Centre for Molecular Biology and Neuroscience (CMBN)

ANNUAL REPORT 08

CENTRE FOR MOLECULAR BIOLOGY AND NEUROSCIENCE

Norwegian Centre of Excellence

UNIVERSITY OF OSLO

RIKSHOSPITALET

The Vision

The vision of the Centre is to be recognized as one of the most innovative research environments to identify, develop and promote new approaches for the treatment of brain diseases and age-related neurological ailments. To achieve the above goal the Centre aims at gaining a thorough understanding of relevant basic biological processes and disease mechanisms.

Table of Contents

2008 marks the expansion of collaborative networks

Ole Petter Ottersen

Tone Tønjum

By Professor Ole Petter Ottersen
Director of the Centre
Professor Tone Tønjum
Deputy Director of the Centre

2008 has been a particularly active year with multiple scientific breakthroughs and a number of international meetings. While interactions between the eleven groups of the Centre form the backbone of most major research projects, we are also seeing an increased number of collaborative projects that engage other environments in the Oslo region, nationally and beyond. This led us to propose that Gaustad Neuroscience Network (established in 2005 to promote translational research at the Gaustad campus - gnnet.com) be expanded, geographically and in terms of its scope. Thus, we are now in the midst of a process that we hope will lead to the establishment of a neuroscience cluster that includes basic and clinical research environments, as well as relevant industry. We are convinced that this initiative will help remove the "translational block" and ensure that discoveries in basic neuroscience be converted into improved prevention, diagnosis or therapy. The formation of a neuroscience cluster is also likely to increase the awareness of unmet needs in clinical practice. Innovation Norway has been very supportive in our endeavours to build better alliances with industry and regional and national research institutions, and we also feel that there is a political backing for such an initiative.

The decision of the University Board to implement the plans for the new building adjacent to Domus Medica was very welcome, but also left us with a significant challenge as expenses for scientific equipment could not be accommodated in the budget. Thanks to a substantial private donation granted by the Letten Foundation in October 2008, we now see that it will be possible to carry out the plans for the imaging centre that will be an integral part of the new building. Efforts are now made to obtain funding also for the other technologies that will be allocated to the new building including high throughput tissue processing, mass spectrometry/structural biology, neuro/bioinformatics, and transgene technology. Our intention is that the building and the technologies therein will serve as a cornerstone in a strong translational research environment with links to national as well as international collaborative partners. In fact, the building will constitute a major strategic asset for the University of Oslo and Regional Health Authority (Helse SørØst) and will represent a competitive advantage in positioning for funding from the European Union and other international funding bodies.

Collaboration between the National Hospital (Rikshospitalet) and CMBN

Frode Vartdal

By Professor Frode Vartdal
Head of the Medical Faculty's division at Rikshospitalet

Since its establishment in 2002 the Centre has educated a number of young scientists. One important issue that emerged in 2008 regards the need to secure the scientific career of our best talents in a time when permanent positions are in short supply. We are now increasing our efforts to ensure that our dedicated young scientists can keep active while positioning themselves for independent funding, e.g., through the European Research Council. Our young scientists constitute the most important asset of CMBN and it is essential that we support their career development with all the means we have at our disposal. The energy and motivation of our young talents continue to impress and their resolve and stamina promises well for the future of CMBN.

Centre for Molecular Biology and Neuroscience (CMBN) includes several research groups which are located at Rikshospitalet University Hospital, and Rikshospitalet has contributed significantly to the funding of CMBN. The CMBN research groups have become increasingly important for the enhancement of both basic and translational research at the hospital. Thus, many of CMBN research groups are increasingly involved in research on disease mechanism in close collaboration with clinical scientists. Moreover, CMBN helps to provide many of the research groups at the hospital with state-of-the art methodology thus contributing to the important issue of realizing translational research activities.

The organisation of the Centre

Board

On August 20th 2008 the Rector of the University of Oslo appointed a new board for the Centre. Professor Ole M. Sejersted continues as Chairman of the board while all other members are new and shall serve until the Centre of Excellence status expires in 2012.

The first meeting of the new Board took place at the beginning of December 2008.

Leader:
Ole M. Sejersted
Oslo University Hospital/
University of Oslo

Mari Trommald
South-Eastern health region

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

Management

Professor Ole Petter Ottersen is the Director of the Centre with overall scientific and administrative responsibilities for the Centre's activities. In his duties he is supported by Professor Tone Tønjum as Deputy Director and Ms. Julia Ferkis as Administrative leader. The eleven group leaders create the Steering group of the Centre and they meet regularly to discuss important scientific 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 Medical Faculty of the University of Oslo and Oslo University Hospital/ Rikshospitalet. Five of the eleven groups are located at Domus Medica of the Medical Faculty and five groups at Rikshospitalet. The remaining one is located at the Faculty of Mathematics and Natural Sciences.

Economy

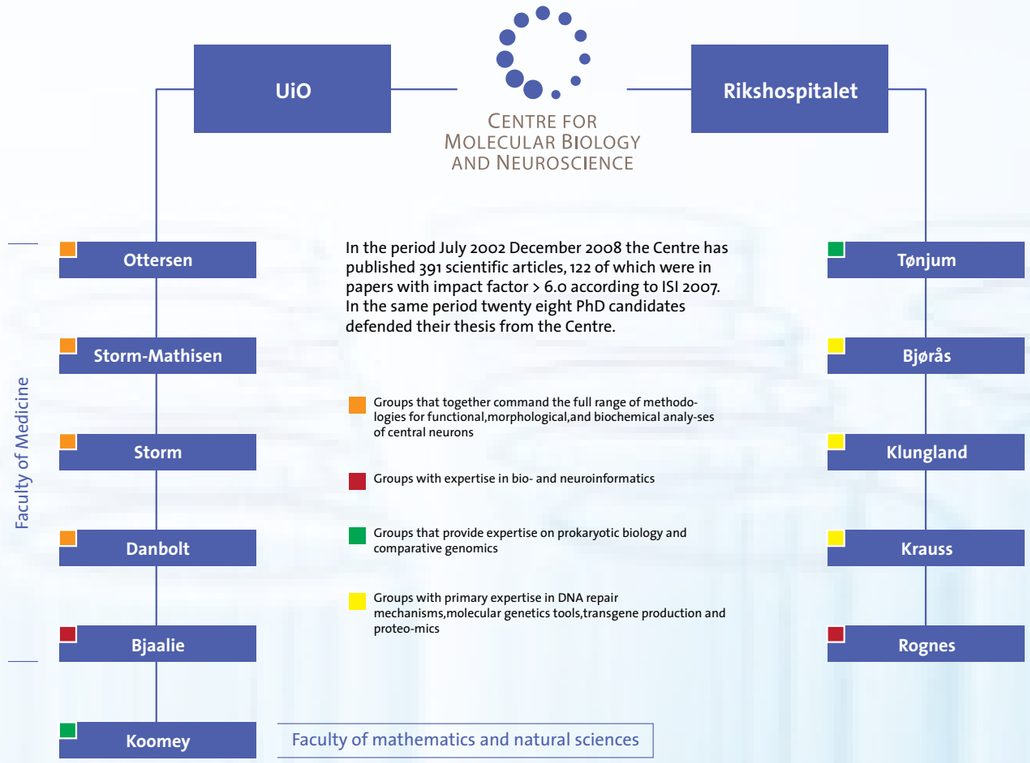
The Centre's total income was NOK 120 million in 2008, an increase of NOK 4 million from the year before. NOK 21 211 000 is the annual centre of excellence grant from the Norwegian Research Council. The two host institutions, the University of Oslo and Rikshospitalet contribute with salaries, office and laboratory space and running expenditures of approximately 1/3 of the Centre's income while other private and public funding contributes with ca. NOK 40 million.

Personnel

As one of the Centre's leading 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 network building can we secure this aim.

Like in previous years the Centre had 16 different nationalities among its scientific personnel and 10 foreign citizens among the technical/administrative staff in 2008. Out of the nine guest researchers we had among the staff last year only one was Norwegian.

Eleven groups providing the context of the Centre



Laboratory of molecular neuroscience

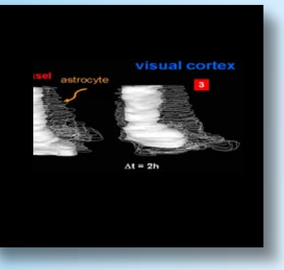
About

The Laboratory for molecular neuroscience investigates molecular mechanisms involved in the development of acute and chronic neurodegenerative disease. It aims at unravelling the molecular basis for cell death and edema development in stroke and other neurological conditions, and explores the pathophysiology of Alzheimer's disease and temporal lobe epilepsy. Long term goals are to identify new molecular targets for neuroprotective strategies in stroke and other conditions involving glutamate excitotoxicity and to develop novel approaches for the treatment of brain edema.

Professor
Ole Petter Ottersen

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, Alzheimer'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.



Swelling of astrocyte, monitored in a living mouse 2h after induction of hypo-osmotic stress. Transcranial multi photon in vivo imaging (courtesy of Gabriele Nase and Johannes Helm).

Projects

- Assessing the role of water channel molecules (aquaporins) in the development of brain edema and in the regulation of ion homeostasis in brain extracellular fluid.

- Exploration of the composition and function of the protein complexes that interact with glutamate receptors and that mediate downstream signalling from these.

- Unravelling the synaptic expression of kainate, NMDA, and AMPA receptors and the mechanisms responsible for their turnover.

- Identification of mechanisms underlying loss of glutamate homeostasis in temporal lobe epilepsy.

- Exploration of mechanisms involved in the formation of beta-amyloid in aging andAlzheimer's disease

Recent achievements: Resolving modes of NMDA and AMPA receptor expression in hippocampal spine synapses (Nature Neuroscience 2:618-624, 1999). Identification of principles underlying expression and regulation of the water channel aquaporin-4 in the CNS (J Neurosci 17:171-80, 1997; J Neurosci 21:3045-51, 2001; PNAS 98:14108-13, 2001). Showing that removal of perivascular aquaporin-4 protects against development of postischemic

edema and delays K+ clearance from the extracellular space (PNAS 100:2106-11, 2003; PNAS, 100:13615-20, 2003, Nature Reviews Neuroscience, 4:991-1001, 2003). Identification of neuronal plasma membrane microdomains that colocalize beta-amyloid and presenilin (Neuroscience, 120:291-300, 2003). Demonstrating loss of glutamine synthetase and perivascular aquaporin-4 in patients with temporal lobe epilepsy (Lancet, 363:28-37, 2004; PNAS 102:1193-8, 2005). Unravelling the molecular organization and function of astrocyte endfeet (PNAS 102: 8030-5, 2005; PNAS 103: 13532 – 6, 2006). Exploring the role of matrix metalloproteinases in epileptogenesis (J Cell Biol 180: 1021 - 35, 2008). Recording volume changes in individual neurons of the intact brain by multiphoton microscopy (Glia 56:895-902, 2008)

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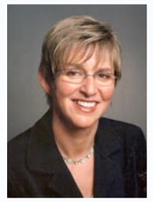
Genome dynamics and microbial pathogenesis



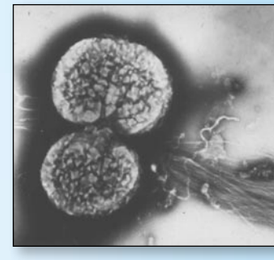
Professor
Tone Tønjum

About

The stability of microbial genomes and gene pools is constantly challenged by horisontal gene transfer and recombination, as well as DNA damage. Mechanisms for rapid genome variation, adaptation and maintenance are a necessity to ensure microbial fitness and survival in rapidly changing environments. Understanding microbial pathogenesis, horizontal gene transfer, genome instability and DNA repair mechanisms requires an interdisciplinary approach of molecular biology, genomics and bacterial physiology. These studies in genetic model bacteria are most important for understanding the balance between cellular fitness for survival and disease development (Nature Microbiol. Rev. 2006). In particular, we are focusing on the identification of DNA binding components contributing to the neisserial transformation system (J Bacteriol 2007), which we suggest is directly coupled to pilus retraction (J Biol Chem 2005). In this context, we have identified a number of novel DNA biding components and defined how they act and interact (Microbiol. 2009). We are also elucidating the effect of defects in DNA repair on host defence and microbial fitness and virulence in a new meningitis mouse model. The group addressing these challenges in molecular and cellular biology and medicine has strong international networks.

Challenges

To dissect owgenome wdynamics affect DNA sequence variability and conservation and thereby influence microbial fitness for survival and pathogenesis. This information will enable us to develop new strategies for prevention and treatment of disease which also has relevance for eukaryotic systems.



EM image of the meningococcus, a major cause of meningitis worldwide, Bergey's Manual 2006

Projects

- Meningococcal pilus biogenesis and DNA uptake: Neisseria meningitidis is the causative agent of meningitis. Pili are the primary virulence factor of this exclusively human pathogen. The transport of these macromolecular structures across membranes is performed by a complex machinery, which is also coupled to transformation of DNA. We hypothesize that DNA uptake during transformation is coupled to pilus retraction (J Mol Biol 2006; J Structural Biol 2006; Microbiology 2009).

- Genomics in the search for novel signature DNA sequences: We are using our combined expertise on evolutionary phylogeny, prokaryote cell physiology and comparative genomics and have defined the DNA uptake sequence as a12-mer (J Bacteriol 2007).

- Effects of the meningococcus on brain water homeostasis: By using cellular and animal models the effect of meningococci on glial aquaporins and other glial and neuronal components are characterized (Neuroscience 2007).

- Intracellular survival of Mycobacterium tuberculosis: We are studying the mechanisms for genome maintenance and thereby fitness for survival in the world's biggest bacterial killer (PloSOne, 2008).

Recent achievements: Antimutator role of meningococcal MutY, MutS and Fpg (Nature Micro. Rev. 2006, BMC Microbiol 2009), the true identity of the neisseria DNA uptake sequence (J Bacteriol 2007), identification of novel DNA binding components (Microbiol. 2009), transformation is conservative and maintains genome stability (Genome Biology, 2008), genetic predisposition for disease (CID 2008)

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Laboratory for molecular biology

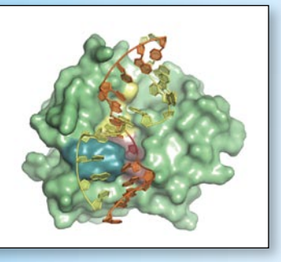
Professor
Magnar Bjørås

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 and adaptation. Focus has been on the repair of endogenous DNA damage and mechanisms for removal of base damage to DNA. At the cellular and organismal level, the aim is to understand mechanisms for genome maintenance in mammalian as well as microbial cells and to develop new interventions for preventing cancer and neurological disease associated with genome instability caused by DNA damage.

Challenges

Cellular genomes are continuously challenged by physical, chemical and biological agents that introduce changes of the chemical structure of the DNA. Intracellular reactive metabolites such as reactive oxygen species and alkylating compounds are important inducers of such changes. Nevertheless, mutation frequencies are low because of very efficient pathways for DNA repair and DNA recombination, which remove DNA damage and conserve at least one functional copy of the genome. Nevertheless, in humans, DNA damage will induce genome instability that is associated with disease and degenerative disorders. Challenges are to understand the mechanisms for cellular protection against DNA damage and its role in cancer, ageing and neurological disease.



Projects

- *Neuroscience databases and atlasing systems*. We develop database applications for image data, from microscopy level to *in vivo* imaging data. We now host a rat and mouse brainwork bench (www.rbwb.org), providing access to repositories, databases, and analytical tools, for circuit level as well as molecular distribution data.

- *Localization in the brain.* We develop and use technologies (robotic microscopy data acquisition, computerised 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 MRI and microPET*. In several project collaborations, tomographical imaging techniques are employed to characterize structural and functional relationships occurring in the brain following experimental perturbations or disease.

Recent achievements: 1.) First publications from the University of Oslo in the area of small animal PET imaging, with establishment of novel mouse and rat brain atlas systems for assigning location to PET data (Hjørnevik et al., Frontiers in Neuroinformatics, doi: 10.3389/neuro.11/004.2007, recently ranked as the 5th mostly viewed paper in the Frontiers journal system, www.frontiersin.org) and identification of slow metabolic adaptations in brain regions involved in modulation of nociceptive signaling and descending inhibition (Hjørnevik et al., Pain, 140: 456-64, 2008). 2.) Establishment of a new journal, Frontiers in Neuroinformatics, ranked as one of the top performing journals in the Frontiers journal system. 3) New tools and databases shared via the Rodent Brain Work Bench (www.rbwb.org). 4.) International coordination in the field of neuroinformatics through the International Neuroinformatics Coordinating Facility (www.incf.org; Bjaalie and Grillner, J. Neurosci., 27: 3613-5, 2007; Bjaalie et al., Neural Netw., 21: 1045-6, 2008; Bjaalie, Frontiers in Neuroscience, doi: 10.3389/neuro.01.022.2008.)

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3-D digital rat brain model reconstructed from a standard stereotaxic atlas. The blue signal in amygdale and adjacent brain areas represent activity during nociceptive conditioning as measured with FDG positron emission tomography

Laboratory of neural systems and graphics computing

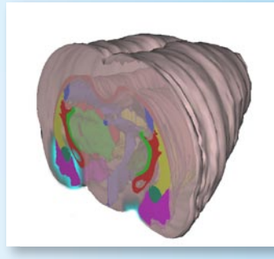
Professor
Jan G. Bjålie/
Trygve B. Leergaard

About

NeSys is a computational neuroanatomy and neuroinformatics laboratory. The research of the group focuses on 1) the development of new and powerful methods for computerized data acquisition, 3-D reconstruction, visualization and quantitative analyses of features in brain tissues, 2) data management and construction of 3-D brain atlases of experimental data, and 3) investigations on organization and re-organization of brain systems architecture in rat and mouse models, and 4) *in vivo* imaging in the context of multi-modality brain atlasing.

Challenges

Much of the research carried out today on rodent models generates high resolution image data, allowing characterization and analysis of brain 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, data management systems and advanced analytical tools are needed. Structure and structure-function relationships are often better understood by introducing 3-D reconstruction and advanced visualization and modelling tools.



Projects

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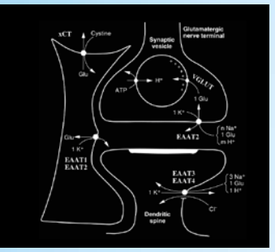
3-D digital rat brain model reconstructed from a standard stereotaxic atlas. The blue signal in amygdale and adjacent brain areas represent activity during nociceptive conditioning as measured with FDG positron emission tomography

Neurotransporter group

Professor Nils Christian Danbolt

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.



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 transporter genes (GAT2, GAT3, BGT1 and EAAT2).
- The role of the GABA transporters in seizure control.
- The importance of EAAT2 in nerve terminals
- Determination of transporter distributions and densities around select synapses.
- Computer modelling of transmitter release, diffusion, removal and receptor activation.
- Laboratory automation: “What a robot can do, a robot should do.”
- Development of systems for data handling and authentication.

Recent achievements: Antimutator role of meningococcal MutY, MutS and Fpg (Nature Micro. Rev. 2006, BMC Microbiol 2009), the true identity of the neisseria DNA uptake sequence (J Bacteriol 2007), identification of novel DNA binding components (Microbiol. 2009), transformation is conservative and maintains genome stability (Genome Biology, 2008), genetic predisposition for disease (CID 2008)

EM image of the meningococcus, a major cause of meningitis worldwide. Bergey’s Manual 2006

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Laboratory for genome repair and regulation

Professor Arne Klungland

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. We focus on the in vivo roles of such genes and therefore generate model organisms carrying defined mutations.

Challenges

Our research focuses on the identification of novel genes with roles in genome repair and regulation. To address this we generate single mutants in mice. Subsequent analysis aim at identifying biological roles, such as cancer, premature ageing and neurodegeneration associated with null mutagenesis of a single gene. We are particularly interested in defining the precise molecular role of individual genes in vivo. Although a protein might be able to carry out a specific reaction in vitro, the exact localization of the protein in vivo, the requirement of specific partners, the regulation of the protein during embryo development, etc, are key regulators for the activity of the protein in vivo. Such factors can even completely change the substrate preference.

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 spermatogenesis.

Projects

Role of FEN1 in DNA repair and replication with focus on cancer development
Modelling triplet expansion in Huntington disease mice.
Role of Alkbh1-8 in DNA repair, epigenetic regulation and tRNA modifications
Stem cells; pluripotency and lineage commitment.
Epigenetic regulation during spermatogenesis.

Recent achievements:

- AlkB Homologue 2–Mediated Repair of Ethenoadenine Lesions in Mammalian DNA (Ringvoll et al., Canc Res 2008).
- Early-Onset Lymphoma and Extensive Embryonic Apoptosis in Two Domain-Specific Fen1 Mice Mutants (Larsen et al., Canc Res 2008)
- 8-Oxoguanine-mediated transcriptional mutagenesis causes Ras activation in mammalian cells (PNAS 2008)

Models of mouse FEN1with the sites interacting with PCNA and the FEN1 active site indicated. We recently described the biological effects of mutating these sites (Larsen et al., 2008)

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Molecular and cellular basis of microbial pathogenesis

Professor
Michael Koomey

About

The main interests of the group lie in studies of how bacterial pathogens cause human disease. Our research primarily makes use of the obligate human pathogens *Neisseria gonorrhoeae* and *Neisseria meningitidis* (the etiologic agents of gonorrhea and epidemic meningitis respectively). Gonorrhea remains one of the most common sexually transmitted diseases contributing to worldwide morbidity, mortality and infertility. Although treatable with antibiotics, no vaccine is available. *N. meningitidis* is a commensal of the human oropharynx that under as yet poorly understood circumstances causes invasive disease and meningitis. Vaccines are available against some but not all disease associated strains. Historically, this work has focused on neisserial bacterial surface organelles termed Type IV pili (Tfp) or fimbriae. Tfp expressing bacterial pathogens are responsible for an extensive amount of morbidity and mortality worldwide. In addition, Tfp are associated with horizontal gene transfer and therefore contribute to the evolution of pathogenic and antibiotic resistant microbes. We have recently used the neisseria findings as a springboard to expand this work to include studies of Tfp expressed by pathogenic species within the genera *Pseudomonas*, *Franscisella* and *Burkholderia*.

Challenges

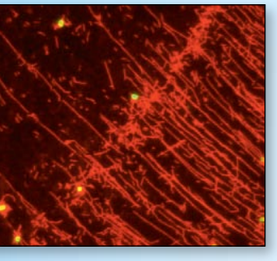
A detailed understanding of the structure and chemistry of pathogen surface components interacting with the human host is essential to the development of efficacious vaccines and anti-infectives. Our recent work has identified novel covalent post-translational modifications of bacterial proteins that likely impact on their functionality and recognition by the host. Efforts to elucidate the biological significance of these modifications require the use of interdisciplinary approaches encompassing reverse and forward genetics, biochemistry, bioinformatics and mass spectrometry. The intention is that by understanding the molecular biology of Tfp and other surface components, it will be possible to design rational approaches to preventing and controlling disease. In addition to working together with the Tønjum group in CMBN, several international collaborations are ongoing.

Projects

- Tfp biogenesis and dynamics of expression
- Tfp structure / function relationships
- O-linked protein glycosylation of neisserial Tfp pilin subunits
- Phosphoform modification of neisserial Tfp pilin subunits (covalent modifications with phosphoethanolamine and phosphocholine)
- General O-linked protein glycosylation systems in Proteobacterial species
- Structure, function and phylogenetics of ccb3 cytochrome oxidase in neisserial species

Recent achievements

Discovery and characterization of protein phosphoform modification (PNAS 2004, JBC 2006, J Bacteriol 2008); effects of pilin subunit structure and composition on function and organelle dynamics (Mol Microbiol 2007, J Bacteriol 2007); molecular characterization of O-linked glycosylation of pilin and its biosynthetic pathway (Mol Microbiol 2007); biophysical characterization of Tfp retraction dynamics (with the group of B. Maier - PNAS 2004, Biophys J *in press*); discovery and characterization of the first general (broad spectrum) O-linked protein glycosylation system in bacteria (PNAS *in press*).



N. gonorrhoeae expressing type IV pili from Pseudomonas aeruginosa (Immunofluorescence microscopy – cell / green, pili / red.)

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Forebrain development and neural stem cells

Professor
Stefan Krauss

About

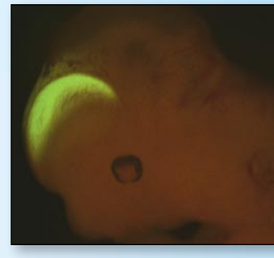
The developmental biology laboratory investigates the signalling mechanisms that control fate specification and proliferation in the mouse cortex.

Challenges

The aim of the ongoing study is to deepen our understanding of signaling pathways that are involved in cortical development, sub-specification of cortical areas, proliferation and communication between cells. The knowledge is used to establish rationale for pathway specific therapeutic intervention.

Projects

- Elucidating signaling pathways and mechanisms in cortical and hippocampal development
- Analyzing the Hh signaling pathway and its cross talk with other signalling pathways
- Investigating Wnt signaling
- Development of Hh antagonists
- Development of Wnt agonists and antagonists



The D6 enhancer allows selective genetic manipulation in the mouse cortex

Institute of Microbiology, Section for cellular and genetic therapy and Centre for Molecular Biology and Neuroscience
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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 function and role in the cell. Advanced statistical and 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.

Model of the 3-dimensional structure of the AlkD enzyme, a member of a new superfamily of DNA glycosylases

Challenges

Huge amounts of molecular biology data is being generated from a range of different technologies. Complete genome sequences from hundreds and soon thousands of organisms are available. Data from many large-scale nucleic acid hybridization experiments, DNA polymorphism studies, molecular interaction experiments and protein structure determination projects is also publicly available. Apparently all this data should enable the extraction of much biological insight, but the main challenge in computational biology is to integrate and make sense of all the data. Computational analyses may be hard, but can be very powerful in many types of studies, saving a lot of work in the wet lab or permitting otherwise impossible studies.

Projects

Sequence similarity: Tools like PARALIGN for particularly rapid and sensitive sequence database similarity searches have been developed. Parallel computing technology is exploited to get the highest performance. These tools are now being used to build gene homology networks and to cluster orthologous genes into groups.

Comparative genomics and DNA repair: General sequence analysis and computational identification of new DNA repair genes is carried out in close collaboration with other groups. Both advanced homology based methods and comparative genomics methods are used. A web portal is being established with an underlying database containing information on DNA repair genes across species.

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 does mutations affect the structure and function of a protein? Docking and molecular dynamics simulations are also used in our studies.

Non-coding RNA genes: The group is developing computational methods to identify new non-coding RNA genes (ncRNA), which are generally poorly annotated. The tool RNAmmer, based on hidden Markov models, has been developed to accurately locate ribosomal RNA genes in genomic sequences. Custom genome tiling microarrays have been designed to study transcription in “intergenic” regions.

Recent achievements: Discovered a new protein superfamily of glycosylases (Mol. Microbiol. 2006), and analysed their mechanism of repair based on a structural model (NAR 2007). Developed software for annotation of rRNA genes (NAR 2007). Characterized mutations in the PCSK9 gene involved in cholesterol metabolism (J Int Med 2008).

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Laboratory of cellular neurophysiology and ion channel function

Professor Johan Storm

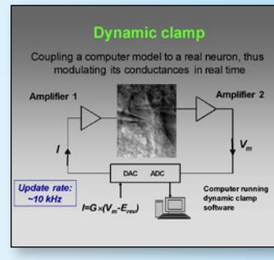
About

Our group is interested in mechanisms of brain function, from molecules to behaviour. Westudy fundamental principles and mechanisms of neuronal signalling in the mammalian brain, in particular the roles of ion channels in central 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, flash photolysis) in brain slices and *in vivo*, molecular genetic (viral vectors and transgenic mice) and pharmacological manipulations, computational modelling (SurfHippo, Neuron), and behavioural tests (water maze etc.).

Challenges

- To determine the functional roles and interplay of multiple signalling mechanisms and ion channel types within different neuronal compartments, and within the entire neuron and small neuronal circuits.
- To elucidate functional roles of specific neuronal populations, signalling mechanisms and ion channel types, in active neuronal networks, and 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.



Dynamic clamp: a live hippocampal pyramidal neurone in a rat brain slice is coupled, via two patch pipettes, to a computational model, thus modulating intrinsic ionic currents. (Hu, Vervaeke & Storm, unpublished).

Projects

- The roles of Kv7/KCNQ/M- and h/HCN-type K^+ channels in neuronal signalling, brain oscillations and electrical resonance, synaptic plasticity, cognitive functions and epilepsy.
- The roles of Ca^{2+}-activated K^+ channels (BK and SK channels) in neuronal signalling, synaptic plasticity, cognitive functions, motor control, epilepsy and neuroprotection.
- The roles of voltage-gated ion channels in neuronal signalling, synaptic plasticity, learning and memory.
- Changes in neuronal signalling during ontogenetic development and ageing.

Recent achievements: Found that BK-type Ca^{2+}-activated K^+ channels mediate neuroprotection and enhance survival after cerebrovascular stroke (ms. submitted). Discovered that BK-type Ca^{2+}-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, *I*NaP, 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 (Guet 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), that KCa1/BK-type K+ channels are essential for cerebellar learning and motor control (*Proc Natl Acad Sci USA* 101: 0474-8, 2004), the role of postsynaptic voltage-gated K^+ channels in regulation of synaptic plasticity (LTP) and integration (*Proc Natl Acad Sci USA* 99:10144, 2002); that Kv7/M/KCNQ-type K^+ channels are essential for intrinsic theta resonance in hippocampal neurons (*J Physiol* 545:783, 2002).

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The synaptic neurochemistry laboratory

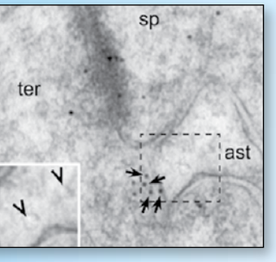
Professor
Jon Storm-Mathisen

About

The group's main interests are the mechanisms underlying synaptic transmission: localization, transport, synthesis, release, action and breakdown of neurotransmitters (glutamate, aspartate, GABA, glycine, monoamines, acetylcholine). These mechanisms are studied in normal and pathological conditions, and during ontogenetic development and ageing.

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 glial cells 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.



Electron micrograph showing NR2B signalling gold particles at the synapse as well as in extrasynaptic membranes (arrows) of nerve terminals (ter) making asymmetric synapses with dendritic spines (sp) in thedentate molecular layer. NR2B particles face astrocytic processes (ast) that containsynaptic-like microvesicles(SLMVs). NR2B is in close proximity to astrocytic SLMVs. Inset, higher magnification showing NR2B gold particles and astrocytic SLMVs (arrowheads). Scale bars, 100 nm. Nature Neuroscience March 2007

Projects

- 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 in experimental models of neurological disease (e.g. Parkinson's disease, epilepsy, ADHD).
- Roles of lactate in synaptic transmission and myelinisation studied in monocarboxylate transporter knock-out mice.
- Signalling at the neuromuscular junction: the roles of glutamate and lactate.
- Identification of gliotransmitters and their roles in neuron-glia communication.
- Synaptic changes during ontogenetic development and aging, and in animals with deficient DNA repair.

Recent achievements: Glutamine transporters, SN (Cell 1999, EMBO J 2001, Eur J Neurosci 2002, Glia 2003, J Am Soc Nephrol 2005) and SA/SAT (PNAS 2000, J Neurosci 2002, J Cell Biol 2002) were molecularly identified and characterized. A role of glutamine has been defined for normal synaptic function (J Neurochem 2008) as well as dendritic retrograde signalling (Cereb Cortex 2009c) and a potential target uncovered in Alzheimer's disease (Neurochem Res 2007). The ultrastructural localization of monocarboxyltate transporters (Cereb Cortex 2005, Neuroscience 2007a) as well as identification of glutamate transporters in glia and nerve endings (Glia 2008, Neuroscience 2008) provides new approaches to understanding brain function. 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). The observations that astrocytes and even non-neural cells (J Cell Sci 2004, J Lipid Res 2007) store and can release neurotransmitter amino acids in a way resembling synaptic release, and that oligodendrocytes have NMDA receptors (Nature 2005), together with findings that glutamate and other neuroactive substances can be co-released from nerve endings (Eur J Neurosci 2003, Molec Neurosci 2004, Cereb Cortex 2009a), 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.

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CMBN group leader at the International Neuroinformatics Coordinating Facility

By Professor Jan G. Bjålie
Group leader and Head of the Institute of Basic Medical Research

The International Neuroinformatics Coordinating Facility (INCF, www.incf.org) coordinates and fosters international activities for discovery and innovation in neuroscience and related fields. Established in 2005 through the Organisation for Economic Co-operation and Development (OECD) Global Science Forum, the INCF catalyzes global knowledge flow and scientific interaction by developing, maintaining and evaluating worldwide programs, standards, guidelines and infrastructures in neuroinformatics to further our understanding of the human brain and its diseases. With its Secretariat at the Karolinska Institutet and Royal Institute of Technology in Stockholm, Sweden, the INCF achieves its international outreach through its national nodes in 14 current member countries across the globe.

Professor Jan Bjaalie, Group leader of the Neural systems and graphics computing laboratory has served as founding Executive Director of the International Neuroinformatics Coordinating Facility (INCF) 2006 – 2008. During his term at the INCF, the central Secratariat with a staff of 12 was established at the Karolinska Institute in Stockholm. The organization started with 10 member countries and four more joined later. Building on extensive community interaction, with 9 workshop reports produced by more than 100 world-leading experts from various disciplines, the INCF has developed and established 1) new programmes for neuroinformatics infrastructure development, 2) a neuroinformatics portal service for the community, 3) an INCF Software Center facilitating the sharing of software tools for neuroscience, and 4) a new congress series for neuroinformatics. Recent achievements includes the hosting of the European mirror of the Allen Brain Atlas and the launching of new standards for large-scale modelling of the nervous system and digital brain atlasing.

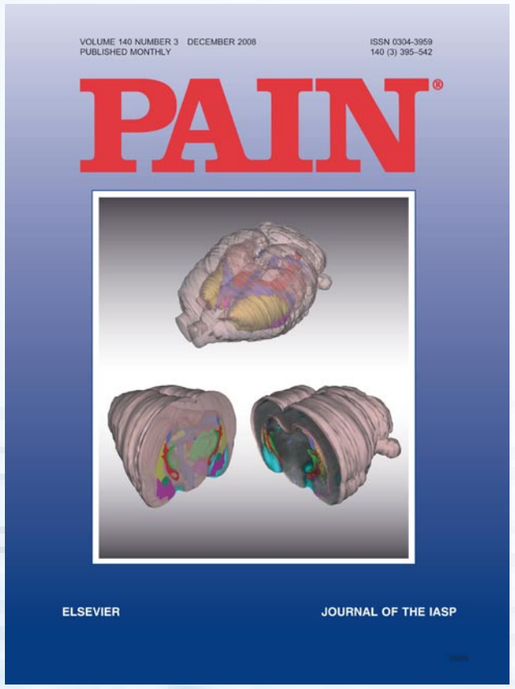
The Norwegian node of the INCF is hosted by CMBN. The node is lead by Gaute Einevoll,

guest researcher at CMBN and professor at the Norwegian University of Life Sciences, and Johan F. Storm, professor and group leader at CMBN. The node supports national neuroinformatics projects, meetings and courses, and map neuroinformatics activities.

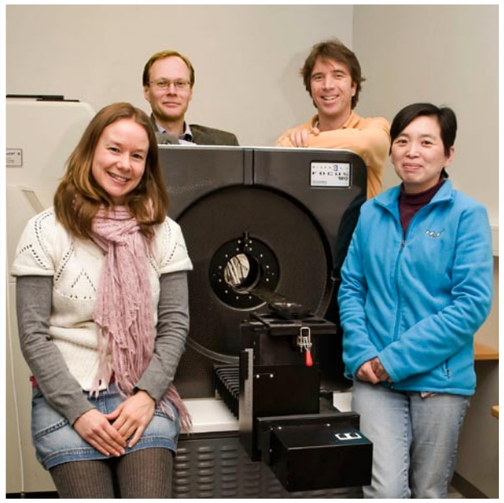
MicroPET at CMBN

Small animal PET (positron emission tomography) scanning was introduced at CMBN in 2005. Following the establishment of experimental protocols and environments for data analysis the first experimental data were collected in 2006-7 with publications in 2007 and 2008. For more information see www.nesys.uio.no/pet/.

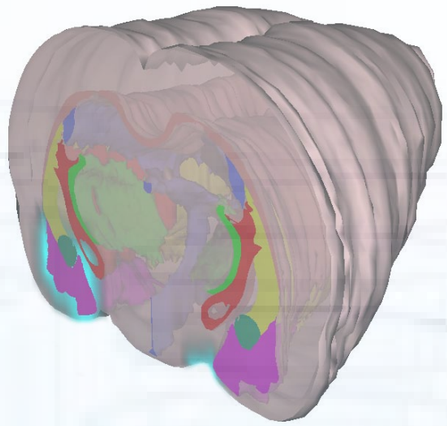
The picture below shows the cover page of the Journal Pain showing registration of positron emission tomography (PET) data to a 3-D digital atlas of the rat brain. The 3-D atlas was used to locate nociceptive-related changes in supraspinal metabolic activity measured using FDG-PET. From Hjørnevik et.al. Pain 2008, 140:456-64. Concerning atlas technology see also Hjørnevik et.al., Front Neuroinformatics 2007, 1:4.



Cover page from the journal Pain, showing registration of positron emission tomography (PET) data to a 3-D digital atlas of the rat brain. The 3-D atlas was used to locate nociceptive-related changes in supraspinal metabolicactivity measured using FDG-PET. From Hjørnevik et al. Pain. 2008, 140:456-64. Concerning atlas technology, see also Hjørnevik et al., Front Neuroinformatics. 2007, 1:4. Used with permission form IASP



The microPET (Siemens) scanner. Front, from left: Trine Hjørnevik (Ph.D student) and Hong Qu (chief engineer). Back, from left: Jan G. Bjålie (group leader at CMBN) and Frode Willoch (senior scientist and PET-research advisor).



3-D digital rat brain model reconstructed from a standard stereotaxic atlas. The blue signal in amygdala and adjacent brain areas represent activity during nociceptive conditioning as measured with FDG positron emission tomography.

Industrial spin-offs

The Centre is in the forefront also with regard to research documentation and quality control

The administrative burden on researchers is increasing. This is not only because of the increasing complexity of legal regulations and research funding, but also because the research activities themselves are rapidly becoming more complicated. This is due to many factors including increasing diversity of biological samples (e.g. due to use of transgenic animals and development of various new experimental designs and model systems), increasing amounts of data (e.g. due to the introduction of robotic systems) and new primary data formats due to novel methods and technology. Further, digitalization of equipment implies that original data are produced in electronic form on the computers connected to the various pieces of equipment.

This has several major implications:

(1) The traditional laboratory notebook does not work very well due to the practical difficulties involved in collecting and authenticating all of the electronic files produced.

(2) Researchers need to handle large amounts of data of many different types and in different formats

(3) To make it worse, the researchers needs are constantly changing. This implies both that powerful database systems are needed, and that these systems need the ability to evolve with the needs of the researchers.

One of the former students Danbolt has invented a database system with a radical new design. This system is being further developed by Science Linker AS. Single user versions of the system has been in use in the Neurotransporter Group since mid 1990s, and a multiuser version since 2003. Because of its success, the three groups at CMBN have now (in the framework of a FUGE project) a collaboration with Science Linker AS. Science Linker AS is setting up network of independent and locally controlled databases designed to organize and keep track of the research activities within each research group and the collaboration between groups.

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PhD degrees 2008

Camilla Haglerød
Glutamate receptor localization and trafficking in the glutamatergic synapse
20 June 2008
Supervisor: Svend Davanger and Ole Petter Ottersen

Gu Ning
Roles of potassium channels in excitability control and spike frequency adaptation in hippocampal pyramidal cells
18 July 2008
Supervisor: Johan F. Storm

Monica Jenstad
Glutamate, GABA and glutamine in synaptic and paracrine signalling
20 August 2008
Supervisor: Farrukh A. Chaudhry

Simen Gylteruwd Owe
Elements of glutamate release, action and reuptake
3 October 2008
Supervisor: Linda Hildegard Bergersen

Tom Tallak Solbu
Role of glutamine transport in synaptic transmission and metabolism
23 October 2008
Supervisor: Farrukh A. Chaudhry

Jeanette Ringvoll Wærsted
Repair of alkylated and deaminated base residues in mammalian DNA
21 November 2008
Supervisor: Arne Klungland

Aleksander Helgøy Holten
Synthesis, release and uptake of transmitter amino acids at central nervous synapses
5 December 2008
Supervisor: Vidar Gundersen

Karin Lagesen
Computational characterization of ribosomal RNAs in prokaryotes
12 December 2008
Supervisor: Torbjørn Rognes

Her kommer billedtext....

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The PhD Forum at the Institute of Basic Medical Research

by Rebecca Carver
PhD student in science communication research and
Leader of the Forum

2008 saw the birth of a new forum for improving the social and academic environment for all PhD students at the Institute of Basic Medical Sciences (IMB) - the IMB PhD Forum. During the autumn 2007 and spring 2008 I spoke to as many PhD students as I could, asking about their life as a PhD student. The message was clear: we often feel isolated and confused, not really knowing what else is going on in the Institute, not knowing who else to turn to for guidance or a social chat, and often unhappy with the courses offered. With encouragement from my supervisor, Jarle Breivik, and fellow PhD student Cecilie Morland from the Institute of Anatomy/CMBN, I invited interested students to a meeting to discuss the possibility of starting up our very own forum in early spring 2008. The main idea of having such a forum was to allow us – the doctoral candidates ourselves – to take a more active part in shaping our own education and social well-being. We want to have courses and events that really cater for our particular needs. Our enthusiasm spilled over and a forum board was officially formed on April 10th, consisting of myself from the Institute of Physiology and Cecilie Morland as joint leaders, and five forum board members:

Lasse Ormel (Anatomy)/Nedim Kasumacic (Physiology)/ Christian Bindesbøll (Nutrition)/

Leif Christopher Lindeman (Biochemistry)/Guro Mørk Johnsen (Nutrition).

We based our initial ideas on the very well run Medical Student Research Program, *Forskerlinjen*, whose students organize one-day seminars with useful workshops. We are grateful for the many fine ideas given us by the daily manager Jarle Breivik, and student representatives and seminar organizers Andreas Gundersen and Jasna Ribic. Using their "dagsseminar" as a model, we organised our very own "Autumn PhD symposium" on 15th October 2008. This was a whole-day seminar packed with topics on how to communicate science, with focus on acquiring transferable skills, generally applicable to everyone. A range of excellent speakers were invited from Norway and America, including Ole Petter Ottersen from CMBN.

The success of our first event has given us the inspiration to continue this initiative. We shall continue to arrange symposia, aiming at having an Autumn Symposium every September/October and a Spring Symposium every March/April. We also intend to arrange more social and learning events, and hope to become an invaluable part of the "official" academic PhD program, though we will need time to establish this properly. We are grateful for the moral and financial support given by the Institute and the Medical Faculty, especially Jarle Breivik, Gunnar Nicolaysen and Sigbjørn Fossum. We are also very grateful for the positive feedback from the PhD students themselves.

Lastly we are pleased to announce that the Forum Board is growing strong; we recently received two new members: Lisa Kjønigsen from the Institute of Anatomy and Harald Hrubus-Strøm from the Institute of Behavioral Sciences. In the future we hope to have a Board representing all six departments, including biostatistics, so that we may be sure to have a truly multidisciplinary board catering for as many interests as possible. We also hope we can set a good example for other institutes in the Faculty of Medicine.

Awards

Anders Jahre's senior and junior prize

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Inauguration of the Kavli Prize

By Professor Jon Storm-Mathisen

A major international event in science 2008 was when the Kavli Prizes were awarded for the first time in Oslo on September 9th. The prizes were presented by His Royal Highness, Crown Prince Haakon Magnus (www.kavliprize.no/nyheter/vis).

I serve as Chairman of the Kavli Prize Committee on Neuroscience, which consists of the following other members, appointed by the Norwegian Academy of Science and Letters (DNVA) among outstanding neuroscientist named by sister academies in Europe and the USA: Linda Buck, Jean-Pierre Changeux, Eric Kandel, Bert Sakmann.

The ***Kavli Prize*** is a joint venture by the DNVA, the Norwegian Ministry of Education and Research, and the Kavli Foundation (based in California). A prize of USD 1,000,000 is given in each of the three fields, astrophysics, nanoscience and neuroscience, to recognize the most significant basic research in the fields that the donator Fred Kavli thinks will bring the most magnificent future progress but which are not sufficiently emphasized by the Nobel Prize.

The vision of Mr. Kavli, the engineer born and educated in Norway who earned a fortune on transducers, is to ***enhance awareness of the importance of basic research***: "Practically everything we touch in our daily lives has been developed or improved through basic research" (F. Kavli, in his address announcing the establishment of the Kavli Prizes, at DNVA 2005). In his presentation of the Kavli Prize in Neuroscience at the award ceremony, which took place in the Oslo Concert Hall, hosted by Aase Kleveland, former Minister of Culture, Storm-Mathisen pointed out that curiosity driven basic research is a hallmark of human culture and indeed an inherent property of the human brain.

The ***Kavli Prize in Neuroscience 2008*** went jointly to Sten Grillner, Thomas Jessell, and Pasko Rakic "*for discoveries on the developmental and functional logic of neuronal circuits*". An in-depth commentary on the work of the prize winners, written by Joel C. Glower, can be found on www.kavliprize.no and will be printed in the journal *Neuroscience*. Interviews with the prize winners have been published in *Nature Reviews Neuroscience* January

Grillner, Kavli, Rakic, and Jessell (left to right) at the award ceremony

2009. The Prize lectures were given during the Kavli Prize Week in Oslo and Trondheim.

The ***selection process*** involved nominations from scientists worldwide. Neuroscience members of the DNVA assisted in the selection of the most qualified nominees. The Neuroscience Prize Committee produced a shortlist and finally decided on the awardees, at a meeting in New York, 28th April 2008.

CMBN researchers co-organized the ***Kavli Prize Inaugural Symposium on Neuroscience*** highlighting salient aspects of brain research in Oslo on September 9th 2008. The organizers were Linda H. Bergersen, Jon Storm-Mathisen (CMBN) and Edvard Moser and Mai-Britt Moser (NTNU). A symposium summary written by Dr. Miriam Sander is published in *Neuroscience*.

GlaxoSmithKline's prize

Janniche Hammer
PostDoc fellow

At Norsk Epilepsiselskaps annual meeting in September 2008 I was awarded GlaxoSmithKline's prize for epilepsy research. This prize goes to young investigators that have contributed to increase the understanding of epilepsy.

Educational activities

As in previous years, CMBN was proud of having Professors Peter Agre, Vilhelm Bohr, Karl P. Giese, Primo Schar and David W. Ussery as **guest professors**.

18 guest lectures were organised in 2008 with prominent international and Norwegian lecturers like Eberhard Fuchs (Gøttingen), Ross O'Shea (Melbourne), Tamas Freund (Budapest), Paola Bezzi (Lausanne) and Ursula Sonnewald (Trondheim), Ragnhild Paulsen (Oslo) and Øyvind Hvalby (Oslo).

One of the five seminars the Centre organised was in collaboration with Gaustad Neuroscience Network and focused on translational research in the region. Another was the third Genome Maintenance Meeting (GMM3) held on August 30th – September 2nd (www.cmbn.no/gmm3). The meeting included speakers, collaborators and participants from Europe, the US, Asia and Australia. Based on the meeting a thematic issue in the journal FEMS Microbiology Reviews was made (editors Bayliss, Casadesus, Rocha and Tønjum) with focus on genome instability and DNA-repair - alltogether 22 chapters and an introduction.

From Choclea to Cortex was the title of one of the six symposia the Centre had the responsibility for last year and was devoted to Professor Kirsten K. Osen's contributions to the field of auditory neuroscience. Kirsten Osen, a pioneer CMBN neuroscientist, is one of the pioneers

in the field of auditory neuroscience and dedicated her career to the study of the cochlear nuclei and other brain regions involved in the processing of auditory information. Professor Osen was affiliated with the Department of Anatomy and is still active as an emeritus professor. She has been involved with many CMBN projects and supervised PhD fellow Janniche Hammer who was awarded a prize in 2008 for her scientific endeavours (A more detailed description of the prize is described earlier in the report). As a tribute to Kirsten Osen on the occasion of her 80th anniversary CMBN arranged above mentioned international symposium at Holmenkollen Park Hotel. This event also marked the publication of a Special Issue of the Journal Neuroscience (see further down).

International Symposium "Physiological and pathophysiological roles of aquaporins in the brain"

June 9th – 10th 2008
by Professor Ole Petter Ottersen

This conference was the first international symposium that specifically focused on aquaporins in the brain, and was arranged by CMBN in partnership with theNordic Centre of Excellence in Molecular Medicine (WIRED) and Gaustad Neuroscience Network (GNN) (www.cmbn.no/events).

The symposium focused on molecular biological and functional aspects of water transport in the brain. Bioinformatics analyses of aquaporins, structure analyses, as well as advanced imaging analyses were included in the program. Furthermore, high-throughput screening for ligands for aquaporin-4 were presented and discussed in relation to plans of a chemical biology platform in Norway.

The discovery of water channels (aquaporins) in the brain has opened a new field in molecular medicine, and aquaporins are possible target molecules in the treatment of brain edema, epilepsy and hydrocephalus. Brain edema is a serious and common condition that lacks an effective therapy. It is the primary cause of death in numerous illnesses of the brain, including stroke, brain trauma, brain tumours and meningitis. It is a paradox that the current principles for therapy are the same as 70 years ago. The discovery of the water channel aquaporin-4 and its role in promoting brain edema, a discovery where Norwegian scientists played an important role, has provided a boost for research aimed at understanding the molecular biology and structure of water channels - as a platform for the development of new therapy.

The target groups for the conference were scientists within biotechnology, fundamental and clinical neuroscience, biology and molecular biology.

The meeting counted 26 national and international speakers and 160 participants. All key persons of the field, like Peter Agre (Nobel Prize winner 2003), Samira Saadoun, Olivera Nesic-Taylor and Marios Papadopoulos held presentations on the symposium.

Neuroscience – the official journal of the International Brain Research Organization (IBRO)

– is edited from CMBN
by Mette Ljungquist Johannessen
Editorial assistant

Neuroscience is one of the major international journals within the field of neurobiology and publishes results of original research on any aspect of the nervous system. Ole Petter Ottersen has served as Chief Editor of *Neuroscience* since January 2006 and is assisted in this capacity by Mette Ljungquist Johannessen, Editorial Assistant since June 2008. *Neuroscience* publishes 28 issues per year with close to 1800 papers. In addition to the regular issues, special issues are devoted to specific topics within neuroscience, preferably 'emergent topics' that open new fields in neurobiological research. The special issues have proved to be very successful in increasing the impact factor for Neuroscience. In 2008 *Neuroscience* published a Special Issue entitled *From Cochlea to Cortex: Recent Advances in Auditory Neuroscience* with Manuel S. Malmierca, Jon Storm-Mathisen and Nell B. Cant as Guest Editors. This special issue was published in honour of Professor Kirsten Osen on the occasion of her 80th anniversary.

Network building in translational research

Even before the term translational research became a phrase on everybody's lip it has been the Centre's strategy to create broad and strong alliances between the basic research community and the clinical environments. This strategy lay behind the establishment of Gaustad Neuroscience Network in January 2005 and ever since the Centre has played an active role in organising seminars and meetings to heighten the awareness of the competence and technologies that are available within the neuroscience community. The ambition is to create an internationally competitive network in translational neuroscience in Norway.

As of today, the network has its own Board consisting of leading basic scientists and clinical researchers of the Gaustad campus. The Board works actively to enlarge the scope of participating environments to include not only Oslo and the Oslo region but the whole of Norway.

To promote network building the Centre has entered an alliance with Innovation Norway in 2008 with the explicit aim of establishing a neuroscience cluster consisting of the best scientific and industrial communities of the field. As part of this work the Centre was participant and/or co-organiser of two international meetings, one in Paris in November and one in London in December 2008 with the purpose of broadening the scope of our national and international contacts.

International networking in translational research is promoted in EATRIS, the European Advanced Translational Research Initiative, where CMBN, represented by Deputy director Tone Tønjum, is fronting the programme on educational training.

The significance of translational research

by Barbra Noodt
Special advisor on science
South-Eastern Health Region

The South-Eastern Regional Health Authority has in its research strategy for 2008-2011 decided to increase the research budget substantially for the coming years. An integrated and coordinated research system at high international level is to be established. This implies both further strengthening of excellent research groups, and that health care in all hospitals of the region is based on research activity. Patients shall benefit from the research results, therefore translational research and innovation have to be strengthened. The establishment of regional research networks, core facilities and research support will be important.

The system is to be coordinated with the universities and university colleges. The Norwegian centres of excellence should play an important role in this process by contributing with their competence, already existing regional infrastructure, schools for PhD students and networks both in basic and translational research.

Collaboration with Innovation Norway

by Special advisor
Ole Jørgen Marvik

Inspired by the success of Oslo Cancer Cluster, the neuroscience community in Norway would like to embark on a similar development. Innovation Norway's health sector team, led by Ole Jørgen Marvik, has expressed strong support for this initiative by CMBN and their colleagues in Trondheim, and taken a leading role in the planning of the emerging cluster. The aim is to qualify for a Norwegian Centre of Expertise application in two years. The theme of the cluster will be "The Ageing Brain", which aligns very well with the Norwegian Government's goals for their five year health initiative managed by Innomed.

University College London has Europe's largest and most productive neuroscience community, and is ranked number four globally. Innovation Norway's London office has recommended an alliance between the emerging Norwegian cluster and UCL and organized a joint one-day seminar to discuss collaboration opportunities on December 8th . The meeting took place at

the Queen Elisabeth II Conference Centre and brought together 51 academicians and company representatives, 34 from Oslo and Trondheim and 17 from UCL. There were a total of 11 companies of which five were Norwegian (Diagenic, Sonowand, Tipogen, HUNT Biosciences and Birkeland Innovation). Most of the companies attended the Genesis Conference the following day and groups form CMBN and the University of Trondheim (NTNU) organized a

joint exhibition booth. A follow-up meeting with UCL was held on January 23rd 2009 and discussions for a joint meeting in Oslo in September 2009 are in progress.

The formation of the neuroscience cluster will undoubtedly be facilitated by harvesting from the experience gained by the Oslo Cancer Cluster.

About Oslo Cancer Cluster

By Bjarte Reve
Managing Director

Oslo Cancer Cluster is a biotechnology cluster solely focused on developing new cancer treatments and diagnostics for the benefit of cancer patients all over the world.

Oslo Cancer Cluster is one of nine Norwegian Centres of Expertise, and the only one in the health sector in Norway. Oslo Cancer Cluster integrates members from the life science industry, research institutions, university hospitals, government and the Norwegian Cancer Society. The aims of the Cluster are to accelerate the development of innovative cancer diagnostics and treatments, and to ensure that patients get access to the new treatments developed.

Oslo Cancer Cluster is a natural regional cluster, where the interaction between members in the Oslo region provides ideal conditions for major synergy. The cluster was established in 2006 as a result of more than 80 years of excellent cancer-related activities in the region. Oslo Cancer Cluster comprises of about 50 members, including industrial companies, academic research institutions, health initiatives and support groups in the field of biotechnology – all with their main focus on cancer.

Oslo Cancer Cluster has more than 50 projects in pipeline. This is an impressive oncology pipeline on the world scale, and most likely the largest one outside the pharmaceutical industry. The members of Oslo Cancer Cluster represent more than 70 percent of the human resources in cancer research in Norway.

Oslo Cancer Cluster will build its own Innovation Park in Oslo right next to the Norwegian Radium Hospital. Unlike other innovation parks, this will include a fully integrated high school as well as companies, research facilities and the clinical trials unit of the Norwegian Radium Hospital. In September 2008 Oslo Cancer Cluster signed an agreement with the Council of Oslo to build the park and it will be up and running in August 2012.

Learning points in developing a biotech cluster

Firm strategic foundation and priorities
The work to develop a vision and aim together with the cluster members was very important in getting enough support and engagement within the Oslo Cancer Cluster in 2008. To make proper priorities has been the most important issue: what shall we do and what we shall not get involved in?

A meeting place between academia, biotech – and bigger firms is attractive
During 2008 we have organised regular Research and Development Forums and this gave both clinicians, cancer researchers and biotech firms a neutral and attractive meeting place to develop new relations. 60% of all cluster members had formal collaboration with each other by the end of 2008.

A specialised biotech cluster gives international attention.
There are few biotech clusters in the world which are so highly specialised as Oslo Cancer Cluster. Our collaborative partner Cancer-Bio-Santé in France is one of the few examples. Cancer is the disease which receives most research and development investments worldwide because of the huge unmet need for a more effective cancer treatment. International journals and big pharmaceutical companies are interested in creating innovation in Norway based on internationally renowned cancer research in the academic community.

120 years of neuroscience in Norway
Fridjof Nansen (1861 – 1930) was the first Norwegian neuroscientist of world format. Nansen's dissertation took place on April 28th 1888 exactly 120 years before the meeting which announced the first Kavli Prize laureates in neuroscience. Researchers from CMBN described the connection between these two important events in an article in the web-journal Forskning.no on April 28th 2008 (www.forskning.no/artikler/2008/april). The University of Oslo's monthly periodical Apollon described how subsequent development leading to the "Oslo School of Neuroanatomy" fostered modern Norwegian neuroscience research, epitomized by CMBN (www.apollon.uio.no/vis/art/2008_4/artikler/hjernen_osloskolen).

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