease and the possible development of treatments.

#### 2020 landmark

**LE** We mapped how the components of a large multifaceted immune system in bacteria (Cmr-B) interact to defend bacteria against intruding phages (virus that attack bacteria). Our results may constitute important knowledge for fighting antibiotic resistance. **J** 

- Professor, Research Director and Group Leader Guillermo Montoya

#### THE TAYLOR GROUP

... uncovers the structure and function of the complex molecular machines involved in transporting molecules across cell membranes. By understanding their biological role, it will ultimately be possible to adapt or modulate these systems for medical purposes.

#### 2020 landmark

**66** Using cryo-EM, we have provided a detailed model of the membrane protein complex that allows bacteria to move. The next step is to investigate if it is possible to inhibit the stator units with chemical compounds and thereby prevent bacteria from moving and spreading.

- Associate Professor and Group Leader Nicholas Taylor

#### PLATFORM RUN BY THE PROTEIN STRUCTURE AND FUNCTION PROGRAM

The Protein Production and Characterization Platform provides CPR with purified proteins and protein complexes of the highest quality and characterizes proteins using biophysical methods. The platform is an important asset as entry point for the cryo-EM facility.



## Proteomics Program

Innovative use of mass spectrometry technology allows the program to map all proteins in a cell (the proteome) to gain a deep biological understanding of cellular processes in health and disease. They can also identify proteins involved in disease and disease biomarkers.

**Professor Matthias Mann Research Director** and Group Leader

#### RESEARCH PROGRAMS

#### THE MANN GROUP

... develops innovative methods for rapid quantification of proteins in body fluids and tissue. By profiling patient samples, they aim to identify novel biomarkers that can be used for patient diagnosis and possibly for prevention and treatment of metabolic diseases, such as diabetes and cancer.

#### 2020 landmark

**LE** Via a vast mapping of proteins across 100 organisms, we offered a comparative view of the functional organisation of organisms across the evolutionary range. By doubling the number of proteins with solid experimental evidence, we provided a valuable resource for the research community available at www. proteomesoflife.org. **33** 

 Professor, Research Director and Group Leader Matthias Mann

#### THE NIELSEN GROUP

... develops novel proteomic strategies and combines this with other protein technologies and bioinformatics to understand how underexplored posttranslational modifications (PTMs)\* of proteins affect mammalian cell biology.

\* Post-translational modifications (PTMs) are chemical groups added to proteins after they are synthesized, affecting protein structure and function.

#### 2020 landmark

**14** We developed an improved strategy to measure physiological levels of ADPribosylation (ADPr) - a PTM involved in fundamental biological processes even from limited starting material. This is a final step toward biomedical and clinical application of ADPr profiling. **39** 

- Professor and Group Leader Michael Lund Nielsen

#### THE OLSEN GROUP

... develops mass spectrometry technology towards increased speed and sensitivity while applying it to biological questions such as mapping cellular signalling via growth factor receptors on the cell surface and the study of ancient proteins (palaeoproteomics).

### 2020 landmark

66 We published a method to analyse cancer phosphoproteomes with increased speed and minimal need for starting materials. The method makes it possible to analyse patient biopsies in clinical and biomedical laboratories and identify activated signalling proteins that can serve as biomarkers or drug targets in diseases. **39** 

 Professor, Vice Director and Group Leader
 Jesper Velgaard Olsen

#### THE CHOUDHARY GROUP

... deciphers the regulatory effects of post-translational modifications in cell signalling by subjecting engineered mammalian cell line models to stateof-the-art quantitative proteomics.

#### 2020 landmark

We contributed to a study that identified a new way to target the stem cells that drive acute myeloid leukaemia (AML), a very aggressive blood cancer. We also collaborated with the Lukas group to reveal how newly synthesized MCM proteins guard against genome instability. 33

- Professor and Group Leader Chuna Ram Choudhary

PLATFORM RUN BY THE PROTEOMICS PROGRAM

The Mass Spectrometry Platform provides technical support and maintenance for research groups in the Proteomics Program to ensure that CPR retains state-of-the-art mass spectrometry technology. Additionally, the platform provides analytical proteomics support for CPR researchers.

# CPR organisation and leadership

Novo Nordisk Foundation Center for Protein Research (CPR) has a clear governance structure tailor-made to maximise efficient governance internally and foster interactions with the Faculty of Health and Medical Sciences at the University of Copenhagen and other Novo Nordisk Foundation-funded centers of excellence.

The governance model incorporates all leaders and principal investigators with top-down advice from the Scientific Advisory Board and bottom-up perspectives from the center's Collaboration, Health and Safety Committee as well as the Student and Postdoc Association.

All key decisions are made by the executive management headed by the Executive Director, who answers directly to the Dean of the Faculty. The CPR executive management team consists of the Faculty Dean, the CPR management, and the Research Directors. The team interacts frequently and on different levels to discuss strategic matters, scientific strategy, finances, and to streamline the day-to-day management.

#### **CPR MANAGEMENT**

Executive Director: Jiri Lukas Deputy Director and Director of Education: Jesper Velgaard Olsen Head of Administration and Finance: Peter Dyrsting

#### CPR SCIENTIFIC ADVISORY BOARD

Once a year, the Scientific Advisory Board evaluates the center's performance, productivity, innovation, synergy and education. The board consists of some of the most

influential scientists of our time, covering world-leading expertise in all of CPR's major research fields. **Angus Lamond** (Chair), Wellcome Trust Centre for Gene Regulation and Expression, Dundee University (UK). Expert in proteomics and advanced imaging. **Andre Nussenzweig**, Laboratory of Genome Integrity, National Institute of Health (NIH), National Cancer Institute, Bethesda (USA). Expert in DNA damage response and mouse models of genome instability disorders.

**Christoph Müller**, Structural and Computational Unit at EMBL, Heidelberg (Germany). Expert in cryo-EM, X-ray crystallography and advanced biophysical and biochemical approaches.

**Michael Yaffe**, Koch Institute for Integrative Cancer Research, MIT (USA). Expert in how signaling pathways integrate at the molecular and systems level to control cell cycle progression and DNA damage responses in cancer.

Naama Barkai, Department of Molecular Genetics, Weizmann Institute of Science (Israel). Expert in systems biology and design principles of biological circuits. Steve Henikoff, Fred Hutchinson Cancer Research Center (USA). Expert in chromatin conformation and epigenetic inheritance.

#### COLLABORATION, HEALTH AND SAFETY COMMITTEE

A dialogue forum where decisions and new ideas are discussed and developed between management and employee representatives. Topics include personnel policy, work/life balance, trust, cooperation, well-being, safety, competence development and finances.

#### STUDENT AND POSTDOC ASSOCIATION

A bottom-up initiative created by students and postdocs to promote internal center synergy. Not a governing body per se, but the association has a direct and positive impact on the strategic decisions made by the management, and its representatives have a regular slot at group leader meetings.

#### CPR GOES GREEN

A bottom-up initative promoting sustainability in the center's daily activities. Works to reduce the carbon footprint of CPR by implementing green initiatives related to waste, energy, water, lab reagents, consumables and daily habits.



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### Publications 2020

The list includes primary research papers, reviews, commentaries and book chapters published in 2020 (print and online ahead of print). CPR authors are highlighted in bold.

#### **PRIMARY RESEARCH**

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Front page: Professor Anja Groth and her group joined Novo Nordisk Foundation Center for Protein Research in 2020. Anja Groth will be Research Director of the new Protein Memory Program. Left to right: Nicolas Alcaraz, Massimo Carraro, Anja Groth and Kathryn Jane Wattam.

