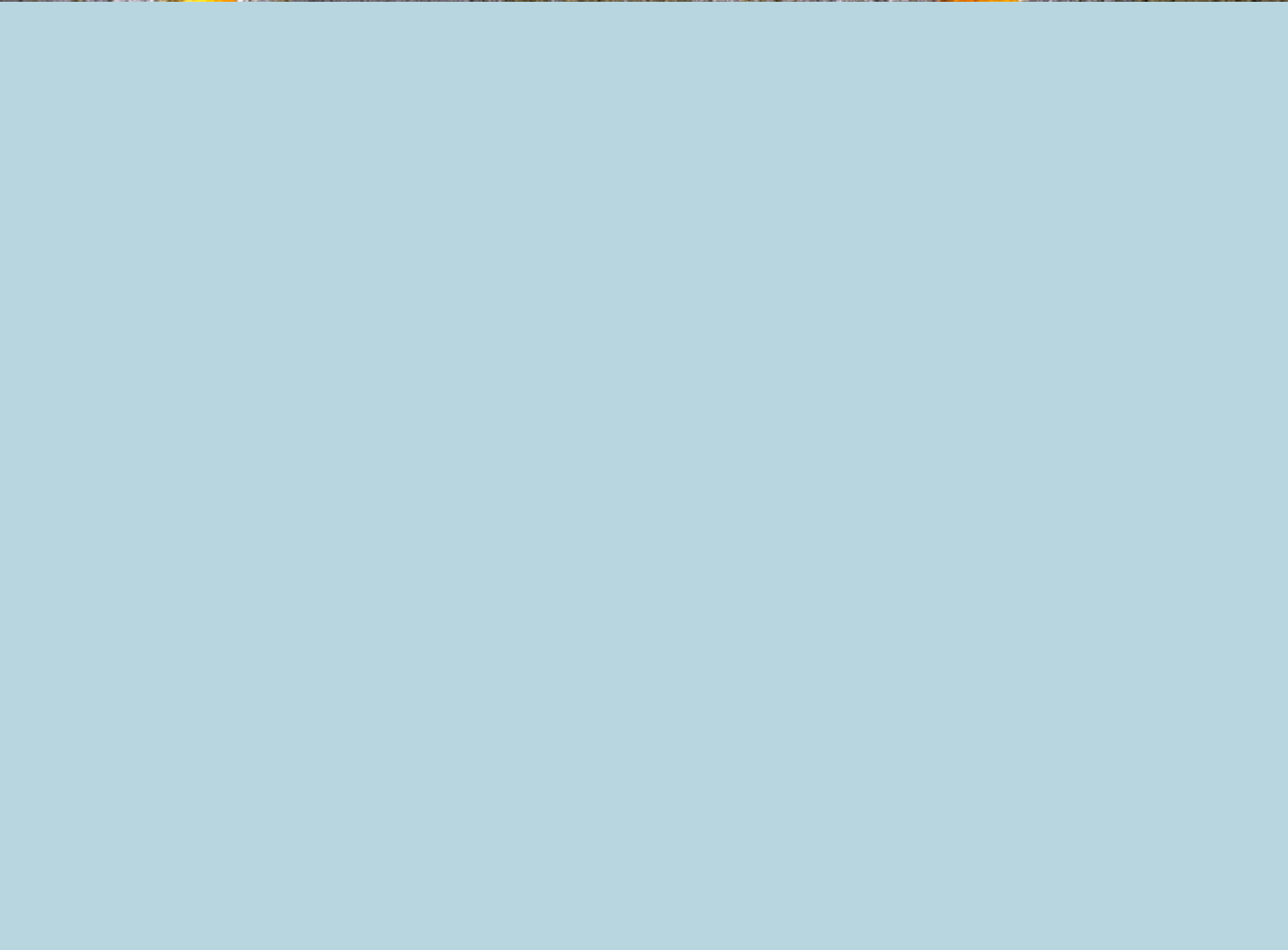




# 2021 ISBUC Letter to the Deans





# Message from the ISBUC Steering Committee

The hardships of the last two years have had a huge impact on the scientific community. Conferences have been cancelled. Opportunities for scientific sparring have been lost. Restrictions on travelling and networking have hit junior researchers particularly hard. Against this background, organisations such as ISBUC have never been so vital.

We are pleased to report that ISBUC has blossomed during the pandemic. Indeed, the willingness of researchers to engage in scientific exchange and networking online opens new possibilities for facilitating interactions between departments, campuses and faculties. Adapting to this new normal, in 2021 ISBUC launched a highly successful online Lunch Talk series as well as a mentoring program for younger researchers and an e-newsletter.

We were lucky enough to schedule the 2021 ISBUC Annual Meeting in a break between corona lock-downs. It

was with much happiness that over 130 staff and students came to the event, as well as a number of researchers from surrounding universities and industry. The meeting featured four international speakers, a panel debate on the future of structural biology as well as presentations and posters from junior researchers.

One of the most exciting pieces of news from 2021 is the development of a new MSc Course on Integrative Structural Biology. ISBUC has been deeply involved in shaping the course and an application to NNF which has secured 2 million kroner to support the course's development and running costs for three years.

In 2021, ISBUC has hired a new cluster coordinator, Lucy Holt, who has done an excellent job of forging new connections between ISBUC researchers and we look forward to working with her for years to come.

We are pleased to report that departments across both faculties continue to invest in structural

biology with a steady-stream of exciting new hires happening across the board. In particular, we see an increasing interest in cryo-EM with three new Associate Professors hired in the last two years. This builds off the huge success of the Core Facility for Integrated Microscopy (CFIM), a centre which ISBUC supports.

Most importantly, we are starting to see an increasing number of interactions amongst ISBUC researchers, resulting in technological break-throughs, high-impact publications and new research grants. A number of these have been initiated by meetings at ISBUC events and all are supported by ISBUC.

All of this, of course, builds upon a foundation of extremely talented boundary-pushing scientists. 2021 was a year which saw UCPH researchers achieve an extraordinary number of research breakthroughs in structural biology. You will find details about all of this, and more, in the coming pages.

Best regards,

Guillermo Montoya  
ISBUC Chairman  
Faculty of Health & Medical Sciences



Bithe B. Kragelund  
ISBUC Co-Chair  
Faculty of Science



Nikos Hatzakis  
SCIENCE



Michael Gajhede  
SUND



Claus Lolland  
SUND



Karen Martinez  
SCIENCE



Søren S.R. Bohr  
SCIENCE



# Meet the rising young stars of ISBUC



The ISBUC community continues to grow. In the last six months alone, 10 new Group Leaders have joined our network. This includes a number of established UCPH researchers who have joined ISBUC after attending one of the many ISBUC events. It also includes a spate of

exciting new hires within structural biology at UCPH. With so many new faces, we would like to take this opportunity to introduce you to some of the young research leaders of ISBUC.



**Henriette Autzen**  
*Associate Professor*  
*BIO, SCIENCE*

**Research achievements:** Henriette determined the first single particle cryo-EM structures of the human TRPM4 ion channel. She has developed new amphiphilic copolymers for isolating membrane proteins in native lipid bilayers.

**Track record:** Henriette has been published in *Science* (2018) and *Chem* (2020). She is the recipient of a DFF Inge Lehmann grant, a Carlsberg Infrastructure grant and a NNF Hallas Møller Emerging Investigator grant.



**Wouter Boomsma**  
*Associate Professor*  
*DIKU, SCIENCE*

**Research achievements:** Wouter develops machine learning models for sequence-structure relationships in proteins, which can be used downstream in protein engineering.

**Track record:** Wouter's research has been published in *Adv Neural Inf Process Syst* (2017) and (2018). He is the co-recipient of a NNF Synergy grant, a Villum Synergy grant and a co-founder of the NNF Collaborative Center for Basic Machine Learning in Life Science.



**Celine Galvagnion-Büll**  
*Associate Professor*  
*ILF, SUND*

**Research achievements:** Celine found a correlation between changes in the lipid profile of human fibroblasts and a higher aggregation propensity of the protein involved in Parkinson's Disease.

**Track record:** Celine has been published in *Brain* (in press) and *Nat Chem Biol* (2015). She has been awarded a NNF Hallas Møller Emerging Investigator grant and a Carlsberg Young Researcher fellowship.



**Martin Gustavsson**  
*Assistant Professor*  
*BMI, SUND*

**Research achievements:** Martin has successfully characterized the structure and function of atypical chemokine receptor 3, a seven-transmembrane protein with unique signaling profile and potential as a drug target in cancer and other diseases.

**Track record:** Martin's research has been published in *Nat Commun.* (2017). He is the recipient of a Villum Young Investigator Grant and a Carlsberg Infrastructure grant.



**Eva Kummer**  
*Associate Professor*  
*CPR, SUND*

**Research achievements:** Eva applies cryo-EM to conduct mechanistic studies of genome maintenance in mitochondria and has produced the first reconstituted mitochondrial translation complex.

**Track record:** Eva's research has been published in *Nature* (2018), *EMBO* (2020), *Mol Cell* (2021), and *Nat Rev MCB* (2021). She is the recipient of a NNF Hallas Møller Emerging Investigator grant.



**Tom Miller**  
*Associate Professor*  
*ICMM, SUND*

**Research achievements:** Tom studies the mechanisms of eukaryotic chromosome replication. Using time-resolved cryo-EM and a new 'Reconstitution in silico' approach, he has revealed how the replicative MCM helicase is loaded to 'license' DNA for replication.

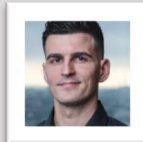
**Track record:** Tom's research has been published in *Nature* (2019) and *COSB* (2022). He was recently awarded a Carlsberg Infrastructure grant.



**Joseph Rogers**  
*Associate Professor*  
*ILF, SUND*

**Research achievements:** Joseph's research has led to the discovery and biophysical characterisation of de novo cyclic peptides, a plentiful source of new drugs and chemical tools.

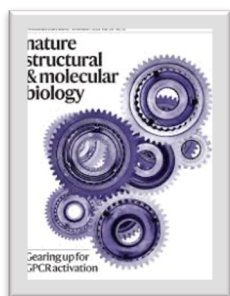
**Track record:** Joseph has been published in *Nat Chem* (2019) and *PNAS* (2018). He is the recipient of a NNF Hallas Møller Emerging Investigator grant.



**Nicholas Taylor**  
*Associate Professor*  
*CPR, SUND*

**Research achievements:** Nicholas has used cryo-EM to produce structures of the stator units that power the bacterial flagellar motor, a human multidrug transporter and the baseplate of a contractile tail bacteriophage.

**Track record:** Nicholas' research has been published in *Cell* (2020), *Nature* (2017) and *Nature* (2016). Nicholas is the recipient of a NNF Hallas Møller Emerging Investigator award and is an EMBO Young Investigator.



## Researchers from David Gloriam's group are honoured with the cover of Nature Structural & Molecular Biology.

ISBUC is proud to announce the publication of two back-to-back articles in Nature Structural & Molecular Biology by talented assistant professors, bioinformatician Albert Kooistra and data scientist Alexander Hauser from the group of David Gloriam at the Department of Drug Design and Pharmacology (SUND). The [first article](#) presents a new online platform for GPCR structure analysis, which is used in the [second article](#) to uncover molecular mechanistic maps of activation of all major classes of human GPCRs.

## Structural analysis of GIP receptor paves way for improved treatments of metabolic diseases

A collaboration led by Mette Rosenkilde (BMI) has predicted for the first time how the GIP receptor works at the molecular level and how it can be regulated. First, researchers 'built' the receptor using a computer programme and the structure of the similar GLP-1R and used the model to simulate interactions. They confirmed their findings by looking at a human cell expressing the GIP receptor and

studying some of the same mechanisms in a petri dish. This involved a cross-disciplinary collaboration with two research groups at CBMR, including ISBUC scientist Thomas Frimurer. The researchers hope the new findings will lead to new and improved obesity and diabetes drugs targeted at both GIP and GLP-1 receptors. This research was published in Structure ([2021](#)).

## Mapping the structure of CRISPR-Cas12j advances the gene editing toolbox

CRISPR-Cas9 has revolutionised biotechnology and the medical sciences. But now researchers may have discovered a new and better genome editing technology. The similar but much smaller CRISPR-Cas12j system was recently found within the archenemy of bacteria – bacteriophages. These tiny viruses can infect and kill bacteria while not being harmful to plants, animals or humans. The CRISPR-Cas12j system

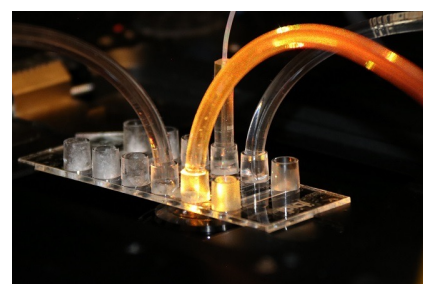
forms part of their defence system and holds vast potential as a gene editing tool. In 2021, a research team led by Guillermo Montoya (CPR, ISBUC Chair) succeeded in mapping the structure of CRISPR-Cas12j3. This is the first step in producing a proper understanding of the CRISPR-Cas12j system and will pave the way for its development as a gene editing tool. This research was published in Nature Communications ([2021](#)).

## Metal ion-induced self-assembly of proteins produces new, dynamic nano-assemblies

A collaboration between ISBUC researchers Knud Jensen (CHEM), Peter Thulstrup (CHEM), Leila Lo Leggio (CHEM), Lisa Arleth (NBI) and others, has demonstrated the possibility of using metal ions to control the self-assembly of higher-order protein structures. The study used the metal ion Fe<sup>2+</sup> and Eu<sup>3+</sup> to synthesize a new terpyridine

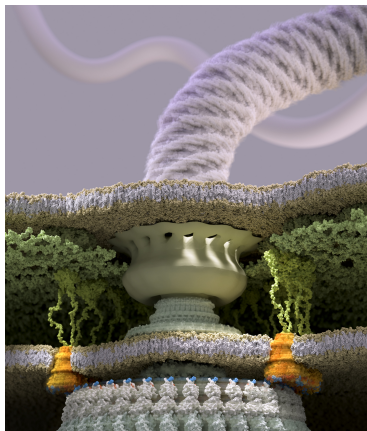
modified insulin and controlled the fractal dimensionality of its self-assembly by manipulating Eu<sup>3+</sup> concentration. This points towards using in vivo control of nano-assemblies as a new strategy to control the pharmacokinetics of peptide and protein pharmaceutical drugs. This research was published in Nanoscale ([2021](#)).

## ISBUC collaboration results in new AI tool to study protein dynamics



A collaboration between Nikos Hatzakis (CHEM, ISBUC Steering Committee), Guillermo Montoya (CPR, ISBUC Chair) and Christian Troels Petersen (NBI) has produced a first-of-its-kind open-access software for analysing images produced by single molecule Förster Resonance Energy Transfer (smFRET). smFRET uses fluorescence tags to track the movements of proteins. The downside is that it produces a very large amount of data which takes a long time to sort through. To overcome this, the researchers used a deep neural network approach to build a model that can do this work automatically. The model works by importing raw images from the microscope, locating the fluorescence tags and producing a map of the molecule's movements. The user friendly software is free and can be downloaded for any major operating systems. Not only that, but it has also proven itself to be more accurate and faster than human analysts. This research was made possible by a collaboration between Guillermo Montoya and Nikos Hatzakis who began collaborating with each other after meeting through the ISBUC network. The research was published in the journal eLife ([2020](#)).

## Cryo-electron microscopy reveals the architecture of the bacterial flagella motor



The ability to move is key for bacteria like some strains of salmonella and *E. coli* to efficiently spread infections. They can propel themselves forward using threads, known as flagella, powered by the flagellar rotary motor. In 2020, a study led by Nicholas Taylor from CPR has demonstrated how this rotary motor is powered. His research showed that the bacterial flagellar motor is powered by yet another even tinier, rotary motor. This research was published in *Cell* ([2020](#)).

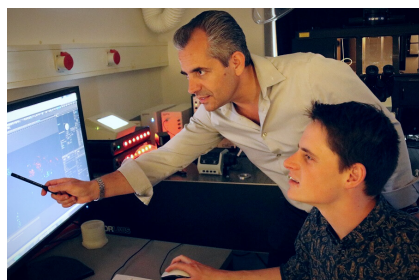
## Industry collaboration results in a new AI tool for predicting protein structure

An industrial collaboration between Thomas Hamelryk's group (DIKU) and the immuno-therapy company Evaxion has produced a new computer model called BIFROST which can efficiently generate possible protein structures for a given protein fragment. The hope is that this will enable the design of "chimera proteins" that can be used in vaccines to elicit the desired

immune system response to viruses while being sensitive to multiple variants. BIFROST is much faster than conventional methods because it only requires a single protein sequence as input. The research was funded by Evaxion and Innovation Fund Denmark and was presented at the International Conference on Machine Learning and published in *PMLR* ([2021](#)).

## ISBUC collaboration uses AI to fingerprint the movements of malfunctional proteins

ISBUC researchers Nikos Hatzakis (CHEM, ISBUC Steering Committee) and Wouter Boomsma (DIKU) have developed a new method for identifying whether a protein is possibly endangering a cell's survival. Their method was developed by feeding a machine learning algorithm microscopic images of a protein's movements, which were then classified automatically. This produces a precise fingerprint of the protein's movement patterns, including its speed, 'gait', directionality, etc. Once trained, the algorithm can compare the characteristics of different proteins and is able to predict their behaviour with more



than 90% accuracy. Thus far, the model has been successfully tested on three biological systems: proteins used for green chemistry in washing detergent, proteins involved in cell division and cancer, as well as nanoparticles used to deliver medication. Wouter and Nikos met at an ISBUC PI Day and this work was published in *PNAS* ([2021](#)).

## Capturing the spaghetti-like structure of the human growth hormone receptor

The human growth hormone affects the growth of muscles and bones, metabolic function and especially the immune system. Possessing a well-ordered exterior that belies the extensive structural chaos found within, the receptor of this hormone has long frustrated characterisation by scientists. But now, a collaboration led by Birthe B. Kragelund (BIO, ISBUC Co-Chair) has produced the first structural image of what the receptor actually looks like, not just on the outside but also on the inside. A true example of integrative structural biology, this structure was produced through a collaboration of 7 research groups, including 3 from ISBUC. The work required the integration of structural data from mass spectrometry, protein chemistry, biophysics, X-ray crystallography, molecular dynamics and modelling, NMR spectroscopy and neutron and small-angle X-ray scattering. The results may eventually help in developing new strategies to treat insufficient growth in height and hormone deficiencies. This research was published in *Science Advances* ([2021](#)).

## ISBUC IN PRINT

214

Publications by ISBUC researchers in 2021

Publications by 2+ ISBUC researchers in 2021

40

7

Publications by 3+ ISBUC researchers in 2021

## ISBUC helps secure NNF grant for new interdisciplinary MSc course in Integrative Structural Biology

ISBUC has helped secure a 2 million kroner grant from the Novo Nordisk Foundation to develop a new interdisciplinary MSc Course in Integrative Structural Biology. The course will be led by Kresten Lindorff-Larsen (BIO).

### Advanced and experimental

The new course will introduce students to the many advanced techniques researchers use to capture biological structure including various X-ray and neutron techniques, electron microscopy, nuclear magnetic resonance spectroscopy, among others. Building on this, the course will teach students to integrate data obtained from these various techniques using state-of-the-art computational modelling and machine learning methods. The course will include visits to large-scale infrastructure facilities in the region, such as ESS and MAX-IV, as well as the state-of-the-art research

infrastructure at UCPH including CFIM, cOpenNMR and CPHSAXS. It will provide students with extensive hands-on experience in both wetlab and computational experiments.

### Integrative & interdisciplinary

The new course will be highly interdisciplinary and involve 12 ISBUC researchers from 5 departments in both SUND and SCIENCE. These include Henriette Autzen (BIO), Poul Martin Bendix (NBI), Wouter Boomsma (DIKU), Heloisa N. Bordallo (NBI), Nikos Hatzakis (CHEM), Kristoffer E. Johansson (BIO), Birthe B. Kragelund (BIO), Kresten Lindorff-Larsen (BIO), Annette E. Langkilde (ILF), Leila Lo Leggio (CHEM), Karen Martinez (CHEM) & Kasper Rand (ILF).

### A networking opportunity

Students and lecturers involved in the course will join a network with students participating in NNF funded courses at DTU, SDU and AU. The course will enable both MSc and PhD

students to meet researchers from across ISBUC and visit their labs, creating new opportunities for interdisciplinary exchange at UCPH.

## BY THE NUMBERS

127

PhD students employed in ISBUC labs in 2021

PhD students graduated from ISBUC labs in 2021

25

119

MSc students supervised by ISBUC researchers

Figures are taken from a survey of 47 ISBUC researchers

## Engaging students with research integrating teaching

In 2021, Birthe B. Kragelund (BIO, ISBUC Co-Chair) launched a new Masters course, which challenges teaching norms every step of the way to create a highly creative and enriching learning environment for students. The course will run again in [2022 and 2023](#).

### Experiments instead of lectures

Besides one introductory lecture, all teaching in the new course is lab-based. Students are formed into small groups and tasked with performing an independent study on an intrinsically-disordered protein (IDP). Each IDP has been pre-selected by an academic or industry partner as being of potential interest and has never been studied by biophysics before. These partners then become mentors for the students while they complete their

experiments.

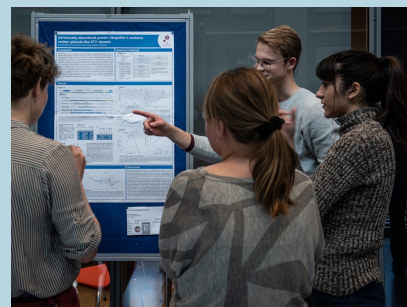
### Students as researchers

Provided only with an agar plate and a colony of bacteria to produce the protein, students are given 80 hours to develop a purification protocol, purify the protein, post a hypothesis, and test this hypothesis using advanced biophysical methods. There are no protocols, no premade buffers, and no pre-tested – or pre-expected -results. The students need to decide, design, and produce everything themselves.

### Posters instead of exams

This innovative format produces real results. In 2021, students made new discoveries about the IDPs they were studying. Results were written up as posters and presented to the academic and industry partners, in lieu of an exam, giving students their

first real taste of life as a researcher.



**Course Title:** Protein Research Lab - Intrinsically Disordered Proteins

**Course Responsible:** Birthe B. Kragelund

**Students:** 17 MSc students

**Partners:** The NNF Research Center Repin (BIO), Galecto Inc, VAR2 Pharmaceuticals and Leo Pharma A/S.

**Funded by:** UCPH research integration, Danish Foundation for Entrepreneurship and Novo Nordisk Foundation

# Innovation and collaboration

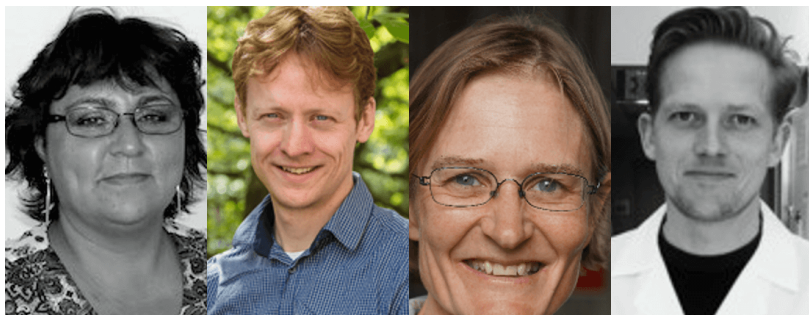
## Kristian Strømgaard awarded KU Innovation Prize and NNF Distinguished Innovator grant

In 2021, Kristian Strømgaard was awarded the prestigious KU Innovation Prize, in recognition of the incredible achievements of his spin-out company Avilex Pharma. Avilex Pharma develops potentially game-changing treatments for acute neurological conditions. After completing successful Stage 1 clinical trial this year, Avilex announced a strategic partnership with Simcere to develop and commercialize its lead compound in greater China in a deal worth DKK1.15 billion.



In 2021, Kristian was also awarded a NNF Distinguished Innovator grant, worth DKK 6 million. This will fund the investigation of a potential drug discovery platform for the treatment of brain diseases by developing compounds that can modulate postsynaptic density.

## Interdisciplinary collaboration receives NNF grant to study mechanical GPCR activation



A new collaboration between Karen Martinez (CHEM, ISBUC Steering Committee), Poul Martin Bendix (NBI), Mette Rosenkilde (BMI) and Christoffer Knak Goth (BMI) is exploring the role of post-translational modifications in the mechanical activation of GPCRs. First, Mette and Christoffer will apply a variety of state-of-the-art techniques to control the post-translational

modifications possessed by GPCRs in their samples. Then, Karen and Poul Martin will apply various forms of pressure and stress to these cells in the hopes of triggering mechanical activation. In Karen's lab, this will involve the development of new nano-devices capable of shrinking and stretching cells. The project was awarded an NNF Exploratory Interdisciplinary Synergy Grant.

## Villum Synergy grant to develop predictive model of protein function and structure

An ambitious new research project between Nikos Hatzakis (CHEM, ISBUC Steering Committee) and Wouter Boomsma (DIKU) aims to develop a machine learning model incorporating protein structure, dynamics and function. Their aim is to build a model with enough specificity to enable useful application in protein engineering. The project builds upon a research collaboration which was initiated at an ISBUC event and has already resulted in a PNAS article (2021). Hatzakis and Boomsma will combine data on lipase structure with smFRET experiments describing lipase function and dynamics in an iterative deep-generative model. This research is funded by a Villum Synergy grant.

### BY THE NUMBERS

27

Industrial PhDs and postdocs in ISBUC labs

Spin-out companies founded by ISBUC researchers

8

Figures are taken from a survey of 47 ISBUC researchers

## New spin-out Dolorestbio aims to develop new drugs to treat chronic pain

In January 2021, a group of researchers from UCPH including ISBUC scientist Kenneth L. Madsen launched new spin-out Dolorestbio. The company aims to treat chronic pain caused by an excess of glutamate receptors in the dorsal horn synapse by selectively targeting the scaffold protein PICK1, which is

responsible for the insertion of these receptors. Their treatment involves the development of a synthetic bivalent peptide that inhibits PICK1 with high specificity and selectivity and has been shown to be highly efficacious in mice (EMBO Mol Med, 2020) and without abuse liability (Frontiers in Cell. Neurosci. 2021).

The research builds off twenty years of collaborative research at UCPH, including partnerships with ISBUC researcher Kristian Strømgaard (ILF) who pioneered the use of bivalent peptides and ISBUC researcher Lise Arleth (NBI) who determined the structure of the PICK1 protein using small-angle X-ray scattering.

# ISBUC activities

## ISBUC under Covid-19: Lunch Talks, a mentoring program and an e-newsletter takes off

Despite the pandemic, ISBUC has blossomed during the last two years.

### ISBUC Lunch Talks

Confined to the home-office, many researchers missed the kind of scientific sparring that arises over lunch or a cup of coffee. To combat this, in 2021 ISBUC launched a new online seminar series, the ISBUC Lunch Talks. Hosted by Professor Claus Lolland (ISBUC Steering Committee, IN), the ISBUC Lunch Talks provide a forum for ISBUC scientists to present and get feedback on ongoing research. With around 40 researchers logging on each month, the ISBUC Lunch Talks have proved so successful that the plan is to make them a permanent feature of the ISBUC community.

### Inside ISBUC e-Newsletter

In 2021, ISBUC launched an internal e-newsletter dedicated to sharing the latest news, research and events relevant to structural biology at UCPH.



### Junior ISBUC mentoring program

The pandemic has been tough on junior researchers who have missed many of the usual opportunities to build their networks both within and outside of academia. To compensate for this, in 2021 the Junior ISBUC Steering Committee launched a mentoring programme for PhD students, Postdocs and Assistant Professors. During the program, 17 mentees were paired with a senior industrial or academic researcher, depending on their future career goals. Feedback on the mentorship program has been hugely positive.

## ISBUC on ISBUC

In 2021, Lucy met with over 20 ISBUC scientists. Here she shares some of the positive feedback she received about ISBUC:

*“I heard about cryo-EM at an ISBUC talk. I used the ISBUC website to find out who to contact. Now I am doing my own cryo-EM studies at CFIM”*

*“It is a nesting bed of ideas”*

*“You have all these events now and then. You start spending time with people and they start asking questions and it evolves into collaborations”*

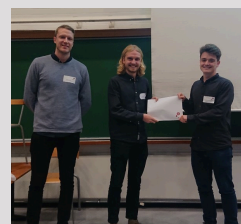
*“It raises the bar and pushes us to do research at the highest level”*

## The 2021 ISBUC Annual Meeting

On October 29th, 2021, ISBUC held its fourth annual meeting. Held during a break between corona-restrictions, the meeting was one of the few large scientific meetings held physically at UCPH last year. So it was with much happiness that over 130 junior and senior researchers turned up. The program included international research leaders Robert Tampé (Goethe University), Sebastian Westenhoff (University of Gothenburg), Lynn Kamerlin (Uppsala University) and Ed Tate (Imperial College). It also included an inspiring panel discussion on the future of structural biology. Importantly, the day provided a rare opportunity for junior researchers to present their research and network with peers outside of their departments during the pandemic.

### Junior ISBUC Poster & Talk Prize

Each year, Junior ISBUC organises a poster and flash talk prize that forms an integral part of the ISBUC Annual Meeting. This year, big congratulations go to Jacob Kæstel-Hansen (CHEM) and Frederik Emil Thomasen (BIO) who won the Best Flash Talk and Best Poster awards.



## Introducing Lucy Holt: ISBUC's new cluster coordinator



In September 2021, Lucy Holt joined the ISBUC community as our new cluster coordinator. Lucy has a PhD in Philosophy of Biology and over ten years experience in science communications, funding and commercial consultancy. Drawing on her past experience, Lucy will focus on building up ISBUC's internal communications, a vital first step towards facilitating interdisciplinary collaborations. She will also focus on securing external funding to bolster the ISBUC community and make new types of interactions possible. Already, Lucy has been instrumental in securing the NNF grant for the MSc Course in Integrative Structural Biology as well as a smaller grant for Junior ISBUC.