

# Protein research and bioinformatics



## Content and application

Proteins are the fundamental building blocks of life. Research in Greater Copenhagen focuses on the significance of proteins and peptides for health, for example using proteins as biomarkers. Protein Research in Greater Copenhagen focuses on designing new proteins to treat neurodegenerative disease such as Alzheimer's and Parkinson's as well as for new personalised treatments. This research stronghold is underpinned by the region's strong competencies in bioinformatics, which employs biodata analysis and register-based health data to identify patterns in the interaction between types of patient, genetics, proteins and health conditions.



## Key environments and star researchers

Denmark has fostered a range of world-leading research teams working with proteins and bioinformatics, especially at the interdisciplinary Center for Protein Research and the Department of Cellular and Molecular Medicine at the University of Copenhagen, combined as well as a whole range of other science and health science environments at the Technical University of Denmark (DTU) and the University of Copenhagen. Leading researchers include Niels Tommerup and Ian Hickson who research the stability of genes and chromosomes and its significance for health. Henrik Clausen and Hans Wandall investigate the significance of sugars for the functionality of cells and proteins, while Søren Brunak combine patient data with large volumes of biological data on protein interactions to discover patterns of importance for the personalised treatment of patients. Finally, Prof. Mathias Mann explores the importance of proteins as biomarkers.



## Prospects for attracting investments

Protein research holds great potential, especially for the biotech sector and the pharmaceutical industry. Research and development form the basis of future diagnostic methods and the treatments of neurodegenerative conditions, cancer, fertility and allergy, for example. Protein research is furthermore an important precondition for developing better methods for drug delivery and personalised medicine. Protein research is closely connected to Greater Copenhagen's strengths in nanotechnology, cancer and diabetes research, and has led to a whole range of promising spin-outs.

## Characteristics of the research area

Protein research is one of the most promising areas in life-science. Research in protein structures and the significance of proteins as well as their interaction with the cells of the human body could open up an entirely new paradigm in the development of new personalised diagnostic and therapeutic methods (personalised medicine).

Protein research in Greater Copenhagen is interdisciplinary and is carried out in a wide range of departments and centres at the University of Copenhagen and DTU. Researchers from many different disciplines collaborate on projects at the Center for Protein Research, which has been awarded funding of about DKK 850m from the Novo Nordisk Foundation.

At the Department of Cellular and Molecular Medicine researchers investigate glycomics and the stability of genes and chromosomes, which is highly significant in understanding and treating a whole range of diseases. At DTU, it is especially DTU Bioinformatics and DTU Bioengineering that are engaged in protein research. Moreover, DTU Bioengineering explores proteins in food and nutrition and the development of new enzymes.

Protein research draws on Greater Copenhagen's strength within bioinformatics, i.e. the use of computers to analyse large volumes of biological data. Bioinformatics can for example be used to identify enzymes and proteins that rapidly and efficiently can be used for identifying genetic patterns and show how new drugs affect patients in preclinical tests.

Bioinformatics benefit from Denmark's leading position in using big data from medical register data, electronic patient records and questionnaire surveys. Using these data and combining them with other forms of biological data enables scientists to mine and identify patterns among different types of patient.

Copenhagen Business School (CBS) also contributes to this research via the BioBusiness and Innovation Platform (BBIP), which is a collaboration between CBS, the University of Copenhagen and DTU. The platform aims to strengthen competencies and specific tools to support bio-based innovation.

### International top quality niches

At the Center for Protein Research, scientists employ a broad, interdisciplinary approach in researching the role of proteins in health, diagnosis and treating disease.

The centre works with protein research from an integrative systems biology approach, i.e. they study the significance of how proteins interact with a whole range of other factors such as genes, sugars, circulation, etc. They investigate the structure of proteins, their interaction with internal cellular processes and how cells communicate with each other via proteins, e.g. when the immune system targets a disease.

The centre furthermore studies how proteins can be used therapeutically and how specially designed proteins can be produced quickly and efficiently. It uses bioinformatics to study proteins by developing algorithms that can recognise interrelationships and patterns in a combination of complex biodata, register data and electronic patient records. These big data studies could for example be crucial for treating cancer and in understanding the immune system and molecular evolution.

The protein research in Greater Copenhagen on the importance of sugars for protein functionality, glycomics, has major potential for supporting future therapies, gene technology and diagnosis. The University of Copenhagen's Center for Glycomics is especially prominent and is among the strongest environments in the world in the field. It is funded by the Danish National Research Foundation.

### Bibliometric key figures

There is no category in the bibliometric database, which fully captures protein research and bioinformatics. The field is interdisciplinary and is reflected in categories such as structural biology, molecular biology and cell biology. With respect to corporate co-publication, Greater Copenhagen takes the lead in all categories.

With respect to the share of articles, which are among the most-cited in the global top 10%, protein research is 2<sup>nd</sup> among the regions of comparison for two of the categories and 1<sup>st</sup> in one of the categories (biochemistry). Finally, Greater Copenhagen is averagely specialized in this area, which reflects the fact that numerous international research environments are engaged in protein research.

Copenhagen is also in front among the regions of comparison in relation to joint publications measured as the number of co-publications with authors from the private commercial sector.

### Key bibliometric indicators

	Specialisation	Output ranking (No. articles)	Highly cited article ranking (%)	Co-publication ranking (%)
Structural biology	0,98	6 (464)	2 (16,4)	1 (13,6%)
Molecular biology	0,68	8 (1122)	2 (18,4)	1 (10,1%)
Biochemistry	1,49	1 (337)	1 (28,1)	1 (12,9%)

Period: 2005 -2015. Regions of comparison: Amsterdam, Berlin, Dublin, Geneva-Lausanne, Hamburg, Helsinki, Munich, Oslo and Stockholm/Uppsala.

Specialisation is an expression of the size of a field of research compared to all research production at University of Copenhagen, DTU and CBS compared with its size in the regions of comparison. A specialisation level 1 indicates that Greater Copenhagen is on level with the regions of comparison. Specialisation of >1 indicates that Greater Copenhagen is more specialised in the field of research than the regions of comparison.

Output ranking measures Greater Copenhagen's position in the field concerned among the regions of comparison in terms of article production (with the absolute numbers of articles in brackets).

Highly cited article ranking indicates Greater Copenhagen's placing in the regions of comparison for the proportion of articles in the field of research in Copenhagen that are among the 10% most cited worldwide (percentage in brackets).

Finally, co-publication ranking indicates Greater Copenhagen's rank among the regions of comparison for the proportion of articles in the field published jointly with the business sector (percentage of overall article production in Greater Copenhagen in brackets).



## Key arguments for the research area's potential to attract investment

There is global demand for new, more efficient ways of conducting early stage diagnostics of diseases.

In these years, the global pharmaceutical industry is challenged by rapid advances within personalised therapies, designed and adapted to the biological characteristics of the individual (personalised medicine). This applies for example to treatment of HIV, cancer, blood disease and neurodegenerative conditions (which basically are caused by changes in proteins). Understanding proteins, peptides (chains of amino acids), glycomics (sugars) and gene stability are absolutely critical preconditions for developing such new diagnostics and treatments.

System biology research at the University of Copenhagen and DTU carries an enormous potential in this field. It has two aims: First, to understand how protein, peptide and glycome interacts with other biological factors in the body. Secondly how nanotechnology can be used to design new proteins. However, research is still relatively fundamental so in many instances returns on investment have very long timescales.

In the short-term, bioinformatics combined with Denmark's consistent register-based health data hold considerable potential with respect to investigating the link between biological characteristics and the effect of different therapies. The research aims to achieve better, more accurate segmentation of patient groups and to optimise drugs that are still at the preclinical stage of development.

### Star researchers and major scientific breakthroughs

Protein research and bioinformatics in Greater Copenhagen have led to a number of breakthroughs. The Center for Glycomics under Prof. Henrik Clausen of the Department of Cellular and Molecular Medicine at the University of Copenhagen has developed a technique in which sugar struc-

tures attach to proteins. These structures stabilise proteins and can determine how long they persist in the human body. CHO cells from hamsters are used to produce human-compatible sugar structures that have been modified using advance genetic editing technologies. The technique can also be used to develop novel, more effective drugs for patients with cancer and other diseases.

The Center for Protein Research has several very promising teams headed by elite researchers, such as Prof. Jiri Lukas, who directs a programme focusing on protein signalling between cells, associated for example with DNA damage, and how these mechanisms can be disrupted. Similarly, Prof. Mathias Mann works with protein-based biomarkers for diabetes and other lifestyle diseases that are an important factor in developing personalised treatments.

Prof. Søren Brunak from the Center for Protein Research and DTU Bioinformatics is one of Denmark's leading protein researchers, working with bioinformatics and register data as the basis for developing more personalised medicine. His research focuses on how different kinds of medicine interact, especially in patients with complex conditions that require them to take many different types of medication.

At the Department of Cellular and Molecular Medicine, University of Copenhagen, Prof. Ian Hickson works on chromosomal instability, which leads to premature ageing in cells in the form of proteins that cannot be regenerated. This is significant for the development of cancer cells, joint disease and neurodegenerative conditions as well as numerous other health issues. He has also received an Advanced Grant from the European Research Council for his research (which indicates excellence at a very high level). Prof. Ian Hickson heads the Center for Chromosome Stability at the Basic Research Center.

Finally, Prof. Niels Tommerup works on designing new proteins for the development of new drugs, primarily focusing on diabetes and obesity. This

area could form the basis for new drugs in future

### **Large talent pool**

Greater Copenhagen is one of the strongest life science regions in Europe, which is also reflected in the pool of talent related to protein research and bioinformatics. The Faculty of Science at the University of Copenhagen offers a Master's programme in bioinformatics in which around 12 students graduate every year. Biochemistry educate 58 graduates annually and Biology/Biotechnology has 57 graduates annually together with 44 in Molecular Biomedicine.

The Faculty of Health and Medical Sciences runs Master's programmes in pharmaceutical chemistry and pharmaceutical science. DTU offers Master's programmes in biotechnology, pharmaceutical technology, system biology, medicine and technology. CBS runs a Master's programme in bio-entrepreneurship, with 13 students completing the course every year. All in all, about 375 Masters students complete their training in this field every year.

In 2015, the Center for Protein Research had 34 postdocs, with 28 at the Department of Cellular and Molecular Medicine. Around 18 PhDs enrol at the Department of Cellular and Molecular Medicine annually, with about 10 at the Center for Protein Research. Every year, between 450-500 PhDs enrol at the Faculty of Health at the University of Copenhagen.

### **Unique research facilities**

High level bioinformatics demands enormous computer power. DTU, the University of Copenhagen and DeiC have jointly invested DKK 40m in a new supercomputer. The computer will among other things be used for processing enormous volumes of patient data, such as DNA data, patient records, etc., in order to identify new patterns between disease, patients and factors such as genetics and lifestyle.

It is expected that in time, analytical results will make it possible to design drugs more cheaply and efficiently, and to target individual patients more effectively. Søren Brunak's research group is among the main users of the computer.

The research environments engaged in protein research all employ state-of-the-art mass spectroscopic equipment (e.g. Nuclear Magnetic Resonance), that can perform advanced structural analyses of proteins. The Center for Protein Research uses microscopic imaging for proteins. At the national level, the Research and Innovation Agency decided to provide DKK 40m in funding to support the establishment of the national PRO-MS Platform, the Danish National Mass Spectrometry Platform for Functional Proteomics.

Finally, we also expect great opportunities from using the super microscopes at ESS and MAX IV in Lund for protein research. This applies for example to studying enzymatic reaction mechanisms, the design of therapeutic proteins and research into new biomembranes.

### **Strong collaboration with leading international research environments**

In Greater Copenhagen, protein research is characterized by close relations with leading international scientific environments. Among other things, Hans Wandall highlight a number of close relations with leading foreign research environments such as Harvard Medical, University of California, University of Pennsylvania and University College London. The Center for Protein Research also works with the German elite research environment at the Max Planck Institute of Biochemistry, where Prof. Mathias Mann also works.

### **Extensive corporate collaborations**

Protein research is carried out in close interaction with the Danish life science sector, including Novozymes, Chr. Hansen and Novo Nordisk. There are also collaborations with international players such as Novartis and Roche. The Novo Nordisk Foundation provided funding for the Center for Protein Research and research on glycomics.

A total of eight licensing agreements were made with companies in this field in 2013-15. The Department of Cellular and Molecular Medicine and the Department of Biomedicine at the University have been responsible for four licensing agreements. Four spin-out companies were also incorporated during the same period (see examples in the box).

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FIDA-tech is a spin-out from the University of Copenhagen that employs innovative technology to analyse and characterise proteins, especially with a focus on diagnosing and monitoring autoimmune disease. The methods are characterised by being significantly faster than existing methods. They only require small samples and are easy to automate. The technology cuts the time needed to test samples by more than 75% and it is more accurate and flexible than existing methods.

Avilex Pharma is a spin-out from the University of Copenhagen that focuses on treatment for hemorrhagic strokes. This is one of the most frequent causes of death and is caused by a lack of blood flow to the brain. The company is developing new drugs using newly developed protein structures that 'dock' with the brains receptors and alleviate pain and protect against the cell death associated with stroke. Novo Seeds, Novo Nordisk Foundation and Copenhagen Spin-outs have invested in the company.