Centre for Molecular Biology and Neuroscience (CMBN)

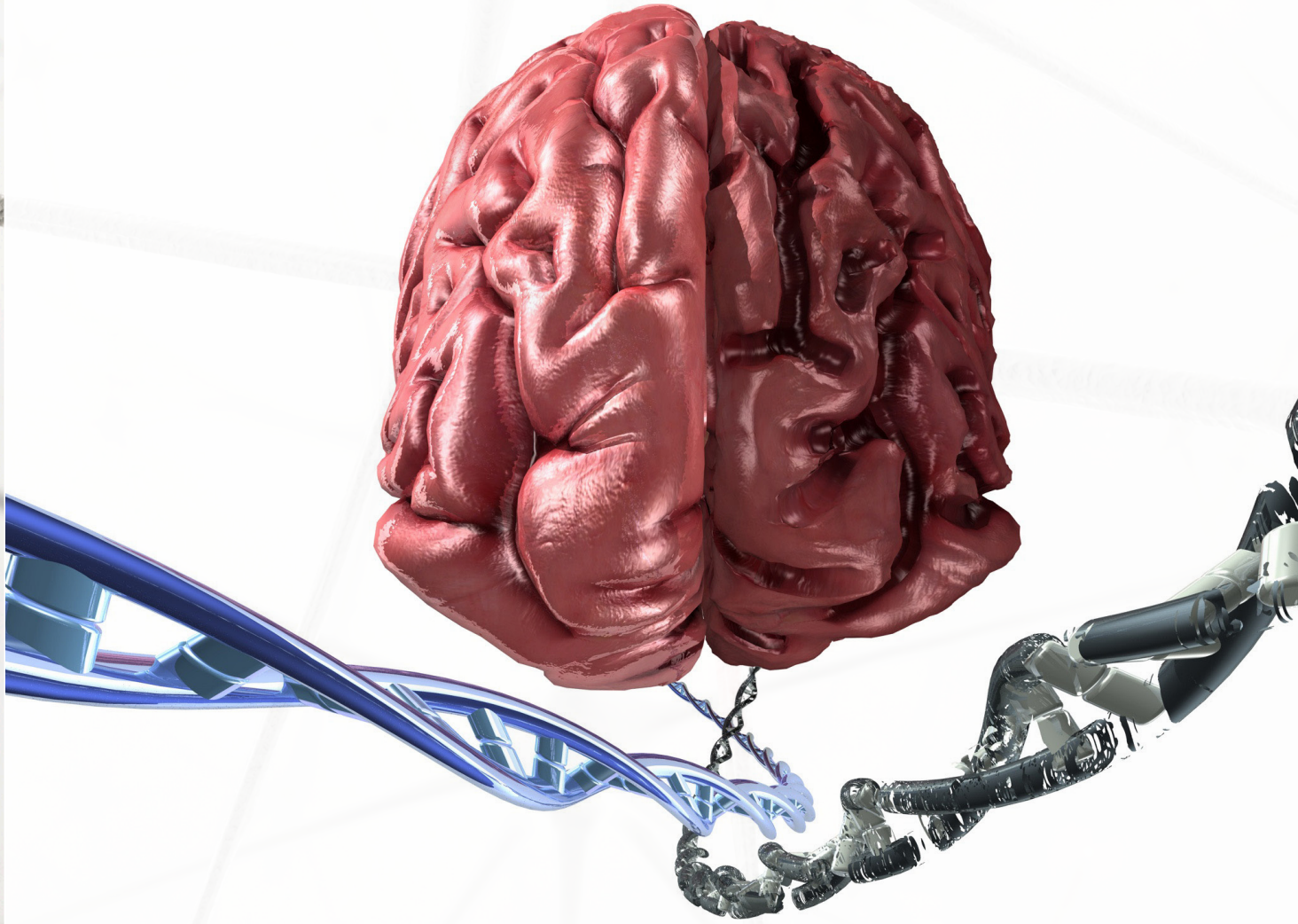
annual report

2011

CENTRE FOR
MOLECULAR BIOLOGY
AND NEUROSCIENCE

Vision

"The Centre shall take on a leading role in elucidating the impact of DNA repair and genome maintenance mechanisms in preventing neurological disease and brain ageing"



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The Directors' view of 2011

Tone Tønjum

Jon Storm-Mathisen

by Professor Tone Tønjum
Director of the Centre and
Professor Jon Storm-Mathisen
Co-Director

Towards innovation

This era of *abundant scientific discoveries* and rapid technological development is prime-time for "innovation", i.e. providing useful spinoffs of basic research. The Centre for Molecular Biology and Neuroscience (CMBN) aims to be recognized as a most innovative research environment in identifying, developing and promoting new tools in the diagnostics and treatment of brain diseases and age-related neurological challenges. Thus, CMBN in its basic nature is a supreme platform for innovation and even commercialization. For CMBN, the year 2011 has been filled by ample new scientific findings - and innovation.

Looking back, 2011 was the year when two anniversaries with great significance for CMBN coincided. Firstly, it has been a magnificent celebration of *the 200 years anniversary for Norway's first university* (the University of Oslo). Secondly, it was 150 years since the birth of Fridtjof Nansen, the neuroscientist, explorer, diplomat and humanitarian. Nansen has also inspired the knowledge transfer network Nansen Neuroscience Network (NNN), linking basic and clinical research environments with relevant industrial partners. This has been a good year for NNN, facilitated by elaboration of communication and website activities on www.nansenneuro.net, together with young NNN collaborators in Trondheim.

Another event that has fuelled the basic vision of the CMBN, is the funding of the NORBRAIN project. A collaboration between the CMBN and the Centre for the Biology of Memory (CBM)-Kavli Institute for Systems Neuroscience and the Medical Imaging Laboratory (MI-Lab) in Trondheim, the revised NORBRAIN application for large scale infrastructure was funded by the Research Council of Norway (RCN), after it in 2010 was included on the RCN "Roadmap for infrastructure". The imaging and molecular equipment built in the NORBRAIN-project will fuel scientific advances even further and enforce the strong translational research network we have built.

The most important goal for CMBN is to make excellent science outstanding, by promoting *quality in science*. Among the breakthroughs in 2011, CMBN scientists have discovered novel modifications of DNA, RNA and proteins, while the expression pattern and levels as well as location of membrane proteins such as aquaporins and their interacting partners have been characterized. Novel DNA repair components and expression patterns exclusively in young stem cells have been described, along with the regulation of glial oligodendrocyte development and myelination by glucose and lactate.

The MindGap exhibition at the Norwegian Techical Museum was opened on April 16, 2011. CMBN scientists have contributed widely to the scientific input at the exhibition, directed by stage director Robert Wilson. To mutually boost the output of the exhibition and its public profile, the Norwegian Brain Council (NBC, Hjernerådet), where CMBN is a founding member, has organized Brainy Saturday (Hjernelørdag). One Saturday a month, scientists give public lectures and PhD students have organized dissection of pig brains to demonstrate brain structure to the public "hands-on". Very successful teaching – new *brain awareness* for young and seniors alike!

Our ambition is to *inspire* the creativity, competence and productivity of our distinguished CMBN scientists and students, to secure and boost their success. At this stage of the CMBN project, a successful exit strategy is on the agenda. In this process, we are particularly grateful to our host institutions, the University of Oslo and Oslo University Hospital, for generously accommodating us. Thereby, the discoveries and knowledge of CMBN can be fully integrated in a long-term perspective, with the outcome and legacy on board.

Message from the Chief Executive Officer, Oslo University Hospital

Bjørn Erikstein

We believe that Oslo University Hospital (OUH) is an excellent arena for translational research, where bridges between basic and clinical science are most evident. Approximately 50 per cent of medical research in Norway is performed at Oslo University Hospital, in close collaboration with the University of Oslo, with extensive national and international networks. In this setting, excellence in science is the basis for advanced patient care.

The scientific vision for Oslo University Hospital is that "Frontier research for better health; Oslo University Hospital shall deliver world-class research as well as lead and strengthen research in Norway, both nationally and regionally. Clinical activity, research and education should be tightly integrated and mutually beneficial in terms of improving quality and competence."

Centre for Molecular Biology and Neuroscience (CMBN) was the first Centre of Excellence in biomedicine in Norway and the first at our institution. CMBN has also in 2011 been successful in generating peak scientific output and communicating science. Amidst the OUH hustling activity, the multidisciplinary competence and advanced infrastructure contributes to the Hospital's translational research in linking basic science and clinical medicine in everyday life. The additional funding of the NORBRAIN project in 2011 for advanced bioimaging and molecular biology equipment is yet another contribution to CMBN-derived infrastructure.

High quality research that supports our prioritised areas of commitment secures the OUH operation and our development of national and multiregional assignments. In this context, the efforts in research related to molecular medicine and brain disease are within the prime strategic areas of the hospital. It is my belief that the legacy of CMBN will contribute to frontline science at OUH beyond 2012.

Message from the Dean of Research, The Faculty of Medicine, University of Oslo

Hilde Nebb

The Centre for Molecular Biology and Neuroscience (CMBN) hosted by the University of Oslo (UoO) in cooperation with Oslo University Hospital has had a Centre of Excellence status since late 2002. Eleven groups form the backbone of the Centre. In total, nearly 200 people are involved in the research at CMBN. Based on its scientific vision and a clear strategic focus, CMBN has excelled notably in the area of DNA repair and genome maintenance mechanisms in preventing neurological disease and brain ageing. 2011 has also been a particularly active year with multiple scientific breakthroughs and a number of international meetings. The focus on advanced technology development has also been very successful, with an immediate impact on the quality of basic research. In order to upgrade their future laboratory facilities, CMBN, together with two other exceptional Norwegian research environments (the Kavli Centre/CBM and MI Lab from NTNU), received 80 mill NOK in 2011 on the NORBRAIN-project – Norwegian Brain Initiative: A Large-scale Infrastructure for 21st century Neuroscience.

The Faculty of Medicine at UiO is proud to host CMBN. Unfortunately, CMBN has only one year left of its Centre of Excellence period. A very important aspect for The Faculty of Medicine is to facilitate a good exit strategy, in close collaboration with the scientists and leadership of the centre, to continue the most valuable elements established over the years. I believe that the successful scientists who are a part of CMBN, even after the termination of CMBN, still will perform science of high international standard and build bridges between scientists both nationally and internationally. They will still be our leading figures with scientific progress, because they know how to succeed and build good science.

Message from the Managing Director of the Center for Healthy Aging

Lene Juel Rasmussen
Managing Director, Center for Healthy Aging, University of Copenhagen, Denmark

Message from the CEHA

A major goal of CMBN is to generate improved understanding about the role of DNA repair and genome maintenance mechanisms to prevent neurological disease and brain ageing. CMBN brings together world-leading scientists on state-of-the-art research for multidisciplinary neuroscience, with a high likelihood for continued success in the years ahead. The Centre has raised a number of outstanding young scientists who have the potential to put Norway on the world map also in the future. The outcome and continuation of the research emanating from CMBN is a necessity for being prepared for the future and the challenges that our society is facing up to with the increasing elderly population. For the Center for Healthy Aging (CEHA), it has been a privilege to follow CMBN in its progress over the years. I am confident that CMBN researchers will continue to provide science of highest international level and contribute to molecular research on brain aging beyond 2012.

Organisation

Board

Ole Sejersted

The Board is responsible for ensuring that CMBN develops in accordance with the current research plan and according to its statutes. The CEO and head of the CMBN board is Professor Ole M. Sejersted Members of the board: Kirsten Sandvig, Oslo University Hospital/ University of Oslo, Torgeir Bruun Wyller, Oslo University Hospital/ University of Oslo, John Torgils Vaage, Oslo University Hospital/University of Oslo, Lars Terenius, Karolinska University Hospital, Sweden. The board of CMBN will serve until the Centre of Excellence status expires in 2012.

Management

Professor Tone Tønjum is the Director of the centre with overall scientific and administrative responsibilities for the activities of the centre. In her duties, she is supported by professor Jon Storm-Mathisen as Co-Director and Ms. Kristine Aa.S. Knudsen as Administrative head and Ms. Anne Haukvik as the Administrative consultant. The eleven group leaders create the Steering group of the centre and they meet regularly to discuss important scientific, strategic and administrative issues.

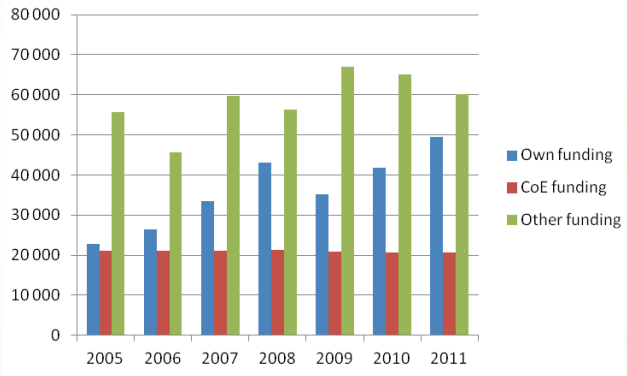
As the Centre of Excellence status is temporary, the centre draws on the competence of the existing administrative staff at its host institutions, the Faculty of Medicine at the University of Oslo and the Oslo University Hospital (Rikshospitalet). Five of the eleven groups are located at Domus Medica of the Faculty of Medicine, UiO, and five groups are located at Oslo University Hospital (Rikshospitalet). One group is located at the Faculty of Mathematics and Natural Sciences, at the Institute of Molecular Life Sciences.

Kristine Aa. S. Knudsen
CMBN Administrative Head

Anne Haukvik
CMBN Administrative consultant

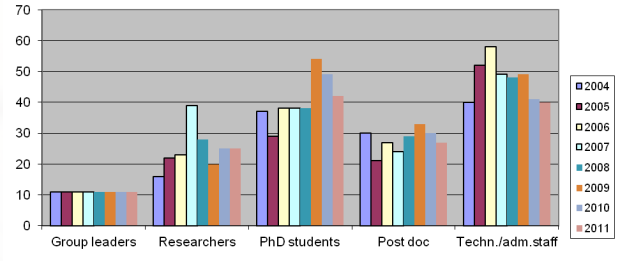
Economy

The Centre's total income was NOK 130,4 million in 2011, an increase of NOK 6 million from the year before. NOK 20,7 million is the annual Centre of Excellence (CoE) grant from the Research Council of Norway. The two host institutions, the University of Oslo and Oslo University Hospital (Rikshospitalet), contribute with salaries, office and laboratory space and running expenditures of approximately 50 million of the Centre's income while other private and public funding contributes with approximately NOK 60 million.



Personnel

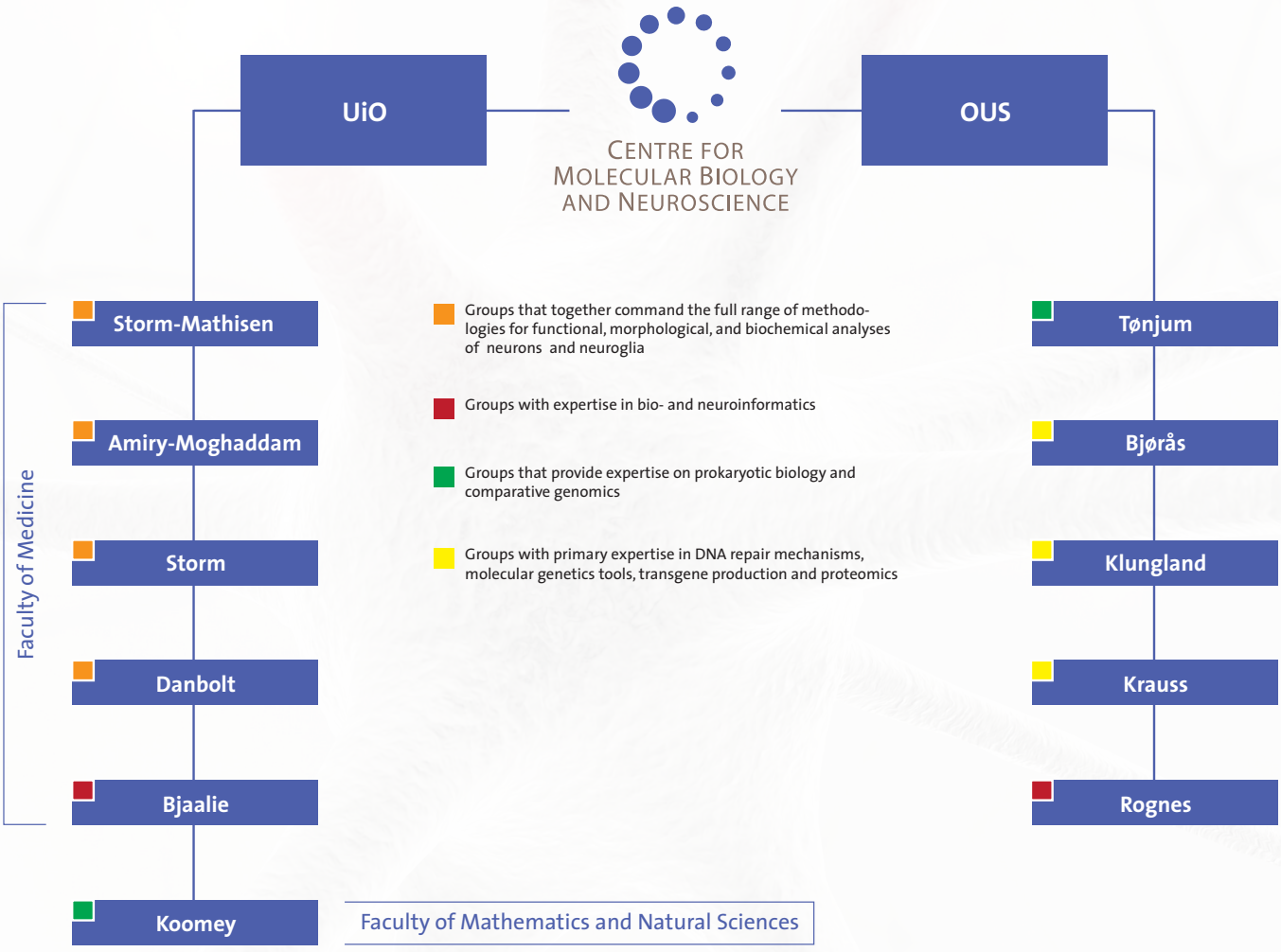
As one of the Centre's strategies is to be internationally leading within our scientific portfolio, it is of primary importance that the composition of our staff reflects this ideology. Only by conscious international networking and recruitment of staff can we secure this aim. The Centre had 25 foreign citizens from 15 different nationalities among its personnel.



Eleven groups providing the context of the Centre

The Centre consists of 11 research groups at the University of Oslo (UiO) and at the Oslo University Hospital (OUS), Rikshospitalet. The Centre activities are mainly situated in the Domus Medica and in the research building at Rikshospitalet, Gaustad. The groups headed by Krauss, Koomey and Rognes are located on other premises in the OUS and UiO within walking distance.

-- Through collaboration we can create more! --

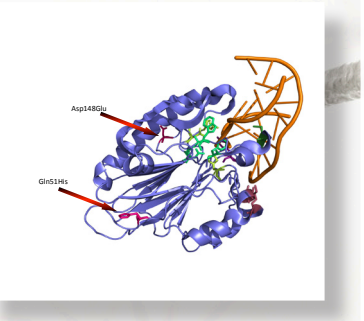


The Genome Dynamics and Pathogenesis Group

Professor
Tone Tønjum

About

Mechanisms for frequent genome variation, adaptation and maintenance are a necessity to ensure cellular fitness and survival in changing environments, for microbes and brain cells alike. Understanding pathogenesis, horizontal gene transfer, genome instability and DNA repair mechanisms requires an interdisciplinary approach of molecular biology, genomics and microbial physiology. Addressing these topics in major pathogens, model bacteria and cellular systems is most important for understanding the balance between fitness for survival and disease development. In particular, we are focusing on the identification of DNA binding components contributing to the neisserial transformation system which we suggest is directly coupled to pilus retraction. We have identified a number of novel DNA binding components and defined how they act and interact. We are also elucidating the effect of defects in DNA repair on host defence, and cellular fitness, and virulence in a new meningitis mouse model. The role of single nucleotide polymorphisms (SNPs) in DNA repair genes in brain aging and cognitive performance are addressed in healthy human cohorts as well as in well-defined patients with mild cognitive impairment (MCI) and neurodegenerative diseases.



Schematic diagram of the predicted 3D structure of the AP endonuklease ApeI, with the SNPs APE1Gln51His and APE1Glu148Asp highlighted (Mech Aging Dev 132: 449-58, 2011).

Challenges

(1) To dissect how genome dynamics affect DNA sequence variability and conservation and thereby influence cellular fitness for survival and pathogenesis.
(2) To understand the evolution of transformation and sexual reproduction.
(3) To develop new strategies for early diagnostics, prevention and treatment of disease.

Projects

- Deconstructing the meningococcal transformation machinery and search for novel vaccine candidates
- Mechanism and evolution of DNA sequence repeats and their influences on genome dynamics and genome stability
- Role of DNA repair helicases in genome maintenance and recombination
- Effects of CNS infection on water homeostasis, brain edema and inflammation
- The impact of DNA repair gene SNP profiles in normal aging and Alzheimer's disease

Recent achievements: Identification of novel DNA binding components (Microbiol 2009, 2011), antimutator role of bacterial MutY, MutS and Fpg (Nature Micro Rev 2006, BMC Microbiol 2009, FEMS Microbiol Immunol 2009), the true identity of the neisserial DNA uptake sequence (J Bacteriol 2007), discovering that transformation/sex is process with a conservative outcome that maintains genome stability (NAR 2004; Genome Biology 2008), identifying DNA repair profiles in common bacterial pathogens (FEMS Microbiology Rev 2009), genetic predisposition for disease (Neuroscience 2007, CID 2008, FEMS Microbiology Rev 2009). Deconstruction of the neisserial DNA Uptake Sequence (International Pathogenic Neisseria Conference IPNC 2010). The genome-wide effects of transformation, mutation and phase variation in Neisseria meningitidis, cellular response to meningococcal meningitis, and the immunoprotective potential of the PilQ complex (IPNC 2010). Defining the gene expression profile of the adaA/alkA operon of Mycobacterium tuberculosis (Mtb) (DNA Repair 2011) and characterisation of Mtb RecG (Keystone 2011). Novel biomarkers for cognitive performance (Mech Aging Dev 2011).

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Synaptic Neurochemistry Laboratory

About

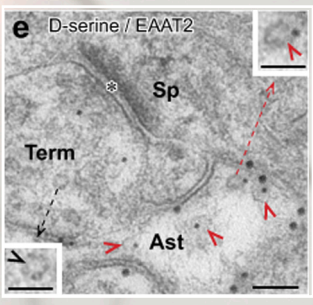
The group's main interests are the mechanisms underlying synaptic transmission and gliotransmission, and the role of metabolism and energy supply for the function of gray and white matter. These mechanisms are studied in normal and pathological conditions (such as ADHD, epilepsy, Parkinson, Alzheimer), and during ontogenetic development and ageing.

Professor
Jon Storm-Mathisen

Associate Professor
Linda H. Bergersen

Challenges

Recent research by our group (see Achievements) has opened possibilities for studying in depth aspects of nervous system functions in health and disease. Important aspects are how nerve endings provide glutamate for synaptic release and how they recover released glutamate for reuse, as well as how synapses provide energy for synaptic transmission and how astrocytes can modulate neuronal function. Our main aim is to study synaptic function under physiological conditions and to investigate how the factors contributing to normal signalling are altered in disease, identifying new therapeutic strategies.



*An astrocyte process (Ast) has synaptic-like microvesicles (red arrowheads) containing D-serine (small particles); the Ast is identified as having glutamate transporter EAAT2 in its plasma membrane (large particles) and is adjacent to a nerve ending (Term) synapsing on a spine (Sp). *, synaptic cleft. Bars 100 nm and 50 nm (insets). From: Bergersen et al Cereb Cortex. 2011 Sep 12. [Epub ahead of print; ISI Impact Factor 6.8]*

Projects

- Identification of gliotransmitters and their roles in neuron-glia communication.
- Role of metabolic precursors of glutamate, including glutamine, for keeping up synaptic release.
- Interplay of glutamate with other neurotransmitters (e.g. aspartate, GABA, dopamine), including experimental models of neurological disease (e.g. Parkinson's disease, epilepsy, ADHD).
- Roles of monocarboxylates (lactate, ketone bodies) in normal brain function, and in disease such as epilepsy; effects of physical activity.
- Synaptic changes during ontogenetic development and in animals with deficient DNA repair.

Recent achievements: The ultrastructural localization of monocarboxyltate transporters (MCTs) (Exp Brain Res 2001, Cereb Cortex 2005, Neuroscience 2007a) and identification of their role in temporal lobe epilepsy (Neurobiol Dis 2011, 2012, Glia 2012), as well as in sustaining myelin structure and function (J Neurosci 2011), and protecting cardiac muscles from ischemic damage (Life Sci 2009) through lactate transport provides new approaches to understanding brain function and developing new therapy in brain diseases . Following the molecular identification of the glutamine transporter family (Cell 1999, several subsequent papers), a role of glutamine has been defined for normal synaptic function (J Neurochem 2008) as well as for dendritic retrograde signaling (Cereb Cortex 2009c), and a potential target uncovered in Alzheimer's disease (Neurochem Res 2008). The identification of proteins, VGLUT1-3 (Neuron 2001, PNAS 2002), that pump glutamate into synaptic vesicles allows the packaging of the transmitter to be characterised in health and disease (J Comp Neurol 2004, 2006, 2007) and modified by gene knock-out (Science 2004). Astrocytes, triggered by e.g. purinergic receptors (Eur J Neurosci 2007), release glutamate from VGLUT containing vesicles to enhance synaptic efficacy (Nature Neurosci 2004, 2007, Neuroscience 2009a). Astrocytes in several brain regions contain synaptic-like microvesicles with VGLUTs (Glia 2011), and glutamate as well as the NMDA receptor modulator D-serine (Cereb Cortex 2011a). The observations that even non-neural cells (J Cell Sci 2004, J Lipid Res 2007, PLoS ONE 2011) store and can release neurotransmitter amino acids in a way resembling synaptic release, and that oligodendrocytes have NMDA type glutamate receptors (Nature 2005), together with findings that glutamate and other neuroactive substances, such as GABA (Eur J Neurosci 2003, Molec Neurosci 2004, Cereb Cortex 2009a) and ATP (Cereb Cortex 2011b), can be co-released from nerve endings, including at the neuromuscular junction (Neuroscience 2007b), suggest novel ways of intercellular communication and potential drug targets. Observations in synapsin knock-out mice that develop epilepsy (Neuroscience 2005, Cereb Cortex 2009b) and in a rat model of ADHD (Neuroscience 2009b) implicate anomalous glutamate signalling in these diseases. Ionotrophic glutamate receptors are implicated in nociception (Mol Neurobiol 2009), and mediate signals that position mitochondria where they are most needed, i.e. at the postsynaptic site of active synapses (Neuron 2009). Inducible expression of a mutated mitochondrial UNG1 DNA repair enzyme in forebrain neurons caused generation of apyrimidinic mDNA and neuronal impairment including reduced size of synaptic contacts (Mol Cell Mol 2010, DNA Rep (Amst) 2011).

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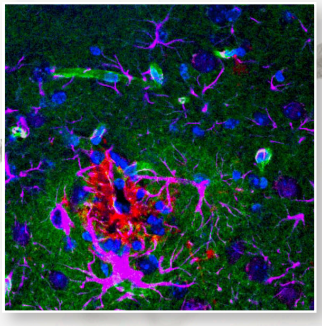
Laboratory of Molecular Neuroscience

Associate Professor Mahmood Reza Amiry-Moghaddam

About

The Laboratory for molecular neuroscience involved molecular mechanisms involved in the role of aquaporin water channels, brain extracellular matrix proteins and astrocytesin normal brain function as well as development of acute and chronic neurodegenerative diseases. It aims at unraveling the molecular basis for cell death and edema development in stroke and other neurological conditions, and explores the pathophysiology of Alzheimer's disease, Parkinson's disease and temporal lobe epilepsy. Long time goals are to identify new tools for early diagnosis for neurodegenerative disorders; and molecular targets for neuroprotective strategies in stroke, epilepsy, Parkinson's disease and Alzheimer's disease and to develop novel approaches for the treatment of brain edema.



Amyloid plaque (red) surrounded by reactive astrocytes in a mouse model of Alzheimer's disease (Photo: Reidun Torp)

Challenges

Neurology continues to lag behind other disciplines when it comes to the range and efficacy of therapeutic strategies. In particular, common neurological conditions such as stroke, epilepsy, Alzheimer's disease, Parkinson's disease and other acute or chronic neurodegenerative diseases call for new therapeutic strategies. Several of these conditions are particularly prevalent among the elderly and will constitute a growing health concern as the population ages. The challenge is to identify new principles of treatment for these diseases.

Projects

- Mechanisms involved in induction and loss of astrocyte polarity in health and disease
- Assessing the role of water channel molecules (aquaporins) and other in the development of brain edema and in the regulation of ion homeostasis in brain extracellular fluid.
- Synthesis of small molecule blockers of the brain aquaporins and assessing their effect on development of brain edema
- Exploration of the composition and function of the brain extracellular matrix proteins in health and disease
- Unraveling novel drug targets and therapeutic strategies in Parkinson's disease
- Exploration of mechanisms involved in the formation of beta-amyloid in aging andAlzheimer's disease

Recent achievments: Unraveling role of AQP4 in cell volume regulation and calcium signaling in astrocytes (Benfenati et al, PNAS 2011; Thrane et al PNAS 2011). Designing and synthesis synthetic peptides potentially binding to AQP4 (Jacobsen et al J Org Chem 2011). Unraveling the pathological roles of astrocytes in Alzheimer's and epilepsy (Alvestad et al., J. Cerebral Blood Flow and Metabolims; Jang et al, J. Alzheimer's disease)

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Laboratory for Molecular Biology

Professor Magnar Bjørås

About

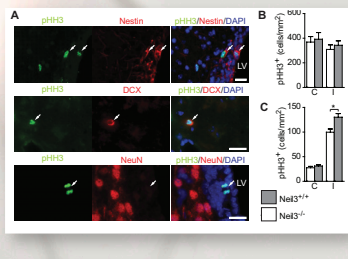
The Laboratory for Molecular Biology investigates basic biological processes associated with cellular responses to DNA damage including DNA repair pathways and mechanism for tolerance, scavenging, cell cycle regulation and adaptation.

Challenges

Challenges are to understand the mechanisms for cellular protection against DNA damage and its role in cancer, ageing, stem cell maintenance and neurological disease.

Projects

Role of oxidative DNA base lesion repair in ageing, cancer and neurological disease.
Biogenesis and maintenance of mitochondrial DNA.
Model studies of DNA damage responses and cell cycle regulation in yeast.
Small RNA genes and small peptides in biological responses to DNA damage.
Mechanisms of DNA repair and genome maintenance in microbial cells and animal viruses.



*Mitotic cell numbers are reduced in the Neil3-deficient striatum. (A) Mitotic (white arrows) nestin+ cells in the SVZ, a mitotic DCX+ cell in the striatum, and NeuN+/pHH3− neurons adjacent to a mitotic cell in the SVZ 3 d after HI. LV, lateral ventricle. (Scale bars, 20 μm.) (B and C) The number of pHH3+ cells was quantified in the SVZ (B) and striatum (C) in two nonadjacent sections from each animal. C, contralateral hemisphere; I, ipsilateral hemisphere. *P = 0.019. n = 4–5 mice. Data represent mean ± SEM*

Recent achievments: Biochemical and structural characterization unravel the monofunctional mode of the human 8-oxoguanine DNA glycosylase hOgg1 by design of separation-of-function mutants. Cell Structure (2011)

Neural stem/progenitor cell proliferation and differentiation are required to replace damaged neurons and regain brain function after hypoxic-ischemic events. We show profound neuropathology in Neil3-knockout mice characterized by a reduced number of microglia and loss of proliferating neuronal stem cells (NSC) in the striatum after hypoxia-ischemia. We propose that Neil3 exercises a highly specialized function through accurate molecular repair of oxidized DNA in NSC. Proc Natl Acad Sci (2011)

The 8-oxoguanine DNA glycosylase (OGG1) is essential for repair of mtDNA damage and NSC viability during mitochondrial oxidative stress. Our results demonstrate for the first time the interdependence between mtDNA integrity and NSC differentiation fate, suggesting that mtDNA damage is the primary signal for the elevated astrogliosis and lack of neurogenesis seen during repair of neuronal injury. J Neurosci (2011)

Yeast Cdc28 regulates cell cycle-dependent processes such as transcription, DNA replication and repair, and chromosome segregation. To gain further insight into the functions of Cdc28, we performed a high-throughput chemical-genetic array (CGA) screen aimed at unraveling the genetic network of *CDC28*. We identified 107 genes that strongly genetically interact with *CDC28*. *Of most interest* these results link cellular ubiquitin levels and the Rad6–Bre1 pathway to cell cycle progression. Proc Natl Acad Sci (2011)

The ada operon of Mycobacterium tuberculosis, which encodes a composite protein of AdaA and AlkA and a separate AdaB/Ogt protein, was characterized. M. these data indicate that M. tuberculosis hypermutator strains with defective adaptive response genes might sustain robustness to cytotoxic alkylation DNA damage and confer a selective advantage contributing to host adaptation. DNA Repair (2011)

2-oxoglutarate (2OG) dependent dioxygenases are ubiquitous iron containing enzymes that participate in a wide range of biological processes. Our results define a new subclass of AlkB proteins (Ofd2 in *Schizosaccharomyces pombe*) interacting with histones, which also might comprise some of the human AlkB homologs with unknown function. PLoS One (2011)

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Neural Systems and Graphics Computing Laboratory

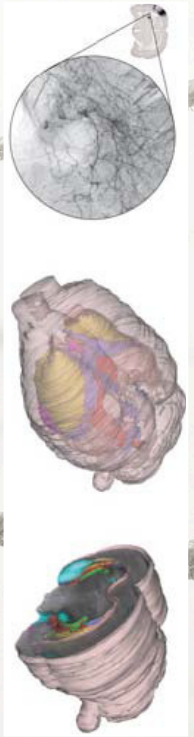
Professor
Jan G. Bjålie

Assistant Professor
Trygve B. Leergaard

About

NeSys is a computational neuroanatomy, neuroimaging, and neuroinformatics laboratory aiming at developing and implementing new technologies for analysis of brain architecture, connectivity, and gene and molecular distribution at the level of regions and whole brain. The laboratory has three divisions:

- **The Experimental Neuroanatomy division** (headed by Associate Professor Trygve B. Leergaard), applies experimental histological techniques to map system level neural connections in the brain, characterize morphological changes in rodent models of neurodegenerative disease, and investigate histological correlates of neuroimaging measurements.



- **The Small Animal PET division** (headed by Professor Frode Willoch) specializes in pain research, in particular opioid receptor binding studies.

- **The Neuroinformatics division** (headed by Professor Jan Bjaalie) develops tools for 3-D visualization and analysis including brain atlases, database applications for management of microscopy and imaging data, and large scale infrastructures for sharing of tools and data.

Challenges

Much of the research carried out today on rodent models generates high-resolution image data allowing characterization and analysis of molecular distribution, gene expression, and connectivity. It is of great importance not only to record more data, but also to integrate data, re-use data in novel combinations, and perform more powerful analyses. To this end, our laboratory develops data management systems and tools for analysis and visualization of brain architecture data. Data accumulated in our systems and analyzed with accompanying suites of tools are used for both hypothesis-driven as well as discovery based research.

Projects

- **Neuroscience databases and atlasing systems:** We develop database applications and brain atlasing systems for image data, from microscopy level to in vivo imaging data.

- **Localization in the brain:** We develop and use technologies (large-scale data acquisition and storage, computerized 3-D reconstruction, and digital atlasing) for efficiently assigning localization to neuroscience data.

- **Brain map transformations:** We study design principles and changes in the architecture of major circuits in the brain following external and genetic manipulations.

- **High resolution structural and functional neuroimaging:** Tomographical imaging techniques are employed to characterize structural and functional changes occurring in the brain following experimental perturbations and disease. We also investigate the spatial distribution and dynamics of opioid receptors in the brain in relation to drug assisted rehabilitation.

Recent achievements: Digital atlas of regional and cellular level expression of transgenic Tet-Off gene promotors across the mouse brain (Neuroimage 54:2603-2611, 2011), Brain wide mapping of the connections of the rat primary somatosensory cortex (PLoS One 6(8):e22669, 2011), Online atlas of the anatomical subdivisions of the rat hippocampal region (Front. Neuroinform. 5:2, doi:10.3389/fninf.2011.00002). Establishment of improved tools and an anatomical template for spatial registration of functional images (J.Neurosci.Methods 199:166-172, 2011). Development of the first population-averaged diffusion tensor imaging atlas of the rat brain (Neuroimage 58:975-983, 2011).

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Neurotransporter Group

About

The Group studies how transporter proteins (in normal and diseased brains of different ages) modulate the extracellular spatiotemporal concentration profiles of excitatory and inhibitory transmitter amino acids. The transporters studied are those able to transport aspartate, GABA, glutamate and glycine across brain plasma membranes. These include the glutamate (EAAT1-5), GABA (GAT1-4), glycine (GLYT1-2) and dicarboxylate transporters as well as the glutamate-cystine exchanger and their anchoring and regulatory proteins.

Professor
Niels Chr. Danbolt

Challenges

The human genome contains almost 400 different transporter protein genes, most of which are expressed in the nervous system. The encoded proteins, including those for glutamate, are subject to sophisticated dynamic regulation, and several of them are doing more than solute transport. They are also ion channels and take part in intracellular signalling. Thus, the transporters are not simply pumps, but these other functions are poorly understood. The overall aim of the Group is to determine the roles of the individual transporter subtypes in order to better understand normal physiology and disease, and to uncover new therapeutic opportunities as disturbed control of extracellular glutamate appears to be an important factor, directly or indirectly, in all neurological disorders (including traumatic injury, epilepsy and stroke) as well as in drug abuse and major psychiatric disorders (for review see: Danbolt, 2001: Prog. Neurobiol).

Projects

- Conditional deletion of genes (GAT2, GAT3, BGT1, EAAT2 and GS).
- The role of the GAT3 transporters in seizure control.
- The importance of EAAT2 in nerve terminals
- Determination of GABA and glutamate transporter distributions and densities around select synapses.
- Computer modelling of transmitter release, diffusion, removal and receptor activation in 3D-models of neuropil
- The roles of transporters in peripheral organs (endocrine pancreas, heart, kidney and liver).
- Laboratory automation: "What a robot can do, a robot should do."
- Development of systems for data handling and authentication, as well as for sample tracking and data exchange between researchers.

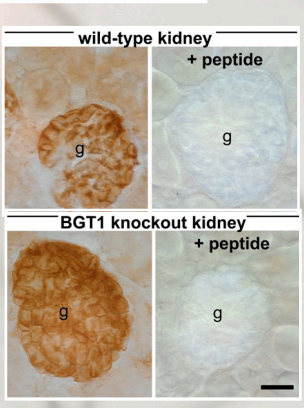

Fig.fra forskning Danbolt Kidney sections from wild-type and BGT1 knockout mice were labeled using a BGT1 antibody. This antibody turned out to cross-react with glomeroli. Pre-adsorption with the antigen (peptide) used to create the antibody, blocked all labeling giving a misleading impression of specificvity

Recent achievements: We created mice without the slc6a12 gene encoding the betaine-GABA transporter (BGT1) and found that the investigational drug EF1502 does not excert its anticonvulsive action by blocking the BGT1 as previously believed (Lehre et al., 2011). Now we report (Zhou et al., 2012) that BGT1 (protein and mRNA) is predominantly expressed in the liver (sinusoidal hepatocyte plasma membranes) and not in the liver, brain or kidney endothelium. BGT1 is also present in the renal medulla, where it localizes to the basolateral membranes of collecting ducts (particularly at the papilla tip) and the thick ascending limbs of Henle. There is some BGT1 in the leptomeninges, but brain parenchyma, brain blood vessels, ependymal cells, the renal cortex, and the intestine are virtually BGT1 deficient in 1- to 3-mo-old mice. Labeling specificity was assured by processing tissue from BGT1-deficient littermates in parallel as negative controls. Apart from providing new information about BGT1, this study illustrates how the the biomedical research community relies directly or indirectly on immunocytochemical data. For instance, interpretation of electrophysiological and pharmacological observations depends on information on where ion channels, receptors, enzymes or transporters Unfortunately, validation of labeling specificity is difficult. A common specificity test is the preadsorption test. This test was intended for testing crude antisera but is now frequently used to validate monoclonal and affinity purified polyclonal antibodies. We assessed the power of this test and show that antigen preadsorption blocked all labeling of both wild-type and knockout samples, implying that preadsorption also blocked binding to cross-reactive epitopes. This can give an illusion of specificity (Holmseth et al., 2012).

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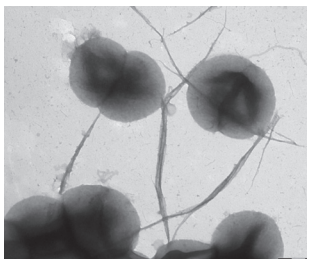
Molecular and Cellular Basis of Microbial Pathogenesis

Professor
Michael Koomey

About

Our laboratory uses human associated species of the bacterial genus Neisseria to address fundamental questions as to how bacterial pathogens cause disease in man. The research has focused primarily on the structure - function relationships of bacterial surface proteins. Recently, we have extended these studies to include investigations of covalent post-translational modifications (PTM) of surface proteins. These efforts have focused primarily on these processes in two, closely related species of causing disease in man: *N. gonorrhoeae* (causing gonorrhea) and *N. meningitidis* (the etiologic agent of epidemic meningitis). In particular, we are harnessing knowledge to understand what factors might dictate the propensity for *N. meningitidis* to colonize the nasopharynx and occasionally cause meningitidis while *N. gonorrhoeae* resides at genital sites. This work is supplemented by studies of *N. lactamica* and other commensal neisserial species that harmlessly colonizes human mucosal sites. We have also expanded our studies of bacterial protein glycosylation to include important species within the genera *Francisella* and *Burkholderia*.



Neisseria gonorrhoeae/ expressing type IV /pili// /(electron microscopy image).

Challenges

Despite the rapid acquisition of bacterial genome sequences, attempts at inferring phenotype from genotype remain difficult tasks. Moreover, covalent PTMs of proteins provide unique sources for structural complexity and diversification and by modifying structure and potentially function, they are likely to play an important role in the parasite-host interaction. We use research strategies combining biochemistry, bioinformatics, and reverse genetics together with advanced mass spectrometric-based proteomic approaches to examine PTM status. Challenges are to understand the basic biology of bacterial surface molecules, identify the components involved in modifying their structure, and to understand the biological significance of PTMs in these model systems. A long-term goal is to understand the evolution and phylogenetic distribution of PTM systems in bacteria. Several collaborations within the Centre for Molecular Biology and Neuroscience and internationally are involved. Incuded among the latter are those with the Feldman (Univ of Alberta, Imperiali (MIT), Maiden (Oxford) groups.

Projects

- Diversity of protein-associated glycan forms in *Neisseria*
- Genetic basis of protein-associated glycan diversification in *Neisseria*
- Effects of protein glycosylation on protein structure and function
- Dynamic interplay between glycosylation and zwitterionic phospho-from modifications
- Roles of glycoproteins in terminal respiratory pathways (oxygen targeting and denitrification)

Recent achievements: Discovery of the first broad spectrum) *O*-linked protein glycosylation in bacteria (Vik et al, 2009), defining structural alterations in a component of cytochrome c oxidase and links to molecular evolution Aspholm et al, 2010), uncovering an evolutionary trajectory for glycan synthesis in a bacterial protein glycosylation system (Børud et al, 2011), identification of the endogenous protein-targeting oligosaccharyltransferase and characterization of the native oligosaccharide in F. tularensis (Egge-Jacobson et al, 2011), and discovery of novel protein substrates of the phospho-form modification system and their connection to O-linked protein glycosylation (Anonsen et al, 2012).

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Forebrain development and Neural Stem Cells | Stem cell pathways

About

Stem cell knowledge is of fundamental importance, both within regenerative medicine, and in tumour medicine. Unsurprisingly, the same signals that control stem cells also play a central role in tumor growth and maintenance. The main interest of the group is to analyze the implications of stem cell pathways in developmental models, stem cells and cancer. The central focus of the group is to deepen our understanding on Wnt/_-catenin and Hh signaling. Having discovered the key morphogen Shh in 1993, the laboratory has continued to contribute to the understanding of Hh and Wnt signaling in various systems. Recently, the laboratory has expanded into using chemical biology approaches to elucidate the ramifications of the two pathways and to identify possibilities for *in vivo* pharmacological intervention.

Professor Stefan Krauss

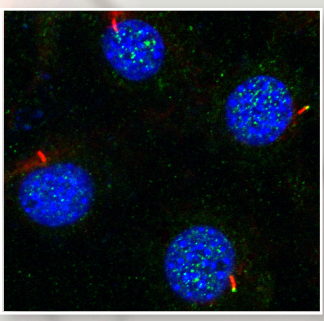
Challenges

Identify functionally relevant druggable targets in Wnt/_-catenin and Hh signaling that can be used for therapeutic intervention.

Projects

- Elucidating the roles of canonical Wnt signaling at different stages of forebrain development
- Analyzing the role of oxysterols in Wnt/_-catenin and Hh signaling
- Analyzing druggable targets in the Wnt/_-catenin
- Developing functional knock-out lines using zinc finger nucleases
- Developing clinical candidate stage Tankyrase inhibitors

Recent achievements: The group has developed an improved differentiation protocol for neural lineage commitment of mouse ES cells. The group has analyzed the interplay between TCF3 and _-catenin. We have developed a novel Wnt/_-catenin inhibitor to clinical candidate stage and are testing the inhibitor in various *in vitro* and *in vivo* models with the aim of initiating clinical trials within 2 years. The group has furthermore identified a novel SMO antagonist that we are currently analyzing.



"FLAG-tagged Gli2 localization in primary cilia upon activation of Hh signalling by the SMO agonist SAG (green: FLAG-tagged Gli2; red: acetylated tubulin; blue: DAPI). Martin Strand / Eline Buchman".

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Bioinformatics Group

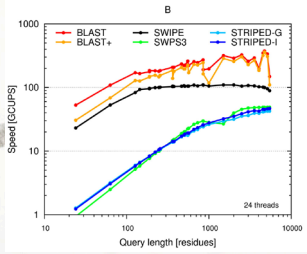
Associate Professor
Torbjørn Rognes

About

The Bioinformatics group uses computational methods to analyse genome sequences, amino acid sequences, and gene expression data, both to identify new genes of interest and to determine their structure, function and role in the cell. Advanced computational tools are both being used and developed. The group is also creating databases and web sites with our tools and generated data. We are involved in many collaborative projects with different research groups.

Challenges

Huge amounts of molecular biology data is being generated from a range of different technologies. New technologies allow extensive sequencing to be carried out to analyse sequence variation, transcription, epigenetics and other phenomena. Complete genome sequences from more than a thousand organisms as well as data from large-scale protein structure determination projects are also publicly available. The main challenge in computational biology is to integrate and make sense of all of this data.



Performance of sequence database search programs. *The speed of the BLAST (red), BLAST+ (orange), SWIPE (black), SWPS3 (green) and STRIPED (light blue, dark blue) programs is indicated in billion cell updates per second (GCUPS) with queries of varying length. (From Rognes, BMC Bioinformatics, 2011).*

Projects

- **Structural bioinformatics:** Computational models of the 3D structure of proteins are created and studied in order to understand the molecular mechanisms of enzyme activities. How do mutations affect the structure and function of a protein? How have the genes evolved? Docking and molecular dynamics simulations are also used in our studies.

- **Tools for sequence analysis:** Extremely rapid implementations of the fundamental algorithm for local sequence alignment that exploits readily available parallel computing technology has been developed (PARALIGN, SWIPE). We are working to improve such tools further and to apply them in important cases, like genome assembly or accurate read mapping of data from deep sequencing.

Recent achievements: We have developed the fastest implementation of the important Smith-Waterman local sequence alignment algorithm (BMC Bioinformatics, 2011). We have also discovered an important mutation in the AP endonuclease in lab strains of *S.pombe* (DNA repair, 2011). Furthermore, we have characterized the role of specific domains in the protein structure of PCSK9 in degradation of the LDL receptor (J Lipid Res 2011; BBRC, 2011) and contributed to the characterization of a PSC susceptibility locus (Nat Genet 2011).

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Laboratory for Genome Repair and Regulation

About

The "Laboratory for Genome Repair and Regulation" studies individual genes and their roles in basic biological processes including DNA repair, post translational regulation and epigenetics. The major rationale behind studying DNA repair and DNA regulation (including epigenetics), is the remarkable similarity, both at the sequence and biochemical levels, between enzymes introducing and removing macromolecular modifications, regardless of whether the target is DNA damage or an epigenetic mark. We focus mainly on enzymes able to hydroxylate a methyl-group (methyl-hydroxylation) and the in vivo roles of such proteins are being addressed by designing model organisms carrying defined mutations in the corresponding genes.

Professor Arne Klungland

Challenges

Our research focuses on the identification of novel genes with roles in genome repair and regulation. To address this we generate single, and combination thereof, mutants in mice. Subsequent analysis aim at identifying biological roles, such as cancer, regulation of mitosis and meiosis, etc associated with null mutagenesis of a single gene. We are particularly interested in defining the precise molecular role of individual genes in vivo. Today we focus on defining roles for a novel class of hydroxylases (which in vitro has been shown to hydroxylate/demethylate DNA, tRNA and histones) in epigenetic reprogramming in pluripotent stem cells and during mitosis and meiosis.

Quest 5-hmC DNA enrichment KIT. Based upon the published method by Robertson and colleagues (Nucl Acids Research 2011, Nature Prot. 2012).

Projects

- DNA Repair by Direct Reversal: Role in cancer.
- **Huntingtons Disease:** Modelling triplet expansion in Huntington disease mice and role of DNA repair.
- **Epigenetics:** Understand and characterize the novel epigenetic modification 5-hydroxymethylCytosine (5-hmC).
- Alternative splicing in meiosis.

Recent achievements: We have succeeded in generating null-mutant mice for 8 Alkb homolog's (Alkbh1-Alkbh8) and are currently characterizing these models. Whereas some homolog's have specificity for DNA repair (EMBO J 2006) other have roles in modifying tRNAs (Nature Comm. 2011). We have also established a novel method for the efficient identification of 5-hydroxymethylCytosine (5hmC) in genomic DNA (NAR 2011, Nature Prot. 2012); see illustration. Moreover, 2011 has been a very fruitful year with 5 publications including several CMBN partners and we have contributed to a study which may explain the pathological and clinical disease features in humans with mutations in SLC9A6 (project headed by Petter Strømme, OUS; Brain 2011).

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Laboratory of Cellular Neurophysiology and Ion Channel Function

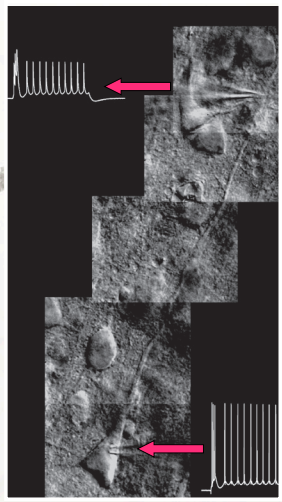
Professor
Johan F. Storm

About

Our group is interested in mechanisms of brain function, from molecules to behaviour. We study fundamental principles and mechanisms of neural signalling and coding in the mammalian brain, in particular the roles of ion channels in cortical neurons and circuits, mainly in the hippocampal-entorhinal memory system and the neocortex. Methods: Electrophysiological and optical recordings (patch clamp, intracellular recording, dynamic clamp, calcium imaging) in brain slices and in vivo, molecular genetic (viral vectors and transgenic mice) and pharmacological manipulations, computational modelling (Neuron, SurfHippo), and behavioural testing.

Challenges

To determine the functional roles and interplay of multiple signalling mechanisms within dendrites, axons and other neuronal compartments, and in small neuronal circuits. To elucidate functional roles of specific neuronal populations and signalling mechanisms including various ion channels, in active neuronal networks, in the brain of behaving animals. To elucidate the roles of neuronal signalling mechanisms in ageing and neurological disease. including ischemia/stoke, neurodegenerative disorders, epilepsy, and memory disorders.



Dual patch clamp recording from soma and dendrite of a cortical pyramidal cell from rat brain (H Hu & JF Storm, unpublished)

Projects

- Functional roles and mechanisms of neuronal oscillations and resonance in the mammalian cortex.
- The roles of voltage-gated ion channels in neural coding, signalling, synaptic plasticity, learning and memory.
- Changes in neuronal signalling during development and ageing.
- Roles of Kv7/KCNQ/M, h/HCN and other ion channels in neuronal signalling, brain oscillations and electrical resonance, synaptic plasticity, cognitive functions and epilepsy.
- Roles of Ca2+-activated K+ channels (BK and SK channels) in neuronal signalling, synaptic plasticity, cognitive functions, motor control, epilepsy and neuroprotection.
- Sunbthreshold signalling mechanisms and neuromodulation in mammalian cortical neurons in vivo.

Recent achievements: We are currently exploring novel signalling mechanisms in axons, including the roles of subthreshold voltage-gated conductances and intrinsic resonance (H. Alle et al.; abstract Germ. Neurosci. Soc. 2012; J.F. Storm, H. Alle, & J. Geiger, FENS Abstracts 2010), and developing new computer models and analysis tools (Murphey & J.F. Storm, Society for Neurosci. Abstr. 2011). By combining double and triple patch clamp recording from the dendrites and soma of CA1 hippocampal pyramidal neurons with computational modelling, we recently found that each cell is found that each cell is equipped with two complementary, spatially segregated mechanisms for theta resonance filtering of synaptic input, one in the apical dendrites and the other perisomatic (Hu et al., J. Neurosci. 2009). Walter Kaufmann et al. (J.Comp.Neurol, 2009), found that large-conductance calcium-activated potassium (BK) channels in Purkinje cell plasma membranes are clustered at sites of hypolemmal microdomains. In collaboration with Peter Ruth's group we found that BK-type Ca2+-activated K+ channels mediate neuroprotection and enhance survival after cerebrovascular stroke (Liao et al. PLOS 2010). We found that SK (KCa2) channels do not control somatic excitability in CA1 pyramidal neurons but can be activated by dendritic excitatory synapses and regulate their impact. (Gu et al. J. Neurophysiol. 2008). We have previously discovered that: - BK-type Ca2+-activated K+ channels can enhance early high-frequency firing and mediate a novel form of spike frequency adaptation (Gu et al., J Physiol 2007). - Discovered that Kv7/M/KCNQ-type K+ channels are present in the perisomatic region but not in the apical dendrites of hippocampal pyramidal neurons (Hu et al., J. Neuroscience, 2007). - Discovered that the persistent sodium current, INaP, paradoxically amplifies afterhyperpolarizations and reduces the frequency (f/I) gain, and strongly modulates spike timing (Vervaeke et al., Neuron 2006); that Kv7/M/KCNQ-type K+channels but not SK channels are essential for excitability control in hippocampal neurons (Gu et al., J Neurophysiol, 2008; Gu et al., J Physiol, 2005); that Kv7/M/KCNQ-type K+ channels are essential for spatial learning and prevention of epilepsy (Nature Neuroscience 8: 51-60, 2005), and that KCa1/BK-type K+ channels are essential for cerebellar learning and motor control (Proc Natl Acad Sci USA 101: 0474-8, 2004).

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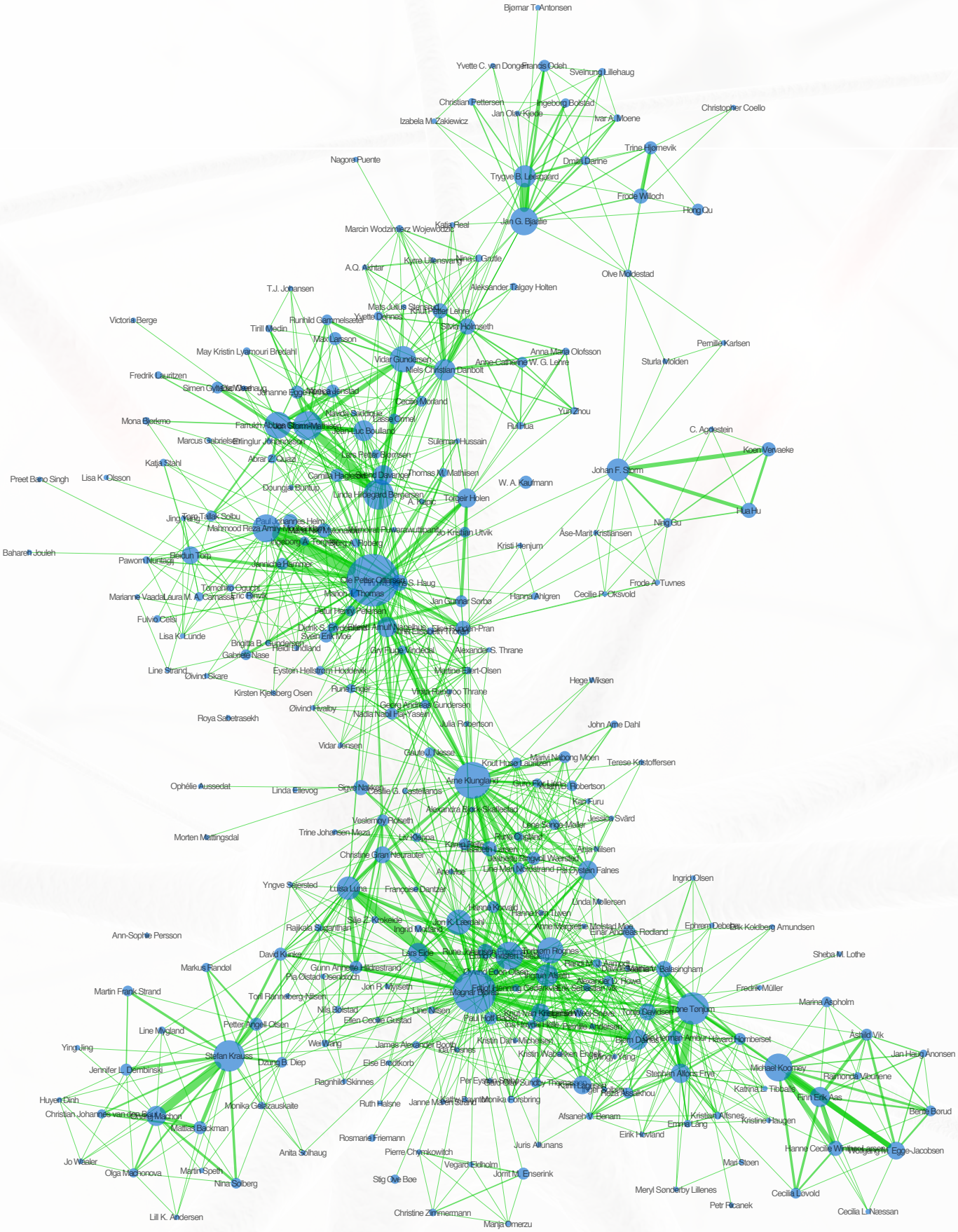
Author Network 2011



Co-publication network graph for all CMBN authors: The network is based on all types of journal articles published since CMBN was established. The area of the circles and the width of the lines are proportional to the number of publications by each author, and by the number of co-authored publications, respectively.

Publications 2011

1. Abu Hossain S, **Chaudhry FA**, Zahedi K, Siddiqui F, Amlal H (2011)
Cellular and molecular basis of increased ammoniagenesis in potassium deprivation
Am J Physiol Renal Physiol, 301 (5), F969-78
PubMed 21795646

2. **Ahlgren H**, **Henjum K**, **Ottersen OP**, **Rundén-Pran E** (2011)
Validation of organotypical hippocampal slice cultures as an ex vivo model of brain ischemia: different roles of NMDA receptors in cell death signalling after exposure to NMDA or oxygen and glucose deprivation
Cell Tissue Res, 345 (3), 329-41
PubMed 21874291

3. Alvestad S, **Hammer J**, Qu H, Håberg A, **Ottersen OP**, Sonnewald U (2011)
Reduced astrocytic contribution to the turnover of glutamate, glutamine, and GABA characterizes the latent phase in the kainate model of temporal lobe epilepsy
J Cereb Blood Flow Metab, 31 (8), 1675-86
PubMed 21522161

4. Arczewska KD, Baumeier C, Kassahun H, Sengupta T, **Bjørås M**, Kuśmierek JT, Nilsen H (2011)
Caenorhabditis elegans NDX-4 is a MutT-type enzyme that contributes to genomic stability
DNA Repair (Amst), 10 (2), 176-87
PubMed 21111690

5. Belova NV, **Dalhus B**, Girichev GV, Giricheva NI, Haaland A, Kuzmima NP, Zhukova TA (2011)
The molecular structure of tris-2,2,6,6-tetramethyl-heptane-3,5-dione aluminium: gas-phase electron diffraction, quantum chemical calculations and X-ray crystallography
Struct. Chem., 22 (2), 393-399

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Structure-function relationships of the competence lipoprotein ComL and SSB in meningococcal transformation
Microbiology, 157 (Pt 5), 1329-42
PubMed 21330432

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An aquaporin-4/transient receptor potential vanilloid 4 (AQP4/TRPV4) complex is essential for cell-volume control in astrocytes
Proc Natl Acad Sci U S A, 108 (6), 2563-8
PubMed 21262839

8. **Bergersen LH**, Sander M, **Storm-Mathisen J** (2011)
What the nose knows, what the eyes see, how we feel, how we learn, how we understand motor acts, why "YY" is essential for ion transport, how epigenetics meet neurobiology in Rett syndrome: seven topics at the 2010 Kavli Prize Symposium on Neuroscience
Neuroscience, 190, 1-11
PubMed 21624437

9. Bøhle LA, Riaz T, **Egge-Jacobsen W**, Skaugen M, Busk ØL, Eijsink VG, Mathiesen G (2011)
Identification of surface proteins in Enterococcus faecalis V583
BMC Genomics, 12, 135
PubMed 21362161

10. **Børud B**, **Viburiene R**, Hartley MD, Paulsen BS, **Egge-Jacobsen W**, Imperiali B, **Koomey M** (2011)
Genetic and molecular analyses reveal an evolutionary trajectory for glycan synthesis in a bacterial protein glycosylation system
Proc Natl Acad Sci U S A, 108 (23), 9643-8
PubMed 21606362

11. **Coello C**, **Hjornevik T**, Courivaud F, **Willoch F** (2011)
Anatomical standardization of small animal brain FDG-PET images using synthetic functional template: experimental comparison with anatomical template
J Neurosci Methods, 199 (1), 166-72
PubMed 21550366

12. **Dalhus B**, **Forsbring M**, **Helle IH**, **Vik ES**, **Forstrøm RJ**, **Backe PH**, **Alseth I**, **Bjørås M** (2011)
Separation-of-function mutants unravel the dual-reaction mode of human 8-oxoguanine DNA glycosylase
Structure, 19 (1), 117-27
PubMed 21220122

13. **Egge-Jacobsen W**, Salomonsson EN, **Aas FE**, Forslund AL, **Winther-Larsen HC**, Maier J, Macellaro A, Kuoppa K, Oyston PC, Titball RW, Thomas RM, Forsberg Å, Prior JL, **Koomey M** (2011)
O-linked glycosylation of the PilA pilin protein of Francisella tularensis: identification of the endogenous protein-targeting oligosaccharyltransferase and characterization of the native oligosaccharide
J Bacteriol, 193 (19), 5487-97
PubMed 21804002

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Spontaneous mutagenesis in Csb(m/m)Ogg1$^{-(/)-}$ mice is attenuated by dietary resveratrol
Carcinogenesis, 32 (1), 80-5
PubMed 21062970

15. **Gammelsaeter R**, Coppola T, Marcaggi P, **Storm-Mathisen J**, **Chaudhry FA**, Attwell D, Regazzi R, **Gundersen V** (2011)
A role for glutamate transporters in the regulation of insulin secretion
PLoS One, 6 (8), e22960
PubMed 21853059

16. **Haj-Yasein NN**, **Jensen V**, **Vindedal GF**, **Gundersen GA**, **Klungland A**, **Ottersen OP**, **Hvalby O**, **Nagelhus EA** (2011)
Evidence that compromised K+ spatial buffering contributes to the epileptogenic effect of mutations in the human Kir4.1 gene (KCNJ10)
Glia, 59 (11), 1635-42
PubMed 21748805

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Glial-conditional deletion of aquaporin-4 (Aqp4) reduces blood-brain water uptake and confers barrier function on perivascular astrocyte endfeet
Proc Natl Acad Sci U S A, 108 (43), 17815-20
PubMed 21990350

18. Hartley MD, Morrison MJ, **Aas FE**, **Børud B**, **Koomey M**, Imperiali B (2011)
Biochemical characterization of the O-linked glycosylation pathway in Neisseria gonorrhoeae responsible for biosynthesis of protein glycans containing N,N'-diacetylbacillosamine
Biochemistry, 50 (22), 4936-48
PubMed 21542610

19. **Helm PJ**, **Ottersen OP** (2011)
Proposal of a new method to measure FRET quantitatively in living or fixed biomedical specimens on a laser microscope
PROC SPIE, 7903, 790331

20. Hereng TH, Elgstøen KB, **Cederkvist FH**, **Eide L**, Jahnsen T, Skålhegg BS, Rosendal KR (2011)
Exogenous pyruvate accelerates glycolysis and promotes capacitation in human spermatozoa
Hum Reprod, 26 (12), 3249-63
PubMed 21946930

21. Holla ØL, Cameron J, Tveten K, Strøm TB, Berge KE, **Laerdahl JK**, Leren TP (2011)
Role of the C-terminal domain of PCSK9 in degradation of the LDL receptors
J Lipid Res, 52 (10), 1787-94
PubMed 21771976

22. Holla ØL, **Laerdahl JK**, Strøm TB, Tveten K, Cameron J, Berge KE, Leren TP (2011)
Removal of acidic residues of the prodomain of PCSK9 increases its activity towards the LDL receptor
Biochem Biophys Res Commun, 406 (2), 234-8
PubMed 21324305

23. Hussain S, Davanger S (2011)
The discovery of the soluble N-ethylmaleimide-sensitive factor attachment protein receptor complex and the molecular regulation of synaptic vesicle transmitter release: the 2010 Kavli Prize in neuroscience
Neuroscience, 190, 12-20
PubMed 21641968

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Insulin receptor substrate 2 is a negative regulator of memory formation
Learn Mem, 18 (6), 375-83
PubMed 21597043

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Stapling of a 3(10)-helix with click chemistry
J Org Chem, 76 (5), 1228-38
PubMed 21275402

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In vitro differentiation of mouse embryonic stem cells into neurons of the dorsal forebrain
Cell Mol Neurobiol, 31 (5), 715-27
PubMed 21424551

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The G157C mutation in the Escherichia coli sliding clamp specifically affects initiation of replication
Mol Microbiol, 79 (2), 433-46
PubMed 21219462

28. Kjonigsen LJ, **Leergaard TB**, Witter MP, **Bjaalie JG** (2011)
Digital atlas of anatomical subdivisions and boundaries of the rat hippocampal region
Front Neuroinform, 5, 2
PubMed 21519393

29. **Korvald H**, **Mølstad Moe AM**, **Cederkvist FH**, Thiede B, **Laerdahl JK**, **Bjørås M**, **Alseth I** (2011)
Schizosaccharomyces pombe Ofd2 is a nuclear 2-oxoglutarate and iron dependent dioxygenase interacting with histones
PLoS One, 6 (9), e25188
PubMed 21949882

30. Kaarbø M, Ager-Wick E, Osenbroch PØ, Kilander A, Skinnes R, Müller F, **Eide L** (2011)
Human cytomegalovirus infection increases mitochondrial biogenesis
Mitochondrion, 11 (6), 935-45
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J Histochem Cytochem, 59 (9), 807-12
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Monocarboxylate transporter 1 is deficient on microvessels in the human epileptogenic hippocampus
Neurobiol Dis, 41 (2), 577-84
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Deletion of the betaine-GABA transporter (BGT1; slc6a12) gene does not affect seizure thresholds of adult mice
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Workflow and atlas system for brain-wide mapping of axonal connectivity in rat
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Proteome Scale Turnover Analysis in Live Animals Using Stable Isotope Metabolic Labeling
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Immunogold Detection of L-glutamate and D-serine in Small Synaptic-Like Microvesicles in Adult Hippocampal Astrocytes
Cereb Cortex (in press)
PubMed 21914633

2. Binder DK, **Nagelhus EA**, **Ottersen OP**
Aquaporin-4 and epilepsy
Glia (in press)
PubMed 22378467

3. Gebhart C, Ielmini MV, Reiz B, Price NL, **Aas FE**, **Koomey M**, Feldman MF
Characterization of exogenous bacterial oligosaccharyltransferases in Escherichia coli reveals the potential for O-linked protein glycosylation in Vibrio cholerae and Burkholderia thailandensis
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PubMed 22391990

4. **Haj-Yasein NN**, **Jensen V**, Ostby I, Omholt SW, Voipio J, Kaila K, **Ottersen OP**, Hvalby O, **Nagelhus EA**
Aquaporin-4 regulates extracellular space volume dynamics during high-frequency synaptic stimulation: A gene deletion study in mouse hippocampus
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PubMed 22419561

5. Herwerth M, **Jensen V**, Novak M, Konopka W, Hvalby O, Köhr G
D4 Dopamine Receptors Modulate NR2B NMDA Receptors and LTP in Stratum Oriens of Hippocampal CA1
Cereb Cortex (in press)
PubMed 21955919

6. Kerty E, Heuser K, Indahl UG, Berg PR, Nakken S, Lien S, Omholt SW, **Ottersen OP**, **Nagelhus EA**
Is the brain water channel aquaporin-4 a pathogenetic factor in idiopathic intracranial hypertension? Results from a combined clinical and genetic study in a Norwegian cohort
Acta Ophthalmol (in press)
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7. Kielland A, **Camassa LM**, Døhlen G, Munthe LA, Blomhoff R, **Amiry-Moghaddam M**, Carlsen H
NF-κB Activity in Perinatal Brain During Infectious and Hypoxic-Ischemic Insults Revealed by a Reporter Mouse
Brain Pathol (in press)
PubMed 22059637

8. **Korvald H**, Falnes PO, **Laerdahl JK**, **Bjørås M**, **Alseth I**
The Schizosaccharomyces pombe AlkB homolog Abh1 exhibits AP lyase activity but no demethylase activity
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PubMed 22365419

9. **Larsson M**, Sawada K, **Morland C**, Hiasa M, **Ormel L**, Moriyama Y, **Gundersen V**
Functional and Anatomical Identification of a Vesicular Transporter Mediating Neuronal ATP Release
Cereb Cortex (in press)
PubMed 21810784

10. Nesvold A, Fagerland MW, **Davanger S**, Ellingsen O, Solberg EE, Holen A, Sevre K, Atar D
Increased heart rate variability during nondirective meditation
Eur J Cardiovasc Prev Rehabil (in press)
PubMed 21693507

11. Roberg-Larsen H, **Strand MF**, Grimsmo A, **Olsen PA**, **Dembinski JL**, Rise F, Lundanes E, Greibrokk T, **Krauss S**, Wilson SR
High sensitivity measurements of active oxysterols with automated filtration/filter backflush-solid phase extraction-liquid chromatography-mass spectrometry
J Chromatogr A (in press)
PubMed 22410154

12. **Solberg N**, **Machon O**, **Machonova O**, **Krauss S**
Mouse Tcf3 represses canonical Wnt signaling by either competing for β-catenin binding or through occupation of DNA-binding sites
Mol Cell Biochem (in press)
PubMed 22270545

13. **Waaler J**, **Machon O**, Tumova L, Dinh H, Korinek V, Wilson SR, Paulsen JE, Pedersen NM, Eide TJ, **Machonova O**, Gradl D, Voronkov A, von Kries JP, **Krauss S**
A novel tankyrase inhibitor decreases canonical Wnt signaling in colon carcinoma cells and reduces tumor growth in conditional APC mutant mice
Cancer Res (in press)
PubMed 22440753

Publication Highlights 2011

If repair processes do not occur as normal, DNA can be damaged or modified and the consequences can be premature aging, cancer or neurodegenerative brain disease. CMBN scientists have identified high levels of 5-hydroxymethylcytosine (5-hmC) at promoters of pluripotent and lineage specific genes in embryonic stem cells, and have also described novel mammalian tRNA modifications (Nature Comm 2, 172). They have also developed a novel method for the identification of the "6th" base in DNA, the newly identified 5-hmC which is produced following hydroxylation of 5-methylcytosine (NAR 39, e55; Biochem Biophys Res Comm 411, 40-3).

Neural stem/progenitor cell proliferation and differentiation are required to replace damaged neurons and regain brain function after hypoxic-ischemic events. DNA base lesions accumulating during hypoxic-ischemic stress are removed by DNA glycosylases in the base-excision repair pathway to prevent cytotoxicity and mutagenesis. Expression of the DNA glycosylase endonuclease VIII-like 3 (Neil3) has been shown to be confined to regenerative subregions in the embryonic and perinatal brains, suggesting that Neil3 exercises a highly specialized function through accurate molecular repair of DNA in rapidly proliferating cells (Proc Natl Acad Sci USA 108, 18802-7). Differentiation of embryonic stem cells into forebrain neurons has been described (Cell Mol Neurobiol 31, 715-27). CMBN researchers have provided a number of discoveries on the structure-function relationships of how DNA repair components exert DNA binding and processing (Structure 19, 117-27; PloS One 6, e25188; DNA repair 10, 296-305; DNA repair 10, 595-602; Microbiol 157, 1329-42).

CMBN scientists have constructed a new aquaporin-4 (AQP4) knock-out mouse (Proc Natl Acad Sci USA 108, 846-51) and have seminal discoveries on AQP4 localization, functions and interactions, highly relevant for glial cell osmolarity and ion flux (Proc Natl Acad Sci USA, 108, 2563-8; Proc Natl Acad Sci USA 108, 17815-20; Glia 59, 1635-42).

Major leaps have been achieved in the understanding of synaptic transmission. Numerous observations on glio- and neurotransmitters and their significance in brain disease have been presented (PloS One 6, e22960). Glutamate and the co-transmitter D-serine are found to be co-released from astrocytic small synaptic-like vesicles to activate perisynaptic glutamate receptors of the NMDA type (Cereb Cortex 2011 Sep 12). This mechanism may be important for memory formation and changed excitability states such as in epilepsy. Furthermore, lactate transporter MCT1 is found to be downregulated in microvessel endothelium and upregulated in neuropil astrocytes in temporal lobe epilepsy, in human surgical specimens (Neurobiol Dis 41:577-84) as well as in animal models (Neurobiol Dis 45:165-76). Lactate is required for oligodendrocyte thriving and myelination, particularly at low glucose concentrations (J Neurosci 31:538-48). The role of the betaine-GABA transporter BGT1 has been monitored in transgenic mice (Epilepsy Res 95, 70-81). Another discovery is on the nature astrocyte polarization in a mouse model for Alzheimer's disease (J Alzheimer Dis 27, 711-22). Mitochondrial damage-induced defenses and differentiation, highly relevant for apoptosis and development of neurons, have been presented (DNA repair 10, 639-53; J Neurosci 31, 9746-51), highlighting how important stem cells and mitochondria are for efficient repair in the brain.

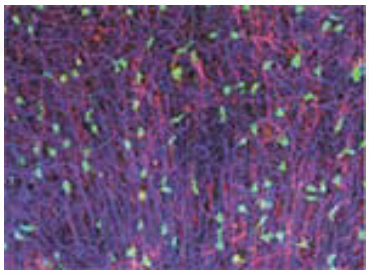
In terms of brain organ structure, a 3D digital brain atlas has been developed (PLoS One 6, e22669; Neuroimage 54, 2603-11; Front Neuroinform 5, 2). Collectively, these findings are relevant for the innovation of treatment against cerebral palsy, stroke, and secondary ischemia after spinal cord injury.

Post-translational modifications (PTMs) in the form of carbohydrate decoration promote cellular cohesion of brains cells and CMBN scientists have discovered novel pathways for PTMs in microbial models (Proc Natl Acad Sci USA, 108, 9643-8; J Bacteriol 193, 5487-97; Biocemistry 50, 4936-48).

Even new drug candidates against adenocarcioma and in the Wnt and cell cycle pathways have been launched (Cancer Res 71, 197-205; PLoS One 6, e19904; Proc Natl Acad Sci USA 108, 18748-53). Finally, novel biomarkers for cognitive performance in a normal life span have been identified, representing promise for early biomakers for neurodegenerative brain disease (Mech Aging Dev 132, 449-58). Collectively, these findings provide extended insight into how cells develop, function and are maintained and, in turn, will represent new potential for early diagnostics, prevention and treatment of disease.

CMBN in the media

Melkesyre beskytter hjernen
Forskningsaktuelt, Institutt for medisinske basalfag, Det medisinske fakultet, UiO, 21 December 2011



Samler og deler informasjon om hjernen
Nyheter, Norges forskningsråd, 8 December 2011

Hjernebilder gir hele bildet
Forskning.no, 18 May 2011

Nansens hjernearv
Forskningsaktuelt, Medisinsk Fakultet, UiO, 28 October 2011

Fred Kavli blir æresdoktor ved UiO og lærer mer om sine favorittfag
Teknisk ukeblad, 02 September 2011

80 mill. kroner til utstyr for hjerneforskning
Aktuelt, Medisinsk Fakultet, UiO, 1 November 2011

Flykter fra kutt
Aftenposten, 04 June 2011

Bioteknologi for bermen
Fritanke.no, 20 May 2011

Fridtjof Nansen - en pioner i nevrovitenskap
Forskning.no, 04 June 2011

Et hjernekraftverk
A-magasinet, 15 April 2011

I hvilken retning kysser du?
Kvinneguiden, 16 March 2011

Combined efforts yield excellence in research
KLIMA21, 03 March 2011

Mange revolusjoner
Forskningsrådet, 24 February 2011

De største spørsmål, de minste ting
Forskningsrådet, 23 February 2011

Mikrober, DNA og cellereparasjon
Tekninsk museum, 09 February 2011

Glutamat - et sant eventyr
Tekninsk museum, 31 January 2011

Alzheimer på cellenivå
Tekninsk museum, 12 January 2011

Det er kjemien som bestemmer
Tekninsk museum, 12 January 2011

Tanketrim og melkesyre
Tekninsk museum, 12 January 2011

DMII/NORBRAIN

NORBRAIN project receives 80 Million NOK grant

NORBRAIN receives 80 MNOK (10.2 Million Euro) from the National Financing Initiative for Research Infrastructure

NORBRAIN (The Norwegian Brain Initiative - A Large Scale Infrastructure for 21st Century Neuroscience -) is an NTNU-coordinated national infrastructure for neuroscience. The project is structured around two Centres of Excellence - the Centre for the Biology of Memory at the Norwegian University of Science and Technology (NTNU) and the Centre for Molecular Biology and Neuroscience at the University of Oslo - as well as one Centre for Research-based Innovation - the Medical Imaging Laboratory at NTNU. The contribution will be used to set up state-of-the-art neuroscience equipment across a broad spectrum of molecular and systems neuroscience. A total of NOK 400 million is being allocated under the National Financing Initiative for Research Infrastructure this year, 80 of which were awarded to NORBRAIN.

We collaborate to get one of the best neuroscience infrastructures in the world. The new state-of-the-art equipment will enhance our opportunity to conduct groundbreaking research. The project also has an international perspective in that it will make it easier for us to receive guest researchers and researchers in training.

This grant is important to highlight the importance of basic functional mechanisms in the brain, of DNA-repair in healthy brain cells, and in aging and disease. This is a unique opportunity to build a state-of-the-art infrastructure, especially in the new Domus Medica II building.

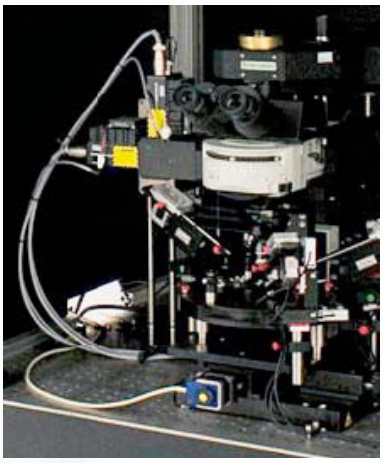


Photo: Gunnar F. Lothe, UiO.

Photo: NTNU

PhD Degrees 2011

1. **Ruth Halsne**
Mitochondrial and cellular effects of mitochondrial DNA damage
Faculty of Medicine, University of Oslo, 21 December 2011
Supervisor: Lars Eide

2. **Liv Kleppa**
Excision repair deficiencies in man and mice; lessons from CSA and Fen1 mutants
Faculty of Medicine, University of Oslo, 19 December 2011
Supervisor: Arne Klungland

3. **Maria-Niki Mylonakou**
Expression, anchoring and functional roles of brain aquaporins: A comparative analysis of AQP4 and AQP9
Faculty of Medicine, University of Oslo, 25 November 2011
Supervisor: Mahmood Reza Amiry-Moghaddam

4. **Lene Songe-Møller**
Alkbh8-mediated formation of wobble uridine modifications
Faculty of Medicine, University of Oslo, 5 October 2011
Supervisor: Arne Klungland

5. **Anne-Catherine Wiersholm Gauslaa Lehre**
Sex matters: Looking into variability. The variability hypothesis, the 2003 Quality Reform in higher education in Norway, and the role of BGT1 in seizure control
Faculty of Medicine, University of Oslo, 21 September 2011
Supervisors: Petter Laake & Niels Christian Danbolt

6. **Didrik Søli Frydenlund**
Pathophysiological roles of aquaporin-4 in CNS disease
Faculty of Medicine, University of Oslo, 20 May 2011
Supervisors: Mahmood Reza Amiry-Moghaddam & Tone Tønjum

7. **Knut Husø Lauritzen**
Mitochondrial DNA damage in forebrain neurons of mice
Faculty of Medicine, University of Oslo, 21 February 2011
Supervisor: Arne Klungland

8. **Thomas Misje Mathiisen**
The gliovascular unit: Structure and functional aspects
Faculty of Medicine, University of Oslo, 4 February 2011
Supervisor: Knut Petter Lehre

9. **Olve Moldestad**
Kv7 voltage-gated potassium channels and mitochondrial DNA toxicity in the forebrain: effects on behavior
Faculty of Medicine, University of Oslo, 14 January 2011
Supervisor: Johan F. Storm

10. **Pia Osenbroch**
Characterization of mitochondrial function in three distinct model systems for Cockayne Syndrome, hCMV-infection and NSC differentiation
Faculty of Medicine, University of Oslo, 13 January 2011
Supervisor: Lars Eide

PhD mid-term evaluations

1. Meryl Sønderby Lillenes
Neurogenetics of ageing: impact of DNA repair and macrophage function in Alzheimer disease
Monday 14 March 2011 at 14:00
Supervisor: Tone Tønjum

2. Izabela Maria Zakiewicz
Towards brain-wide connectivity mapping: a digital atlas of the complete output projections of the rat primary somatosensory cortex
Faculty of Medicine, University of Oslo, April 4, 2011
Supervisor: Trygve B. Leergaard

3. Fredrik Lauritzen
The role of monocarboxylate transporter 1 in mesial temporal lobe epilepsy
Friday 18 March 2011 at 13:00
Supervisor: Linda H. Bergersen

4. Kristian Alfsnes
Transformation, DNA repair and phase variation in Neisseria meningitidis -- impact genomic conservation and variation
Tuesday 29 March 2011 at 11:00
Supervisor: Tone Tønjum

MLS[UiO]

As a part of the celebration of the University of Oslo's 200 years, MLS [UiO] (Molecular Life Science at the University of Oslo) organized the competition, "Tell about your research". The competion challenged young scientist within the field of Molecular Life Science to tell about their research at UiO in a way that non-specialists can understand and find interesting.

Three first places with a prize of 10 000 NOK were awarded, five second places awarded with 5 000 NOK and five third places awarded NOK 1 000. We are pleased that three of the winners were from the CMBN.

First prize

Johanne E. Rinholm,
IMB/CMBN Postdoc Melkesyre beskytter hjernen.

Second prize

Kristian Alfsnes, OUS/Med.fak./CMBN Stipendiat,
Genetiske signaturer og dialekter: En studie av sex hos meningokokkbakterier.

Meryl S. Lillenes, OUS og Ahus/Med.fak./CMBN
Stipendiat Arvestoffet, aldring og Alzheimers sykdom: til forundring, fascinasjon og fortvilelse.

Young scientists supported in 2011

An important part of the common investments has been dedicated as support for young and promising scientists. This support is meant to provide salary while recruiting individual funding and generate a basis for the development of independent research groups. The scientists are also offered practical support, advice and infrastructure.

The CMBN scientists receiving this support must on a competitive basis apply for further financing from national and international funding agencies.

Torgeir Holen
Has been writing applications during the CMBN funding year, and finished several different publications on epilepsy, aquaporins, brain ultrastructure and olfaction.

Elisabeth Larsen
"The support gave me the opportunity to establish a laboratory modeling human diseases using induced pluripotent stem cells. Our focus is currently neurodegenerative diseases and DNA repair".

Conferences, celebrations, seminars

Jon Storm-Mathisen

We congratulate Jon Storm-Mathisen with his 70th birthday on January 16th, 2011.

Jon Storm-Mathisen was the first to visualize amino acids microscopically (Nature 1983; Nature 1986). With OP Ottersen this technique was extended to electronmicroscopic quantification (TINS 1987), showing with V Gundersen that glutamate and aspartate are concentrated in and released from synaptic vesicles in excitatory nerve endings (J Neurosci 1998). Early work with F Fonnum showed -for the first time- GABA to be synthesized in inhibitory neurons in the brain (Brain Res 1970), and showed excitatory nerve endings to have glutamate uptake (Nature 1977). Studies with NC Danbolt and the labs of BI Kanner and E Seeberg discovered the first glutamate transporter GLT1 (Nature 1992), and work with FA Chaudhry and RH Edwards identified the first glutamine transporters SN1 and SAT1 (Cell 1999; EMBO J 2001), and vesicular glutamate transporters VGLUT2 and 3 (Neuron 2001; PNAS 2002). He is listed by ISI Highly Cited (http://highlycited.com/names/s). H-factor 63.

Fourth EU-USA conference on DNA base damage and repair

The fourth EU-USA conference on DNA base damage and repair was organized in Oslo, Norway on May 18-22, 2011.

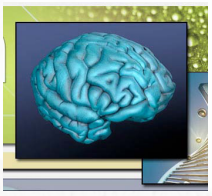
The aim was to bring together leading scientists from Europe and USA on DNA repair of base lesions.

The main scientific focus of this meeting was on DNA repair mechanisms and mutagenesis. Most mutagenic and carcinogenic agents induce covalent changes in the structure of the DNA and living organisms have evolved a large number of gene functions specifically designed to repair or tolerate such alterations without loss of viability or development of disease.

DNA repair mechanisms are probably the most important cellular protection against the development of cancer and are also essential for living cells to survive in an environment that would otherwise cause unacceptable mutation frequencies. The importance of DNA repair for normal life existence has been verified by discoveries of coupling between transcription and repair, by association between DNA repair and cell-cycle checkpoints, and by identification of nucleotide excision and mismatch repair genes being essential for prevention of cancer and neurological disease in man.

Healthy Brain 2011: Aging and Brain Disease

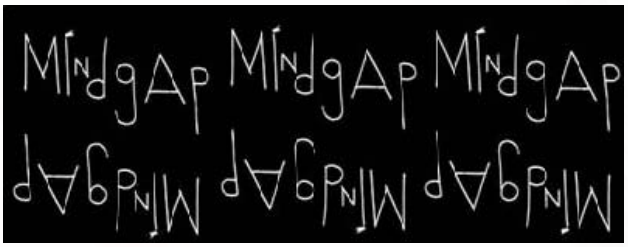
The Healthy Brain 2011: Aging and Brain disease was organized at Oslo University Hospital, Rikshospitalet, 6-7 June 2011.



The conference brought together world-leading scientists to discuss the state-of-the-art and current perspectives on the neurobiology of normal brain aging and early diagnosis and treatment of neurodegenerative disease. The incidence of diseases such as Alzheimer's disease is rising with the increase in the aging population and has profound impact on the quality of life and on health care costs. To meet this challenge, we need improved understanding of healthy brain aging and the pathophysiological processes underlying brain diseases related to aging. Research relevant to these topics spans multiple levels from clinical investigations and neuroimaging to molecular biology and genetics. Our aim was to elucidate the current standing of the field and discuss roadmaps for future efforts to unravel the aging process and generate targeted prevention and treatment.

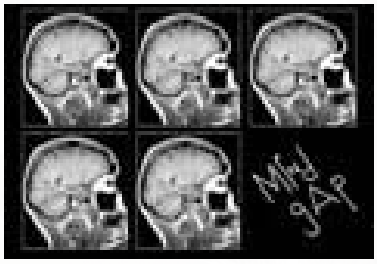
"The Healthy Brain - Aging and Brain Disease" was part of the celebrations of the 200th anniversary of the founding of the University of Oslo, and of the 150th anniversary of the birth of Fridtjof Nansen, the founder of Norwegian neuroscience (before earning fame as a polar explorer, oceanographer, diplomat, and Nobel peace prize laureate).

MindGap



The exhibition MindGap is about the brain and brain research. It was opened on April 16th, 2011 at the Technical Museum and will stay open until the end of 2012. CMBN has been central in the planning and scientific content of the exhibition and has also contributed economically. The University of Oslo is the main partner for the exhibition and the exhibition is part of the 200th anniversary celebrations of the founding of the University of Oslo, Norways first University.

"Hjernelørdag"



CMBN has taken part in "Hjernelørdag" organized by our collaborators in The Norwegian Brain Council in connection with the MindGap exhibition. Researchers from CMBN have demonstrated dissection of pig's brains and talked about brain disease and research.

The Fridtjof Nansen Science Symposium 2011

CMBN scientists organized the neuroscience part of The Fridtjof Nansen Science Symposium 2011 at the Norwegian Academy of Science and Letters April 28th 2011, marking the "nascence" of Norwegian neuroscience (Nansen's doctoral dissertation April 28th 1887). http://english.dnva.no/c26889/kalender/vis.html?tid=48931

Mini-symposium: Microbiology in the environment and society

CMBN and BIG organized a mini-symposium on Microbiology in the Environment and Society January 21st at Oslo University Hospital, Rikshospitalet. Bernhard Schink (University of Konstanz, Germany) talked about Microbial life at its energetic limits, Jim Prosser (University of Aberdeen, UK) addressed Nitrification in acid soils: explaining the impossible, while Fergus Priest (Heriot Watt University, Edinburg, UK) talked about Lactic acid bacteria in Scotch whisky fermentations and their influence on whisky flavor.

Mini-symposium on aquaporins

CMBN organized a mini-symposium on aquaporins Friday February 25ft 2011. The speakers included Rector at UiO Ole Petter Ottersen gave an introduction, Professor Peter Agre (Johns Hopkins Hospital, Baltimore, US) who talked about Aquaporins in malaria plasmodiums and consequences for therapy, senior researcher Erlend A. Nagelhus (NCMM, CMBN) who addressed In vivo two-photon imaging of aquaporin function in brain and Professor Tone Tønjum (CMBN) spoke about Aquaporin expression in bacterial meningitis and senior researcher Mahmood Amiry-Moghaddam (CMBN) talked about Aquaporins in the gliovascular unit: Structure and function

CMBN seminar: Promyelocytic Leukemia (PML) and autophagy in development and disease

CMBN organized the seminar PML and autophagy in development and disease, at Oslo University Hospital, Rikshospitalet the October 4th 2011.

Seminar: Women in Science - Bridging science and Career Development

November 10-11, 2011 CMBN arranged a seminar at the Norwegian Academy of Science and Letters called Women in science: Bridging science and career development. CMBN invited frontline female scientists in molecular biology, DNA repair and neuroscience to lecture on their research and share their experiences.

Innovation achievements

Bjørås group:

Received RCN FORNY-support for the innovation project : "Small toxic membrane peptides to treat bacterial infections".

Received support from Inven2 to establish the company "QOTICS Ltd" (Oppstartsfirma)

Klungland group:

Novel method licenced by Zymo research (licensed to Robertson, Dahl and Klungland)

A novel strategy for the identification of the 6th base in genomic DNA: 5-hydroxymethylcytosine (5-hmC) was developed. This base is probably crucial in the reprogramming occuring in the fertilized egg and is particularly abundant in the brain. The method is available through ZYMO research either as a kit or through a service which also includes analysis of captured, 5-hmC enriched, DNA by real-time PCR, microarray or deep sequencing. The kit is based upon the published method:

Robertson AB, Dahl JA, Vågbø CB, Tripathi P, Krokan HE, Klungland A (2011)

A novel method for the efficient and selective identification of 5-hydroxymethylcytosine in genomic DNA. Nucleic Acids Research, 39, e55

Krauss group:

Patent 1
Title: Azole derivatives as Wnt pathway inhibitors (title on published WO patent application)
Priority application: EP09251497.5, Priority date 05.06.23009 PCT application: PCT/GB2010/001118, International filing date 07.06.2010. Publication: WO2010139966, International publication date 09.12.2010.
The application is filed in US, EPO, Canada, Australia, Japan, China and India.

Patent 2
Title: Compounds
Priority application: US 61/420,942, 08.12.2010
PCT application: PCT/GB2011/052441, 08.12.2011

Patent 3
Title: Wnt pathway inhibitors
Priority application: US61/579094, 22.12.2011

Cooperation: the Centre for Healthy Aging (CEHA), The Brain Council, Norway and the NansenNeuroscienceNetwork (NNN)

In the last year CMBN has developed cooperation with several neuroscience partners.

CEHA

Center for Healthy Aging is a research center at University of Copenhagen that focuses on interdisciplinary aging research for the advance of better health and reduced frailty.

CEHA is generating improved understanding of healthy aging, and pursuing a groundbreaking path towards understanding the pathophysiological processes underlying diseases related to aging. CEHA research relevant to these topics spans multiple levels, from clinical investigations and imaging to molecular biology, genetics and social as well as humanistic studies. CEHA brings together world-leading scientists to conduct state-of-the-art research on critical aging-related topics, from the molecular biology of normal aging to societal aspects of the aging process. CEHA is a unique arena for multidisciplinary science and translational research on healthy aging, which has a high likelihood for continued success in the years ahead. The ongoing successes of the Center are a MUST, helping Denmark and many other countries to be well - prepared to cope with aging itself, as well as the challenges that face our society in adapting to the increasing size of the elderly population. CMBN Director Tone Tønjum serves on the CEHA Board, and CMBN researcher Linda H Bergersen is from 2011 part-time Professor Neurobiology of Aging at the CEHA.

http://healthyaging.ku.dk/

HJERNERÅDET

The Norwegian Brain Council

The Norwegian Brain Council is working to raise awareness around diseases in the brain and support research and development related to diagnostics, treatment, prevention and rehabilitation. The Norwegian Brain Council constitutes of most of the organizations that have a particular interest diseases in the brain in Norway. The Brain Council have several outreach arrangements for the public and are applying for “TV-aksjonen” 2013.

CMBN was one of the founders of Brain Council in Norway and plays a central role in the Brain Council. The CMBN participated and contributed to several of the activities organized by the Brain Council as a part of our responsibility of sharing knowledge about the brain with the public.

http://www.hjerneradet.no/

NANSEN NEUROSCIENCE NETWORK
connecting brain science and industry

NNN

The Nansen Neuroscience Network is founded as an independent organization by industry, academic research groups and clinicians with a particular interest in neuroscience. The Nansen Neuroscience Network is a member association with its origin in Norway and profiles itself as the Norwegian knowledge hub in neuroscience.

Neuroscience is on the threshold of discovering the underlying mechanisms for complex mental and cognitive functions, considered by many to be the most challenging and exciting questions in science. It is also one of the fastest developing areas of medical research, and one in which Norway excels and is making significant contributions.

However, in order to leverage this knowledge further, we need to more actively integrate different sub disciplines, spanning from gene regulation and synaptic biology to neural systems, bioinformatics, biobanks, medical imaging, psychiatry and studies of behavior. We need the formation of research centers and open networks consisting of scientists with complementary skills and insights.

NNNs aim is to shorten the way from research to product, to increase the cooperation between industry and academia, and to raise awareness about Neuroscience. CMBN was one of the founders of NNN in 2010 and has played a vital role in developing the organization. The cooperation with NNN is important for our continued interaction with national and international players in research based “innovation” in neuroscience.

http://www.nansenneuro.net/

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