

UNIVERSITY OF COPENHAGEN
NOVO NORDISK FOUNDATION
CENTER FOR PROTEIN RESEARCH



Annual Report 2022

Novo Nordisk Foundation
Center for Protein Research



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 and growth 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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➔ A world-leading protein explorer

Since its foundation in 2007, Novo Nordisk Foundation Center for Protein Research (CPR) has pursued the ambition of becoming a world-leader in exploring how proteins drive fundamental biological processes in humans. The research performed in the center will contribute to new ways to diagnose, prevent and treat diseases.

The impactful results of CPR are possible thanks to a unique strategy implemented by the employees and the management with the support of the Faculty of Health and Medical Sciences, University of Copenhagen and external partners. The strategy focuses on tackling 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:

- 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 2022, CPR employed 248 staff members from 40 different countries, compared to 235 in 2021. CPR employees fall into three main categories: scientific personnel, research support and administrative support, of which scientific personnel constitute 71%.





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AMBITION

03
A world-leading protein explorer

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.



TECHNOLOGIES

06
Combining technologies to grasp the protein world

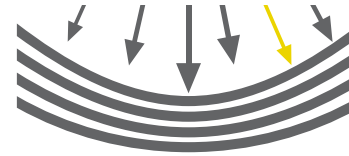
The technologies available in CPR span the entire spectrum from mapping all protein variants in a cell to visualizing how individual proteins assemble in functional networks that drive fundamental physiological processes.



CHALLENGE

07
The unexplored protein world

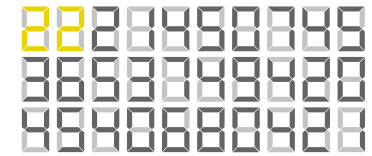
While the basics of the human genome, the DNA, was roughly mapped in 2001, the expression of the DNA in proteins - the human proteome - is still widely unexplored. Take a look into how proteins are made in a cell.



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2022 served as the midpoint of CPR's current funding period, generously provided by the Novo Nordisk Foundation. The cornerstone of CPR's success lies in assembling the best minds and cutting-edge protein technology under one roof.



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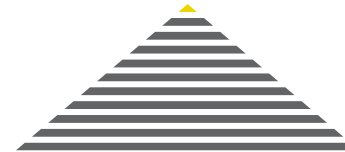
A graphic overview of how CPR research programs complement each other and a map of CPR's network of external collaborators.



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GOVERNANCE

Organisation and leadership
40

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.




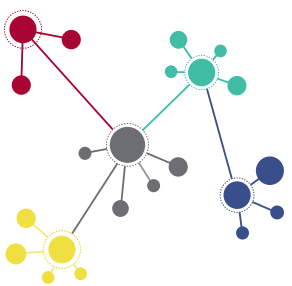

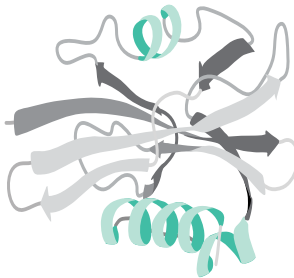

PUBLICATIONS

Full overview of CPR publications
42

In 2022, CPR researchers published 141 articles, including 132 primary research articles and 9 review articles. Find the full reference list here.

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 visualizing 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.

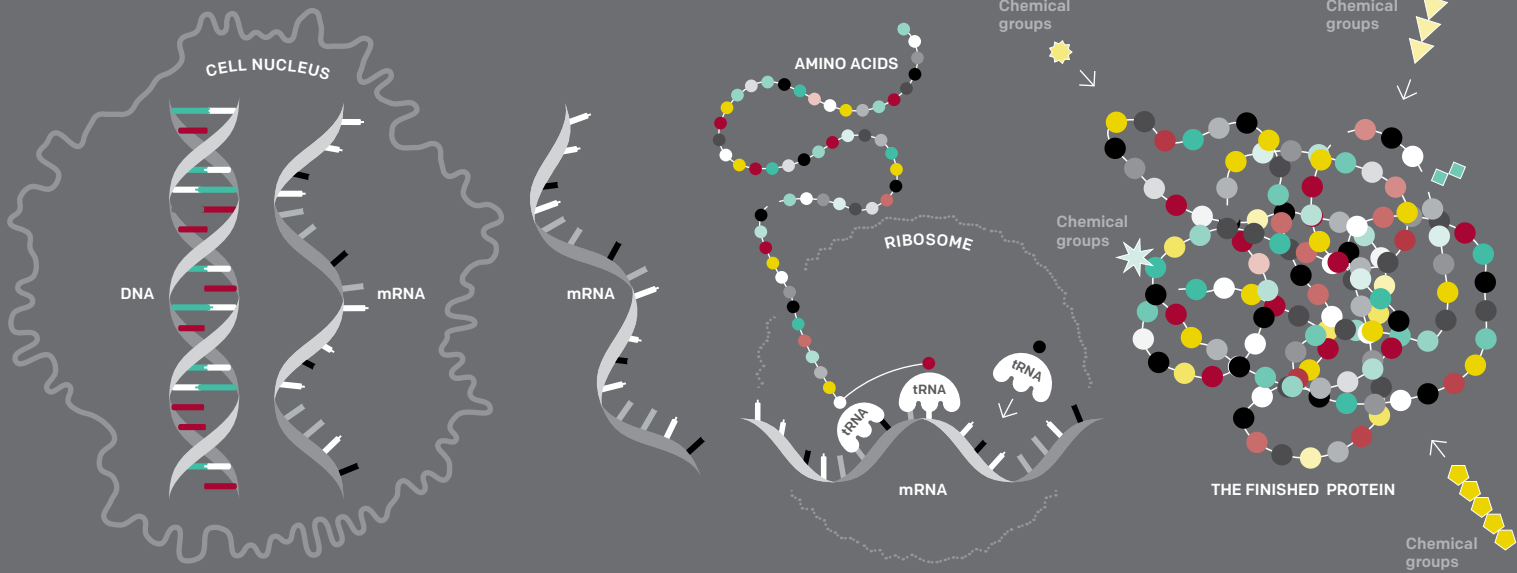
Technology	Mass spectrometry	Big data management and analysis	Protein imaging	Cryo-electron microscopy and x-ray crystallography	Functional genomics
	<p>Analyses all protein variants in a sample.</p> 	<p>Predicts how proteins interact and cooperate.</p> 	<p>Investigates protein function in living cells.</p> 	<p>Deciphers the structure of individual proteins and protein complexes.</p> 	<p>Explores genome organisation and function.</p> 
What the technology can do?	Reveals the identity and amounts of proteins and their modifications 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. Visualizes how proteins move around over time, how they interact and the effects on the cell.	Studies molecules and molecular 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 understand 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 investigate and functionally complement the results from mass spectrometry and big data analysis.	Protein characterization and structural studies contribute to the understanding of a protein's function, thus complementing all other protein technologies at CPR.	In a cross-disciplinary approach, functional genomics is combined with CPR technological strongholds such as proteomics, structural biology, and big data analysis to reveal protein function in genome regulation.

CHALLENGE



The quest to understand the human proteome

HOW PROTEINS ARE MADE IN A CELL



THE DNA HOLDS THE CODE

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 mRNA TRANSPORTS THE CODE

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 ASSEMBLES THE PROTEIN

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.

THE PROTEIN IS MODIFIED AND READY

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 so-called 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, muscles 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.

CELL MEMBRANE

© ILLUSTRATION BY MARIANNE BOM / KIBERG & GORVENSEN



Realizing CPR mission, the midway checkpoint

The year 2022 served as the midpoint of CPR’s current funding period, generously provided by the Novo Nordisk Foundation. Our primary focus is to pinpoint areas within protein research where groundbreaking discoveries can be made, particularly in disease prevention.

The cornerstone of success for the Novo Nordisk Foundation Center for Protein Research (CPR) lies in assembling the best minds and cutting-edge protein technology under one roof. Our primary focus is to pinpoint areas within protein research where groundbreaking discoveries can be made, particularly in disease prevention. We are grateful for the continued opportunity to pursue this mission, made possible by our funding support. The year 2022 served as the midpoint of CPR’s current funding period (2020-2024), generously provided by the Novo Nordisk Foundation.

We are privileged to benefit from the active involvement of a deeply committed and hands-on Scientific Advisory Board (SAB) consisting of some of the most influential scientists of our time, each possessing world-leading expertise in the major research fields covered by CPR. In April, CPR hosted the SAB for a two-day visit to evaluate CPR’s performance, productivity, innovation, synergy, and educational efforts. Ulla Wewer also participated, marking one of her final commitments before stepping down as Dean of The Faculty. Following the meeting, André Nussenzweig stepped down from the board after serving as a valued member since 2013. CPR expresses sincere gratitude to both Ulla and André for their invaluable contribu-

tions over the years; their guidance and support have been indispensable to the sustained success of CPR.

One of the most important tools CPR uses to uphold scientific excellence is quinquennial review of research group leaders and their group’s scientific achievements and performance. In June 2022, Nicholas Taylor and his research group underwent their first quinquennial review. During a one-day site visit, a panel comprising of top international experts provided constructive feedback to Nicholas aimed at refining his research and leadership strategies for optimal success. Nicholas Taylor received the highest rating on CPR’s scale (‘outstanding’) and based on this evaluation, CPR’s management decided on the financial allocation to the group (2020-2024) and supported Taylor’s enrolment in the University’s recently established promotion program, expectedly from July 2023.

At CPR, optimization of protein technology is central for the mission. This year, the Olsen Group published a new streamlined pipeline for analysing proteins in bones, which enables analysis of 200 samples per day. This severely reduces time and cost. The method can help archaeologists to rapidly determine the species of bone fragments found in archaeological excavations.

We are proud that as a natural extension of our passion for basic research, CPR continues to give insight into areas that can give knowledge into different areas of disease. As an example, the Rasmussen Group published a new approach involving deep-learning to map bacteriophages, which are viruses that infect and kill bacteria, in the human gut. This information may help improve treatment of gastrointestinal diseases such as inflammatory bowel disease.

This year, CPR organised a keynote presentation by Bobby Bovell from Living Institute, focusing on diversity and inclusion. This event was mandatory for all CPR employees and aimed to cultivate a shared understanding of inclusion and diversity within the organisation. Following the keynote, staff were provided with a link to an inclusion survey, designed to assess the level of inclusion at CPR and identify any perception gaps.

Jiri Lukas

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

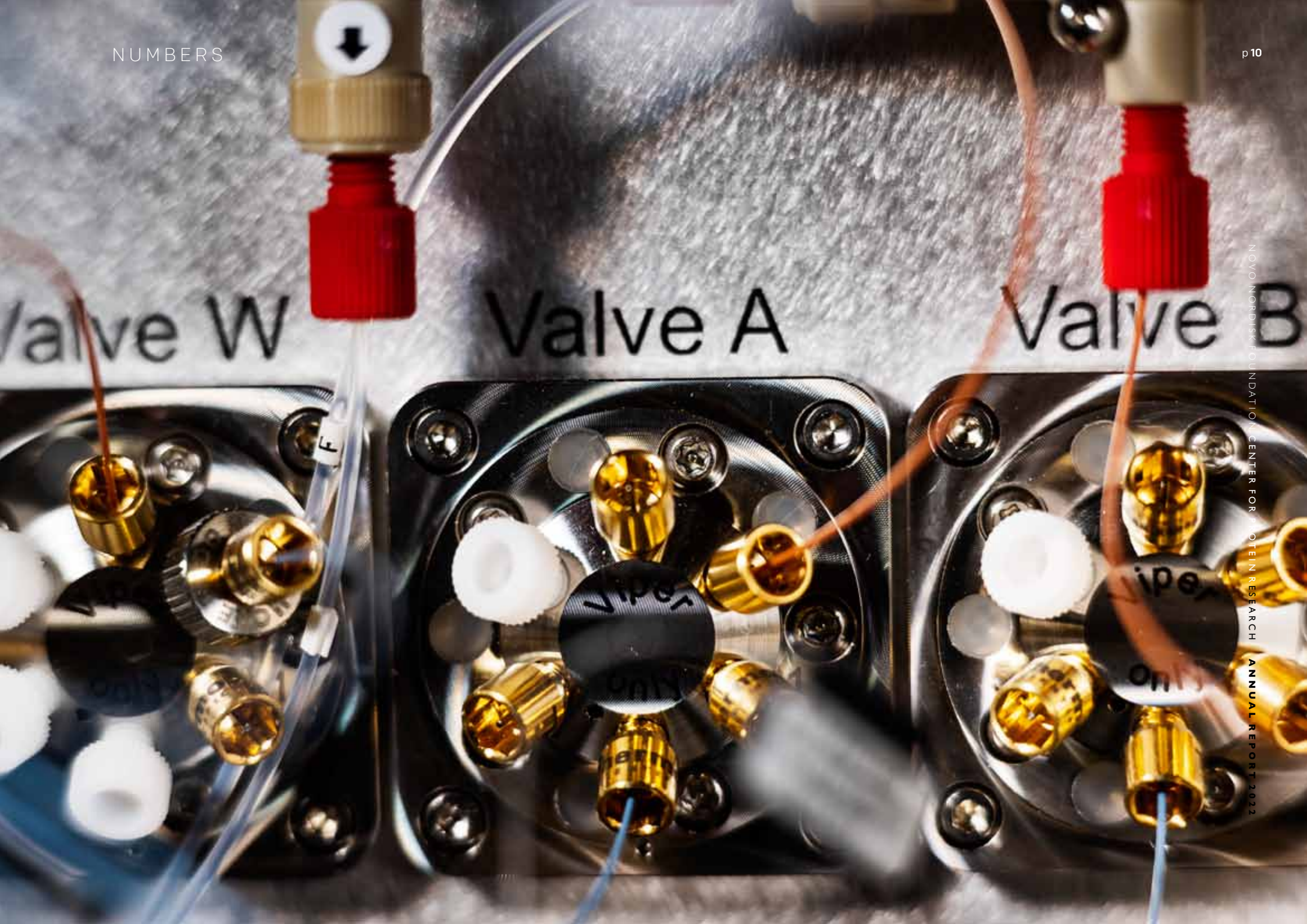
CPR'S VISION

...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 mechanism based 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.

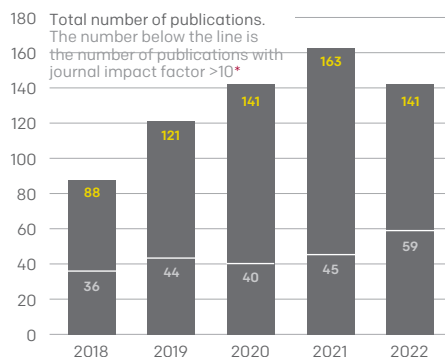


NUMBERS



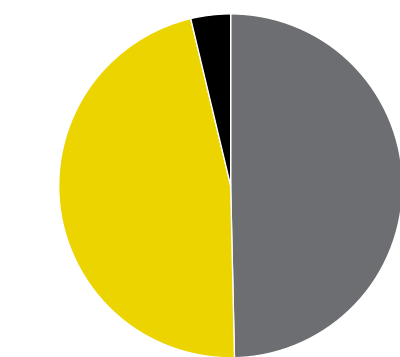
Selected numbers: CPR activities in 2022

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.

Annual funding and distribution



- NNF center grant 119.7 million DKK
- Competitive research grants 112.4 million DKK
- University of Copenhagen funds 9 million DKK
- Total 241.1 million DKK

No. of courses

No. of attendees

	Under graduates	PhD students	Post-docs	Mixed Audience**
CPR organised and co-organised	2 • 55	4 • 105	3 • 50	2 • 53
Faculty of Health and Medical Sciences at UCPH*	7 • 190	7 • 170	- • -	2 • 36
Outside Faculty of Health and Medical Sciences in DK and abroad*	9 • 238	3 • 75	- • -	5 • 80
Online resources organised by CPR	- • -	- • -	- • -	1 • ***
Total	18 • 483	14 • 350	3 • 50	10 • 169

- * Excluding CPR organised courses.
- ** Mixed audience covers undergraduate students, PhD students, postdocs and academic staff.
- *** Continuously accessed.

No. of outreach events



events
in 2022

RESEARCH OUTPUT

In 2022, CPR researchers published 141 articles: 132 primary research articles reporting on original research and 9 review articles. Commentary and book chapters are not included in the diagram.

More than four out of ten of the articles (42%) were published in journals with impact factor above 10.

FUNDING

In 2022, the total turnover of CPR was 241.1 million DKK.

- Almost half of the turnover was attracted as competitive grants (112.4 million DKK), supplementing the Novo Nordisk Foundation center grant of 119.7 million DKK.

TEACHING ACTIVITIES

Approximately 1,052 persons attended 45 courses taught by CPR researchers in 2022.

CPR's educational activities draw on the research excellence and unique opportunities associated with being a university-based research center.

OUTREACH

CPR researchers want to share their knowledge on protein research. In 2022, they participated in 91 outreach events:

- 48 press and media interactions
- 13 broadcast e.g. TV/radio/podcast
- 9 talks
- 12 focused websites, blogs or social media channel
- 9 activities such as workshops, visits and open day.



Cancer cell evolution is exposed by a new method leading to the most beneficial treatment

Why do some people not respond to cancer treatment? Researchers at CPR have come closer to answering this important question using their newly developed method called 'Deep Visual Proteomics'. DVP may help to expose cancer tumor evolution leading to the most beneficial treatment for each individual patient.

It is always difficult to determine why certain illnesses arise in our bodies. Old age, risky behavior, such as smoking, or genetics can all be parts.

However, the exact individual reasons for serious diseases such as cancer remain elusive and therefore the most beneficial treatment is not obvious. This leads to both missed treatment opportunities and unnecessary treatment.

Now, a new ground-breaking method called 'Deep Visual Proteomics' could help change just that.

The method has been invented by an international team of researchers driven by Andreas Mund, Associate Professor at CPR and Professor Matthias Mann, also at CPR, and has been applied to human tumors. The new technology was described in a study published in the top scientific journal 'Nature Biotechnology' in 2022.

"Our new technology, Deep Visual Proteomics, could become a game changer for molecular pathology in hospitals. With this method we can identify thousands of proteins and determine which ones drive the disease by taking a tissue sample and analysing just

the tumor cells in it," explains Andreas Mund, who is the first author of the study.

"This identification of all proteins is called proteomics and it reveals the mechanisms that drive tumor development. In turn, this can directly expose new therapeutic targets from a single tissue slice of a cancer patient biopsy. It makes visible a whole cosmos of molecules inside these cancer cells," says Andreas Mund.

IMPORTANT TO PATHOLOGY DEPARTMENTS

The researchers are very interested in proteins because proteins are ultimately the most important molecules in almost all diseases.

"When something goes wrong inside our cells and we become sick, it is quite certain that proteins are involved. Because of this, mapping the protein landscape can help us determine why a tumor could develop in a particular patient, what vulnerabilities that tumor has, and what treatment strategy might prove the most beneficial," says Professor, Research Director and head of the research team at CPR, Matthias Mann.

In the study, the researchers applied 'Deep Visual Proteomics' to cells from patients with acinic cell carcinoma and with melanoma. This was done in collaboration with researchers and pathologists at the Zealand University Hospital, Roskilde.

FOUR DIFFERENT TECHNOLOGIES

Deep Visual Proteomics integrates advances from four different technologies into a single workflow.

First, advanced microscopy generates high-resolution tissue maps. Second, machine learning algorithms are used to classify cells accurately before a laser micro dissects single tumor cells which are collectioned. Then, at last the normal and diseased cells of a particular type are analysed by ultrasensitive mass spectroscopy, mapping the protein landscape, which can help understanding the mechanisms of health versus disease.

"Using these technologies, we can effectively connect the physiological characteristics of cells seen under microscopes with the functions of aberrant proteins. This was not previously possible, and we are very convinced that this method can be applied to other diseases, not just cancer," says Andreas Mund.



Associate Professor Andreas Mund at the microscope used for the Deep Visual Proteomics method.

REFERENCE

Mund, A., Coscia, F., Kriston, A. et al. Deep Visual Proteomics defines single cell identity and heterogeneity. *Nat Biotechnol* 40, 1231–1240 (2022).
<https://doi.org/10.1038/s41587-022-01302-5>

CONTRIBUTORS

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The Biological Research Centre, HU
Science for Life Laboratory, KTH – Royal Institute of Technology, SE.



PhD Fellow Francisco Tenjo-Castaño co-authored the publication on the new genetic tool, CAST, which can insert large pieces of DNA into the genome.

REFERENCE

Tenjo-Castaño, F., Sofos, N., López-Méndez, B. et al. Structure of the TnsB transposase-DNA complex of type V-K CRISPR-associated transposon. *Nat Commun* 13, 5792 (2022).
<https://doi.org/10.1038/s41467-022-33504-5>

CONTRIBUTORS

Montoya Group, CPR, DK.



New CRISPR technology ready to manage larger pieces of DNA

The discovery of the structure of a fundamental part of the new CRISPR technology makes it possible to transport larger pieces of DNA than previously. Soon the technology is ready for the next steps on the way to clinical application in human cells thanks to researchers from CPR.

CRISPR technology has revolutionized genetic engineering and research for curing many genetic disorders within the past decade. However, CRISPR technology is limited by the fact that genetic scissors can only cut and paste relatively small pieces of DNA from and into the genome.

Now the next genetic tool in the form of a CRISPR-associated transposon system, called CAST, can insert large pieces of DNA into the genome. The background for this is that researchers at CPR have paved the way for further developing the CRISPR system.

“We have both characterized the structure of the transposon part of CAST and introduced genetic changes so that we can insert large pieces of DNA into the genome we cut into. All this represents steps on the way to use the technology on human cells at some point in the future,” explains Guillermo Montoya, Professor, Research Director, and Group Leader at the Protein Structure and Function program at CPR.

TRANSPORTING UP TO 30,000 BASE PAIRS

CRISPR technology works by making a double break on the DNA target to remove a genetic dis-

order. A donor sequence is then introduced, which the body's own repair mechanisms insert at the double break.

“A genetic disorder could be the result of various mutations at a specific place on the genome, and CRISPR could be used to cut out the mutated part of the DNA and replace it with a functioning sequence. This means that CRISPRs targeting the different mutations will need to be used to correct the complete gene,” says Guillermo Montoya.

Until now researchers have been limited by working with pieces of DNA comprising a few hundred base pairs. But by using the CAST system it is possible to transport up to 30,000 base pairs.

DETERMINED THE STRUCTURE OF TRANSPOSONS

“This enables us to insert parts of genes or small genes and regulatory regions to control the genes. We could start to redesign cells, opening new avenues to synthetic biology,” says Guillermo Montoya.

The research was published in the high-ranked scientific paper ‘Nature Communications’ in 2022.

The researchers used cryoelectron microscopy to analyse the structure of the CAST system by trapping proteins in a vitrified sample, which enabled them to determine the structure of the protein atom by atom.

This process has, explains Guillermo Montoya, for the first time shown what the transposon looks like and where it needs to be altered to make it change function. But since the CAST system originates in bacteria, it needs to be developed to be used on human cells.

“In our experiments, we have already shown how small genetic changes can increase the speed and precision of the protein. This shows that the system can be changed and optimized for laboratory or clinical use,” says Guillermo Montoya and concludes:

“Once researchers develop the CAST system to be applied to solve human problems, the possibilities are almost endless. It will enable treatments to be developed for more complex illnesses, requiring major genome structural changes.”



New blood test tool can warn about the state of severe diseases

A revolutionary pipeline to test if a person has alcohol-related liver disease and predict whether the disease will progress has been developed by a research team led by Matthias Mann in collaboration with clinicians. The pipeline minimises the need for liver biopsies and has diagnostic potential for a range of diseases.

About a third of the world's adult population live with fatty liver disease. While this does not necessarily affect an individual's health, it does increase the risk of developing severe liver disease such as cirrhosis and liver failure.

Assessing the risk and severity of a liver disease requires patients to attend a specialised clinic or a hospital to get either a liver biopsy – an invasive process associated with possible complications such as bleeding – or advanced imaging tests.

In 2022, a research team led by the Mann Group at CPR, introduced a much more accessible method to gain potentially life-saving information. From a simple blood sample test the researchers were able to predict patients' risk of developing severe alcohol-related liver disease:

"By analysing a blood sample, we could predict the presence of key liver pathological features and patient outcomes with performance that is equal to or better than existing state-of-the-art clinical tests," says postdoc Lili Niu, first-author of the study published in Nature Medicine.

Detection of such different types of e.g. liver injury is important because it creates a better foundation for developing disease management plans for the patients in the future:

"Given the high prevalence and often asymptomatic progression of liver diseases, there is an urgent need to implement screening programs in at-risk populations for early diagnosis," says Lili Niu.

Clinical Professor and Chief Physician Maja Thiele, Odense University Hospital (OUH), agrees: **"No doubt this is the future. It is a fantastic screening tool and answers everything we need to know about the patient's disease from a single blood test,"** says Maja Thiele, who was responsible for recruiting and investigating the 659 participants for the study in collaboration with her colleagues from the hospital and University of Southern Denmark.

In the study every participant's blood sample was analysed by mass spectrometry, which measures proteins with extreme precision. The researchers were able to identify more than 300 proteins from each blood sample. After identifying and measuring the amount of these

proteins, they used machine learning to find the so-called biomarkers, which are related to how the liver disease progresses:

"We identified three sets of biomarkers that detect fatty liver, inflammation, and liver fibrosis, which are the three key pathological features of progressing alcohol-related liver disease. It is biomarkers for these features we are looking for in the blood sample, because they can help indicate the liver health status and predict how the disease is going to progress in the individual patient," Lili Niu says.

Because of the promising results, Matthias Mann and his collaborators are interested in rolling out this blood-screening tool to the general population or at-risk populations such as persons with alcohol overuse.

"But it's not 'plug and play'. We do expect the tool to be implemented in practice, but it will take more than only a few years," he says and emphasizes that the diagnostic potential of the new tool goes far beyond liver disease: **"Mass spectrometry-based analysis of blood samples has great potential for discovery of new biomarkers that can be used to predict a wide range of diseases."**


Given the high prevalence and often asymptomatic progression of liver diseases, there is an urgent need to implement screening programs in at-risk populations for early diagnosis," says Lili Niu, first author of the study published in Nature Medicine.

REFERENCE

Niu L., Thiele M, Krag A & Mann M. et al. Noninvasive proteomic biomarkers for alcohol-related liver disease. *Nat Med* 28, 1277–1287 (2022).
<https://doi.org/10.1038/s41591-022-01850-y>

CONTRIBUTORS

Mann and Rasmussen Groups, CPR, DK
Odense University Hospital, Odense, DK
Novo Nordisk Foundation Center for Basic Metabolic Research, DK.



Søren Brunak and Simon Rasmussen have shown that the application of multiple omics technologies in biomedical cohorts has the potential to reveal patient-level disease characteristics and individualized response to treatment.

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Allesøe, R.L., Lundgaard, A.T., Hernández Medina, R. et al. Discovery of drug-omics associations in type 2 diabetes with generative deep learning models. *Nat Biotechnol* (2023).
<https://doi.org/10.1038/s41587-022-01520-x>

CONTRIBUTORS

Brunak and Rasmussen Groups, CPR, DK
Novo Nordisk Center for Basic Metabolic Research, DK
University of Copenhagen and Technical University of Denmark, DK
IMI Direct Consortium.



“Bartender” model predicts how drugs or lifestyle changes affect a person

A model based on numerous studies of people with type 2 diabetes can make a new type of prediction in relation to how a certain drug – or lifestyle changes – will affect a specific person at the molecular biological level. The model is developed by scientists at CPR.

People tend to respond differently to treatment with a certain drug, towards dietary changes or changes in exercise habits in relation to the effect on biomarkers of disease and health. Now, researchers from CPR have developed an advanced model for integrating many types of data on people’s molecular, biological, and clinical characteristics.

The model is based on a deep learning framework that integrates data from patients with type 2 diabetes. It receives twelve different types of data related to e.g. diet, exercise, smoking, medication use and clinical data. According to Søren Brunak, Research Director of the Disease Systems Biology Program and Professor at CPR, the model is the crowning achievement of several years of development within pharmaceutical research:

“We have increasingly moved away from using just one data type at a time to understand biological systems. Previously, researchers often used either genomic data, metabolic data or questionnaire surveys but are now trying to integrate different deep data types for each person. Numerous processes are linked in a living being, and determining how a per-

son’s genes will affect metabolites, if the person has a certain type of lifestyle, is important,” says Søren Brunak and continues:

“Our model integrates many very different data for the first time. One can characterize the model as a kind of bartender, because it can mix complementary data ingredients into a cocktail, we can learn from as a whole and not just the ingredients separately.”

BASED ON PEOPLE WITH TYPE 2 DIABETES

The deep-learning model is based on data from 789 patients with newly diagnosed type 2 diabetes, originally made from one of the most comprehensive mappings of diabetes biology. The data have been generated in the Innovative Medicines project DIRECT that has been running for more than 12 years. Based on this previously developed deep-learning framework, the model can receive data, learn from them, and predict how a certain drug would affect a given person.

“We can ask what will happen if you give a person a new drug that the person didn’t receive previously. Then we can determine how this drug will affect the proteins, lipids or metabolites, that we may be interest-

ed in either increasing or reducing,” explains another leading researcher behind the study, Simon Rasmussen, Associate Professor and Group Leader at CPR. However, the model is not yet ready to be used in routine care, because this requires large quantities of expensive omics data on each person.

“These types of patient-level omics data are likely to become more cost-effective in the future. Then, the effects of medication in a clinical setting can more easily be predicted, thereby identifying what likely would be most effective for a specific person with a specific illness,” says Simon Rasmussen.

This is possible because the model also applies to people with other illnesses, for example cancer. In this case the oncologist may consider four or five anticancer treatments:

“The oncologist can test drugs digitally on a person and determine how each drug would affect relevant biomarkers for cancer before deciding on treatment. To train a model on other diseases we again need to have multi-omics and other data available from those types of patients,” he says .



A unique method for studying changes in chemical markers on DNA

Specific changes in DNA occur in human cells throughout life when cells divide. A new method to study these important epigenetic changes in mammalian cells opens new avenues in research into cancer, ageing and drug discovery.

Virtually all cells in an organism, including humans, contain the same genetic information, but which genes are expressed determines a cell's function. This cell-specific gene expression is regulated by the cell's so-called epigenome, which consists of proteins bound to DNA, as well as direct chemical modifications to DNA.

One of the most important epigenetic regulators in mammalian cells is DNA methylation, a chemical marker that turns off regions of the genome that should not be expressed. Therefore, the methylation patterns on DNA will differ between different cell types, e.g. between liver and blood cells.

NOVEL USE OF MASS SPECTROMETRY

When DNA is replicated during cell division, the epigenetic marks associated with the DNA, including DNA methylation, are diluted. The newly created DNA strands then need to re-establish the level and pattern of methylation that existed prior to replication.

Much about these processes has been unknown until recently. But in 2022, a new method to study specific changes in DNA methylation after replication has been developed by researchers from CPR and published in *Nature Cell Biology* in early 2023. The

method, named iDEMS, is highly sensitive and based on quantitative mass spectrometry.

"The novelty in our work is that we didn't use sequencing methods widely used in this field. Instead, we used mass spectrometry and this enabled us to understand the kinetics of how post-replicative methylation is maintained," says Dr. Kathleen Stewart-Morgan from the Groth group at CPR and co-first author of the report.

The researchers found that DNA methylation levels increased steadily after replication, and after four hours the levels on replicated and genomic DNA were equal. This indicates that this process is slow overall and is outpaced by cell division.

"Over time, cells don't have enough time to re-establish their methylation after replication, meaning that the methylation of the genome in the resulting cells is diluted with each cell division," says Kathleen Stewart-Morgan.

This is the first time very clear kinetics for methylation re-establishment have been shown. "This helps explain why loss of DNA methylation is a common feature in cells that have divided many times, such as cancer

cells which are very proliferative and aged cells that have replicated many times over a person's lifespan."

USEFUL WHERE EFFICIENCY IS KEY

The researchers also used iDEMS to study another genomic marker, DNA hydroxymethylation, a rarer marker than methylation.

"We found that the 'parental' DNA strand always has more hydroxymethylation than the 'daughter' strand, supporting earlier work which indicated that this marker distinguishes DNA strands based on age," says Kathleen Stewart-Morgan and continues:

"There was no point at which the levels of hydroxymethylation were equal between the 'parental' and 'daughter' strands throughout the cell cycle. This opens new questions about how this difference may be used by cells, for example during DNA repair."

Looking to the future, iDEMS will be useful in profiling both methylation and hydroxymethylation dynamics in e.g. ageing and cancer evolution. As it provides a simple, fast readout, iDEMS could be useful where efficiency is key, such as in medical settings and drug discovery studies, according to Kathleen Stewart-Morgan.

Dr. Kathleen Stewart-Morgan expects the new method to be useful in profiling both methylation and hydroxymethylation dynamics in ageing and cancer evolution.

REFERENCE

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CONTRIBUTORS

Groth group, CPR, DK
MRC London Institute of Medical Sciences, UK.





Seeing so many people getting engaged in grassroots initiatives and being interested in putting sustainability in science on the agenda motivates me a lot to continue the work, says Ann Schirin, CPR Goes Green.



A grassroots movement fighting for sustainability grown big

CPR Goes Green started as a grassroots initiative at CPR almost four years ago. Now the initiative has spread to many places at the Faculty of Health and Medical Sciences.

Almost four years ago CPR's PhD student Nikoline Borgermann had the idea to start a grass root initiative, promoting a green transition within laboratories. Early onwards Ann Schirin Mirsanaye and other like-minded people at the Novo Nordisk Center for Protein Research (CPR) joined in and CPR Goes Green was founded with the goal to combine top notch science with sustainability.

"We formed a little grassroots initiative and had different people joining us. PhD students, postdocs, lab technicians and administrative staff got together, and our main goal was to look into topics of sustainability relevant for our everyday (lab) work life, including the area of trash sorting inside the labs as well as the kitchens and offices," says Ann Schirin, Chair of CPR Goes Green in 2022.

Over the years, the sustainability initiative has spread to other places at the Faculty of Health and Medical Sciences at the University of Copenhagen.

700 PEOPLE FROM ALL AROUND THE WORLD

"Seeing so many people getting engaged in grassroots initiatives and being interested in putting sustainability in science on the agenda motivates me

a lot to continue the work we've been doing," says Ann Schirin.

"We thought 'let's not reinvent the wheel' but try to connect with each other and learn from others, for example when it comes to creative ideas of re-using consumables in the labs," says Ann Schirin.

That made CPR Goes Green together with Nikoline Borgermann, now owner of the consulting firm Ava Sustain, the driving force to organise the first "Sustainable Research Symposium" in Scandinavia. The goal was to create an international community of people interested in improving the ecological footprint of research and learning more about practical, hands-on tips to help people making a green impact in their labs.

"I think a lot of people get frustrated in science when thinking about the huge environmental impact wet labs have. Our work is important and necessary, but we need to get better and become role models at reducing the carbon footprint of our work. The symposium enabled the opportunity to create a community of scientists who would like to do better and be more sustainable," says Ann Schirin.

The idea of the symposium was to create a regular platform where once a year scientists could come together and get inspired and motivated by and from each other.

NOT A GREEN POLICE

From the beginning it was important for the CPR Goes Green-team to include the rest of the center. They sent a questionnaire asking everybody if they had anything they wanted the team to look into.

"One important part was to ensure early onwards, that we are not functioning as a 'green police', but rather include everyone at the center into to the process of becoming more sustainable. We always tried to display ourselves as a group of people who are interested in sustainability and are happy to look into certain topics to find good solutions," Ann Schirin says.

"We started to look into sorting solutions and became the front runners in helping to setup a functional trash sorting system in the kitchens and in the labs including the design of signs and tables to make sorting as easy as possible for every lab member, which ended up having an impact on a lot of labs at the faculty and other departments."



2022

Brief Highlights

SHARING INNOVATIVE TECHNOLOGY

At CPR it is a core priority to facilitate access to world-class innovative technology to CPR researchers and the surrounding research community. CPR is for instance sharing the cryo-electron microscope (cryo-EM) facility, the Protein Research Infrastructure (PRI) and its protein production. In 2022, a new detector for the high-end cryo-EM was acquired that will improve the resolution of detection for all users of the facility, and PRI became fully established as a go-to proteomics facility for the wider Danish research community in need of mass spectrometry analysis.

FUNCTIONAL GENOMICS

As leader of the Genomics Platform, Anja Groth has expanded the scope of the platform by successfully implementing functional genomics, which is now offered to researchers at CPR and reNEW, the Novo Nordisk Foundation Center for Stem Cell Medicine. The platform is a joint venture between the two centers and facilitates the entire pipeline of functional genomics from experimental design to data analysis. In 2022, the platform entered in an agreement to open up to users from Department of Cellular and Molecular Medicine at the University of Copenhagen.

THE TEACHING PORTFOLIO

CPR has contributed to expanding the teaching portfolio within areas of CPR's technological strongholds. Most of the restrictions caused by the covid-19 pandemic were lifted in 2022, which meant

that CPR were finally able to offer a CPR summer school, which provided a comprehensive, theoretical and practical training in the application of state-of-the-art techniques in cellular and molecular biology characterizing protein mechanisms of action in living cells. Due to the level of laboratory and group work in the course, it had not been held since August 2019. New topics were added since the center has expanded with new groups and areas, allowing Anja Groth, Eva Kummer and Nils Krietenstein to contribute to the course.

YOUNG RESEARCHERS' CONFERENCE

Young researchers at CPR had the opportunity to develop skills outside of the lab by organising a conference for their peers through the FEBS-IUBMB-ENABLE collaboration. The ENABLE project, initially funded by the EU, gives young researchers from all over the world access to conferences dedicated to PhDs and postdocs in the life science field. The conferences allow the participants to learn new scientific advances and interact with renowned scientists in a setting they would not find anywhere else. During the conferences, a full day is dedicated to workshops and career events to educate and improve the skills of the participants.

ATTRACTION OF EXTERNAL FUNDING

In 2022, CPR researchers secured a total of 105 million DKK in external funding, of which some examples are mentioned here. Three Marie Skłodowska-

Curie Actions (MSCA) European Postdoctoral Fellowships were attracted by talented researchers in the Brunak and Montoya groups. Group Leader Julien Duxin entered a MSCA Doctoral Network (RepliFate) designed to train the next generation of European researchers in the field of DNA replication, cell fate and cancer. Research Director Guillermo Montoya was awarded 15,884,125 DKK from the Novo Nordisk Foundation for a new detector for the cryo-EM. He also secured 3,750,000 DKK for an extension of the 'CryoNET network' that coordinates the national cryo-EM facilities in Denmark and Sweden. Three group leaders attracted grants: Nils Krietenstein was awarded a Lundbeck Foundation Fellowship (10,000,000 DKK), Julien Duxin was awarded a NNF Hallas-Møller Ascending Investigator grant from the Novo Nordisk Foundation of 9,440,226 DKK, and Chuna Ram Choudhary was awarded 9,999,872 DKK from the Novo Nordisk Foundation. Assistant Professor Kathleen Stewart-Morgan was awarded a NNF Hallas-Møller Emerging Investigator grant from the Novo Nordisk Foundation for her new research group established from January 2023 at the Department of Cellular and Molecular Medicine, at the University of Copenhagen. Additionally, a total of 13,900,00 DKK were obtained from the Independent Research Fund Denmark to fund five different projects.



Researchers leaving CPR in 2022	→ To these sectors	→ In these regions
PhD	6 → Academia	10 → Denmark 13
Postdoc	10 → Industry	9 → EU 8
Assistant Professor	5 → Other*	4 → Outside EU 2
Associate Professor	2 →	→
Total	23 → Total	23 → Total 23

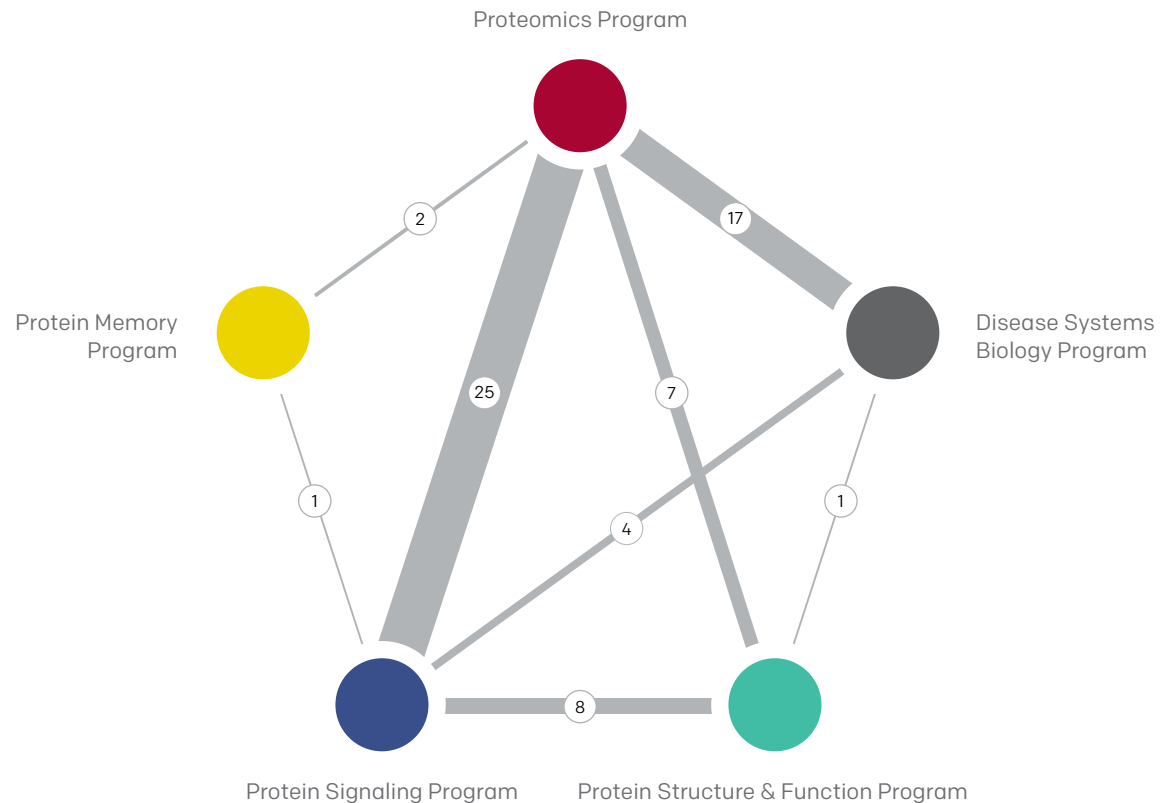
* The category 'Other sector' covers hospitals and research foundations



Internal and external synergy

Collaboration and exchange of ideas are of high priority at 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.

CPR is a highly integrated research center. With all research, knowledge and technology located closely together, CPR has been able to establish an interdisciplinary environment where research programs complement each other and collaborate extensively.



SYNERGY BETWEEN CPR RESEARCH PROGRAMS

Synergies illustrated by the number of program-to-program shared research publications in 2018-2022. The number of collaborations is represented by the thickness of lines (1-25).

Network created with Cytoscape 3.9.1.



Internal and external synergy

CPR actively interacts with the Faculty of Health and Medical Sciences at the 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.

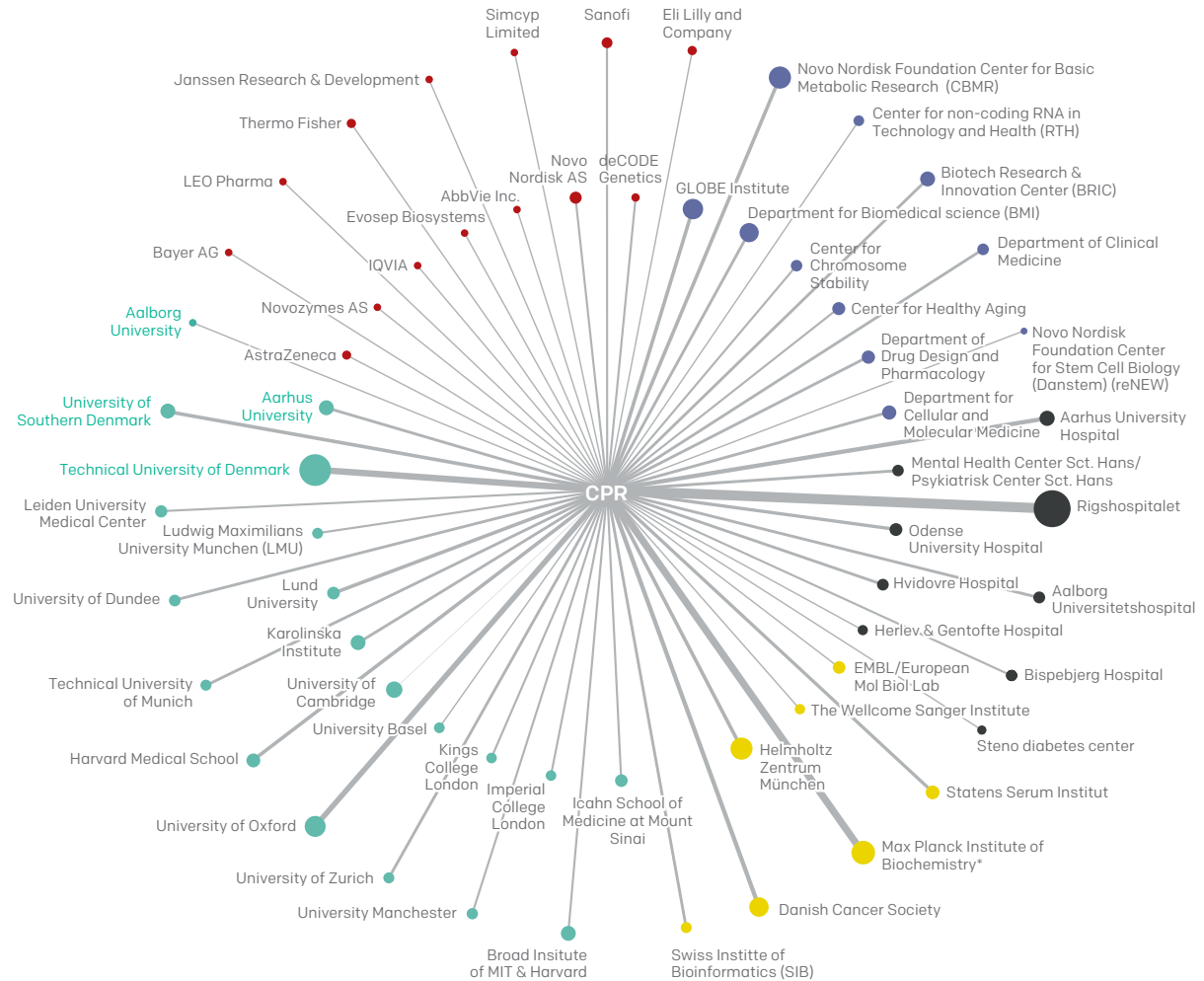
SYNERGY BETWEEN CPR AND EXTERNAL COLLABORATORS

Synergies illustrated by the number of published collaborations with external partners in 2018-2022. The 61 most frequent partners across five different categories are shown. The number of collaborations is represented by the thickness of lines (3-113).

Network created with Cytoscape 3.9.1.

- Faculty of Health and Medical Sciences, University of Copenhagen
- Hospital
- Research institution
- University
- Corporation

* A substantial share of the 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.
 ** A substantial number of the collaborations with the Technical University of Denmark (DTU) are related to Søren Brunak's appointment as Professor of Bioinformatics, Department of Health Technology, DTU.
 *** A substantial number of the collaborations with Danish Cancer Society (DCS) are related to Elena Papaleo's appointment as Group Leader of Computational Biology Laboratory at DCS.







Research programs and technologies in 2022

The research groups at CPR are organised into five research 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.



Professor Anja Groth
Research Director
and Group Leader



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. How cell identity is copied to new cells is essential to understand how we maintain healthy life, delay aging and avoid disease.

THE GROTH GROUP

... elucidates how chromatin organisation is copied and epigenetic information passed on during cell division to maintain cellular function. The group develops innovative genomics and proteomics technologies to understand chromatin replication and epigenome maintenance.

2022 landmark

“ In collaboration with other researchers, we examined how the histone chaperone NASP binds histones alone and in a complex with the ASF1 chaperone. We identified two unique binding modes for NASP chaperoning of histones, explaining how it contributes to histone homeostasis and maintenance of chromosome organisation. We also developed a novel quantitative mass spectrometry technique named ‘iDEMS’ to analyse DNA methylation and hydroxymethylation. This research showcased how DNA methylation is re-established post-replication during cell division. iDEMS holds promise for future applications, including tracking methylation dynamics in contexts like ageing and cancer progression. ”

- Professor, Research Director
and Group Leader
Anja Groth

THE KRIETENSTEIN GROUP

... studies 3D folding of human chromatin – the fundamental organisation of DNA and its associated proteins inside the cell – to understand how this folding helps establish and maintain cell-type-specific gene expression patterns. The aim is to study how mutations can contribute to the development of disease by changing the 3D organisation of genomes.

2022 landmark

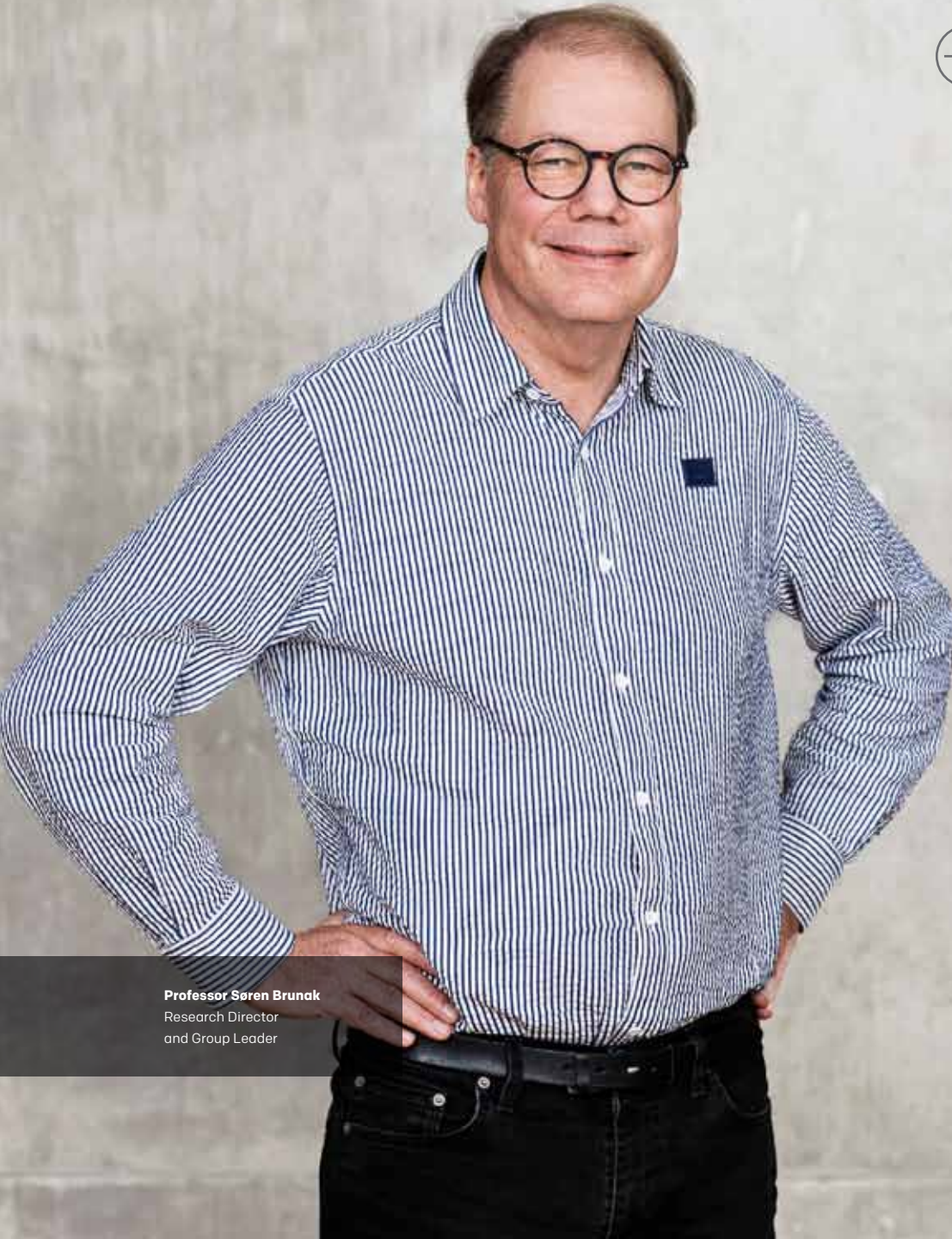
“ We have successfully established the lab securing both important funding and excellent group members. We are now expanding on high-resolution 3D technology to study post-translational modifications in the 3D nuclear environment. ”

- Associate Professor
and Group Leader
Nils Krietenstein



PLATFORM RUN BY THE PROTEIN MEMORY PROGRAM

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



Disease Systems Biology Program

The program is leading in developing innovative tools to analyse 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 population-wide 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 better treatment of diseases and complications.

2022 landmark

“ Type 2 diabetes (T2D) is complex and heterogeneous. A soft-clustering method was used to characterize newly diagnosed T2D patients based on 32 clinical variables, and we investigated associations with glycemic deterioration, genetic risk scores, circulating omics biomarkers, and phenotypic stability. Four clusters represented dysfunction patterns across combinations of T2D etiological processes. Remarkably, 65% of the patients remained outside the archetype clusters, reflecting the mixed etiologies characterizing the T2D population. ”

– Professor, Research Director
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.

2022 landmark

“ We published an updated version of the widely used STRING app for Cytoscape (Doncheva et al., *Journal of Proteome Research: Cytoscape stringApp 2.0: Analysis and Visualization of Heterogeneous Biological Networks*). Cytoscape is a software platform for visualizing complex networks and integrating these with any type of attribute data. The Cytoscape stringApp facilitates visualization of protein-protein interaction analyses from STRING. We also co-authored several papers with the Olsen and Mann groups in the Proteomics Program. ”

– 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 massive amounts of omics data, they aim to increase the understanding of human diseases for more precise diagnostics and treatments.

2022 landmark

“ We developed a deep learning based method for integration of large multi-modal datasets. We used the method to integrate and analyse genetic, registry and hospital information for 40,000 individuals of which half had mental disorder diagnosis of either depression or schizophrenia. One of the main results was the discovery of clinically relevant clusters of patients that are now being pursued for use in drug discovery pipelines. ”

– 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.



Professor Niels Mailand
Research Director
and Group Leader



Protein Signaling Program

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

THE MAILAND GROUP

... employs CRISPR/Cas9- and proteomics-based screening approaches to obtain detailed molecular insights into the signaling processes promoting cellular stress management, which is critical in many disease contexts. This knowledge provides opportunities for the development of novel targeted treatment strategies.

2022 landmark

“ Together with collaborators at CPR including other research programs, we discovered a critical role of the protein SCA1 in promoting error-free DNA replication-coupled repair of DNA interstrand crosslinks (ICLs). The proteins regulating repair pathway choice to promote faithful ICL resolution have been poorly defined but the new findings establish SCA1 as a novel and integral component of the repair pathway. ”

- Professor, Research Director and Group Leader
Niels Mailand

THE NILSSON GROUP

... investigates the function of essential enzymes called protein phosphatases in signaling processes in human cells and the role of binding motifs in virus-host protein interactions. Understanding how they each function may advance rational drug design for a range of diseases.

2022 landmark

“ In collaboration with the Danish Cancer Society and the Mailand and Montoya groups, we have shown that the small molecules iHAP1 and DT-061 selectively kill cancer cells, but not by reactivating PP2A complexes, which had otherwise been reported. Instead, iHAP1 is a microtubule poison and DT-061 disrupts both the Golgi apparatus and the ER and lipid synthesis associated with these structures and they cannot thus be used for dissecting PP2A-B56 biology. ”

- Professor and Group Leader
Jakob Nilsson

THE LUKAS GROUP

... explores how proteins that guard the integrity of the human genome assemble into functional pathways, how they organise 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.

2022 landmark

“ Together with collaborators with scientist from the Center for Chromosome Stability, Department of Cellular and Molecular Medicine at the University of Copenhagen, we have solved the so called “MCM paradox” that for decades hampered tracking active sites of DNA replication in living human cells. ”

- Professor, Executive Director and Group Leader
Jiri Lukas

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.

2022 landmark

“ Together with collaborators at CPR including other research programs, we discovered a critical role of the protein SCA1 in promoting error-free DNA replication-coupled repair of DNA interstrand crosslinks (ICLs). The proteins regulating repair pathway choice to promote faithful ICL resolution have been poorly defined but the new findings establish SCA1 as a novel and integral component of the repair pathway. ”

- Associate Professor and Group Leader
Julien Duxin



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.



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

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.

2022 landmark

“ We determined and published the structure of CRISPR-Cas12j3, also known as Cas-phi3, which may be redesigned as a new and better genome editing technology than the existing CRISPR-Cas9 due to its smaller size, which means it should be possible to include longer sequences to facilitate editing than for its larger cousins. ”

- 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 biomedical purposes.

2022 landmark

“ We published a study in the cryo-EM structure of human thyroglobulin, which has an important role in thyroid health and disease. We also published a review article on the class of molecular membrane motors (5:2 motors) which we have previously done some landmark work on and remain an active topic of research in the group. We also contributed to a study describing the expression, purification and characterization of human proton-coupled oligopeptide transporter 1. ”

- Associate Professor
and Group Leader
Nicholas MI Taylor

THE KUMMER GROUP

... investigates the biology of human mitochondria, which are energy-producing cell compartments, to understand how they maintain their DNA and how they produce functional RNA species. Their work can shed light on the molecular triggers of mitochondrial disorders that are frequently caused by mutations in the involved protein factors.

2022 landmark

“ We have successfully established a highly qualified group and set up a competitive research agenda. For this, we integrated advanced experimental pipelines for insect and mammalian protein production as well as cryo-electron microscopy, which will form the basis of our research in the coming years. ”

- Associate Professor
and Group Leader
Eva Kummer

**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

THE NIELSEN GROUP

... develops novel proteomic strategies and combines this with other protein technologies and bioinformatics to understand how underexplored post-translational 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.

2022 landmark

“ We published a new function of the sumoylation pathway in differentiation of adipocytes. This study also provides an in-depth resource of the dynamics of the SUMO-chromatin landscape, SUMO-regulated transcription and endogenous sumoylation sites during adipocyte differentiation. ”

- Professor and Group Leader
Michael Lund Nielsen

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.

2022 landmark

“ We have pioneered Deep Visual Proteomics (DVP), an innovative technique that combines deep learning-powered image analysis, laser microdissection, and ultra-sensitive mass spectrometry. DVP provides unmatched insights into spatial proteomics at subcellular resolution within tissues. Additionally, our proteomics expertise has been integral to collaborative studies with the Nilsson and Maillard groups at CPR, yielding key insights into protein function. ”

- Professor, Research Director and Group Leader
Matthias Mann

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).

2022 landmark

“ We published a rationale for combination therapy in acute myeloid leukemia. We used subcellular phosphoproteomics to devise rational combination therapies to enhance selinexor treatment efficacy in responders and overcome resistance in non-responders. ”

- 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 state-of-the-art quantitative proteomics.

2022 landmark

“ We published a preprint paper on the mechanisms by which gene expression in mammalian cells is tuned across different cell types and tissues. Our findings uncovered that expression of mammalian genes is quantitatively adjusted in different cell types by altering the strength of promoters and gene proximal enhancers. This finding helps in understanding how quantitative expression in genes enable the emergence of functionally diverse cell types. ”

- 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

Jiri Lukas, Executive Director.

Jesper Velgaard Olsen, Deputy Director and Director of Education.

Peter Dyrsting, Head of Administration and Finance.

CPR SCIENTIFIC ADVISORY BOARD

Every 1.5 years, 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.

André 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. Stepped down after the 2022 SAB visit.

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 post-docs 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 initiative 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.





Publications 2022

The list includes primary research papers, reviews and book chapters published in 2022 (print and online ahead of print). CPR authors are highlighted by colours.

Proteomics

Protein Signaling

Disease Systems Biology

Protein Structure and Function

Protein memory

CPR Associate Member

PRIMARY RESEARCH

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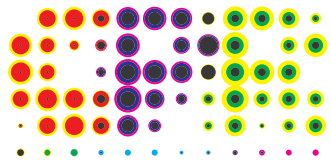
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