Neuroscience Special Lecture Announcement and Invitation:

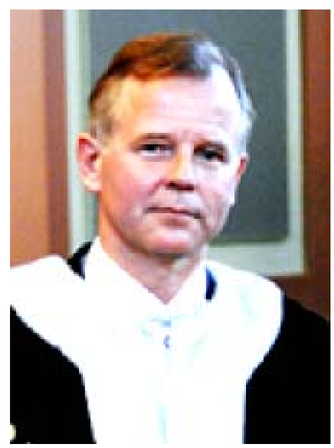
Date: Wednesday 6th January 2010

Place: Conference Room A, Neuro-Behavioural Biology Center, Institute of Molecular Biosciences, Mahidol University, Salaya Campus, 999 Phutthamonthol 4 Road, Salaya, Phutthamonthol, Nakornpathom 73170 Thailand

Time: 9.00 -12.00 AM

Special lecture 1:

The History and Future of Norwegian Neuroscience - *In the perspective of the Thailand-Norway Research Collaboration*



Professor Dr. Ole Petter Ottersen, MD, PhD
President, University of Oslo, Oslo, Norway
Former Director of CMBN and Professor, Department of Anatomy, Institute of Basic Medical Sciences, University of Oslo, Oslo, Norway

Background:

BRAIN RESEARCH FOR GENERATIONS: **Jan B. Jansen** and **Alf Brodal** established the so-called ***Oslo School of Neuroanatomy***, which became world famous for its brain research. Young researchers have been able to maintain its international reputation. The brain research undertaken at the University of Oslo remains in the world's top league.

In the 1930s a unique research environment was founded in Norway, which later was to develop into what in other countries is known as the Oslo School of Neuroanatomy.

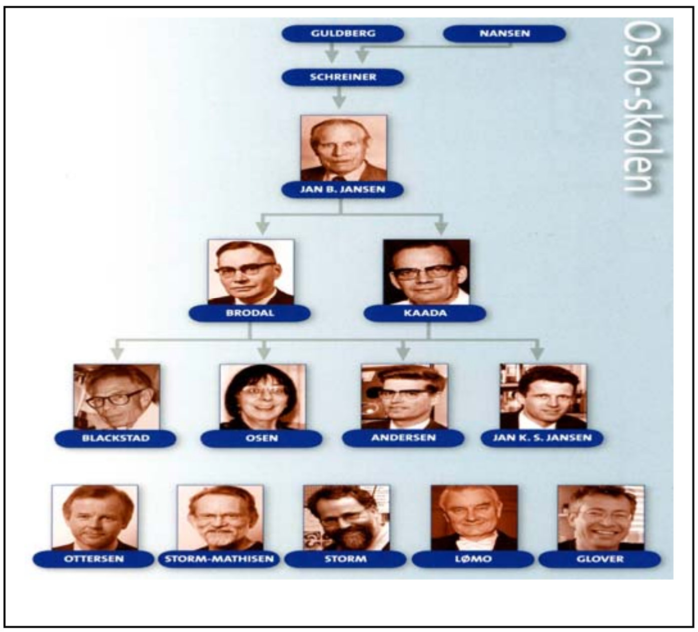
Over the years a handful of men and women have succeeded in placing Norway on the world map: **Ibsen, Munch, Undset, Heyerdahl, Solskjær**. And others too. To have the world's attention focused on a researcher is rare, and in Norway it is close to unthinkable.

Nevertheless, at the University of Oslo there are still men and women who have made a resounding impact in international scientific circles: They have produced new and pioneering research on one of the most complex phenomena in the universe – the human brain. We are not talking about two or three researchers, but an entire research environment which has been at the forefront over long periods, even decades.

Established "The Brain Lab"

How did it all start? What happened after **Fridtjof Nansen** strapped on his skis? Not much, and really nothing that could be compared to Nansen's achievements over a few short years before 1888. To be sure, during the period between the expedition to Greenland and the voyage with ***"Fram"*** he worked intermittently at the Anatomical Institute at the University of Kristiania (the former name of Oslo). Collaborating with the institute's professor, *Gustav Adolph Guldberg,* he investigated the brains of whales and other mammals.

More important, however, was this: The research tradition that these men founded made Professor Guldberg's successor, Professor *Kristian Emil Schreiner,* recruit a young and promising student, ***Jan B. Jansen****,* and ensure that he was able to study modern neurohistology in Chicago at one of the leading laboratories of the time. In 1929 Jansen returned to Norway to start the so-called brain laboratory at the Anatomical Institute, which at that time, and even during Dr Nansen's time, was located in the central university building on Karl Johan Street. This was to constitute the start of the Oslo School of Neuroanatomy.



The start of an adventure

– The laboratory was a fairly simple affair. Two chairs, two microscopes, a pair of scissors and a microtome (an instrument used to slice thin sections of tissue). The thought of it makes me smile. Nevertheless, the laboratory turned into a Mecca for Norwegian students of medicine and constituted the foundation for the strong brain research environment at the Anatomical Institute, says Professor Emeritus ***Per Andersen****.*

As a young medical student he became associated with this environment. Today he is 78 years old, and world famous for his research on the function of the contact points (synapses) between nerve cells.

– **Dr Jansen's** research focused on the structure of the cerebellum. International research institutions were impressed by the systematic representation of the cerebellum that Jan B. Jansen had succeeded in producing. While we gradually have established a solid understanding of the function of other parts of the brain, we still struggle to understand the cerebellum – a part of the brain that mainly governs coordination of movement, balance and posture. For me, it was inspiring to observe the enormous respect that this researcher enjoyed internationally, Andersen says.

In collaboration with his student ***Alf Brodal**,* **Dr Jansen** founded the so-called Oslo School of Neuroanatomy. This research group was soon to attract attention in other parts of the world.

Magnetic power of attraction

– **Dr Brodal's** ideas and the intensity of his work acted as a magnet for young researchers, from Norway as well as abroad. In other countries, researchers started to refer to the "Oslo School of Neuroanatomy" and to Oslo as the "capital of the cerebellum", Andersen says.

Alf Brodal made use of new methods to map nerve pathways in the brain, mainly in the brainstem and the cerebellum, where he documented hitherto unknown nerve fibre connections. In the period from 1940 to 1979, Dr Brodal was considered one of the ten leading neuroanatomists in the world. He was nominated as a Nobel Prize candidate on several occasions.

An impressive feature of the Anatomical Institute is the fact that the younger researchers who continued the efforts of Dr Jansen and Dr Brodal have been able to maintain the international reputation of the institute. A number of their students continued their legacy, including *Fred Walberg* as well as several collaborators from Norway and abroad, he says.

Another prominent scholar in this field was ***Theodor Blackstad**.* His research on the nerve fibre connections in the hippocampus, a part of the cerebral cortex that is especially important for learning and memory, laid the foundation for all subsequent research on this part of the brain.

– In 1959, Dr Blackstad established Norway's first laboratory for electronic microscopy. The laboratory at the Anatomical Institute was one of the first in the world to use this new method to study nerve tissue and to map nerve pathways in the brain.

Already in his early days as a medical student, Per Andersen came into contact with the neuroscience research environment at the Anatomical Institute, at the time when Dr Jansen and Dr Brodal were its leading scholars.

– Gradually I was included in the circle of researchers around ***Birger Kaada**.* He was Norway's first neurophysiologist and had his own laboratory at the Anatomical Institute. Another colleague was Dr Jansen's son, ***Jan K. S. Jansen**,* who discovered the two ways in which our muscle spindles (sense organs of muscles, necessary for the control of movements) are governed: dynamically and statically. This finding was of fundamental importance and attracted a lot of attention.

For the first time

Early in the sixties, Dr Andersen visited the laboratory of the later Nobel Prize laureate Sir *John Eccles* in Canberra. This collaboration had a large impact on Andersen's scientific efforts, and also for Eccles' own research, according to the Nobel laureate himself.

– I have made three discoveries that I find valuable, Andersen says modestly:

– In 1962, Eccles and I showed that a certain type of synapse in the cerebellum and in the hippocampus, the memory centre, are inhibitory. This was the first time that anybody had identified an inhibitory synapse.

– In the hippocampus, my collaborators and I detected what the electrical signals used by the cells actually look like when recorded. This interpretation has later been used by many scientists. In addition, we found that the nerve fibres in the hippocampus mainly have a parallel course, meaning that slices can be cut from the hippocampus without severing the nerve fibre connections. Based on this finding, my group developed a method to keep slices of the hippocampus alive in dishes with saline, preserving parts of the nervous network intact and open to detailed study. The method was a success and is currently used by a large number of laboratories all over the world, Andersen says.

The first woman to be appointed professor of medicine in Norway, *Kirsten Kjelsberg Osen,* also belongs to this research environment. She is a leading authority on the complex auditory pathways of the brain, and the papers that she published in the sixties opened the gates to a flood of new studies in this field.

At the same time, working in the laboratory of Per Andersen, ***Terje Lømo*** and his collaborator ***Tim Bliss*** from London discovered how nerve contacts (synapses) can be trained, a phenomenon called **long-term potentiation (LTP).**

– This is currently the most popular model for cell changes responsible for learning and memory.

– Brave as Nansen

A key person in the current research environment is ***Jon Storm-Mathisen****,* who is also a student of Per Andersen and Theodor Blackstad.

– In the seventies, together with ***Frode Fonnum and Fred Walberg***, he made the first findings to show that gamma-aminobutyric acid (GABA) is the most important inhibitory signal substance in the brain, and that glutamate is the key excitatory signal substance. The balance between these two is crucial for the brain to function. In 1983, Storm-Mathisen, along with ***Ole Petter Ottersen*** and others, published a pioneering article in Nature.

– Until then, nobody had succeeded in creating a method that could make amino acids like glutamate and GABA visible under the microscope. Jon was courageous and original in the same manner as Nansen: He had the excellent idea of injecting the amino acid in a “fixed” form under the skin of a rabbit. The rabbit’s immune cells developed antibodies that attached themselves to the amino acid. Tissue samples could then be treated with antibodies and processed to make the antibodies visible: the signal substances in the tissue became directly visible under the microscope. This was a real breakthrough, Andersen claims.

Storm-Mathisen’s method was so innovative that the editors of Nature first rejected the article. Today the immunocytochemical demonstration of amino acids has become so commonplace that the original articles are no longer cited. Storm-Mathisen has produced a number of further research breakthroughs and has published more than 220 articles in international scientific journals. He is one of the most cited researchers in the world.

In collaboration with Dr Storm-Mathisen, Ole Petter Ottersen developed the method further, and the amount of amino acids in the cells and the cell components can currently be measured with the aid of an electron microscope.

– Ole Petter Ottersen has also studied how the glutamate receptors are distributed in different synapses and is responsible for much of the pioneering research on the water channels in the brain cells. These channels can allow too much water to flow into the brain, as can happen in the case of a stroke, Dr Andersen explains.

One of Per Andersen's students, ***Johan F. Storm**,* studies the activity of the individual brain cells, and how the electrical signals are generated and regulated. He has discovered several ion channels that regulate the sensitivity of the nerve cells. ***Joel Glover*** is another key researcher.

– Glover is a student of Jan K. S. Jansen and studies the nerve cells in the spinal cord. He investigates how nerve cells develop and connect, and whether it will be possible to repair the connections in the case of injuries by placing stem cells in an injured area, Andersen says.

Best even today

Today the Anatomical Institute has been renamed the Department of Anatomy within the Institute of Basic Medical Sciences. Many of the researchers who graduated from the **"Oslo School of Neuroanatomy"** are currently found at the **Centre for Molecular Biology and Neuroscience**, one of Norway's Centers of Excellence in Research.

Never before have so many prominent scholars of neuroscience and biomedicine joined forces in Norway to investigate matters related to the brain. Their goal is to generate further knowledge on the molecular and genetic mechanisms for transmission of signals, aging and cell decay in the nervous system.

– There can be no doubt that the brain research group at the University of Oslo has remained at the absolute forefront to this day, Per Andersen concludes.

BESTSELLER

– My father had a remarkable ability to collect and present scientific material with a highly critical eye, says Professor **Per Brodal** at the Department of Anatomy, University of Oslo. In his hand he holds the book "Neuroanatomy" by the brain researcher Alf Brodal, first published in 1943 and later issued in several new editions and translations.

– The book is known all over the world, the author's son states. Another well-known book is "The Central Nervous System", which was read by Norwegian medical students as early as in the fifties. Per Brodal himself has updated this seminal publication. In his hand he holds his own book "The Central Nervous System", which was issued in its fourth edition last year. It was published by Oxford University Press and has received favourable reviews internationally.

– My ambition is to bridge the gap between basic science and clinical application, Brodal Jr. states.

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Special lecture 2:

How hardwired is the Brain?

Professor Dr. Ole Petter Ottersen, MD, PhD

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THE BRAIN IS MALLEABLE
The brain is capable of being altered by outside forces or influences

- Plasticity at the level of synapses and glia: *multiphoton imaging technology*
- Plasticity (mobility) at the level of neurotransmitter receptors: *single molecule tracking*
- Plasticity is restrained by extracellular matrix molecules: *the importance of extracellular matrix proteinases*

Special Lecture 3:

Organotypic Cultures as a Model of Parkinson´s Disease: A Twist to an Old Model

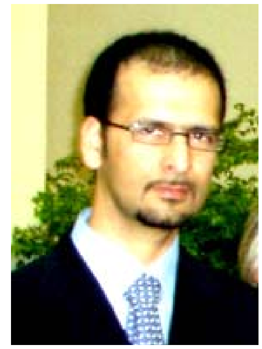
Dr. Reidun Torp, PhD

Senior Researcher,
Center of Excellence for Molecular Biology and Neuroscience (CMBN),
Institute of Basic Medical Science, Faculty of Medicine, University of Oslo,
Oslo, Norway

Abstract:

Organotypic cultures from the ventral mesencephalon (VM) are widely used to model Parkinson's disease (PD). In this method, neurotoxic compounds have traditionally been applied to the media to induce a uniform dopaminergic (DAergic) cell death in the tissue slices, regardless of the variation existing among slices. This study demonstrates a refinement of the toxic induction technique. We show that unilateral application of 6-hydroxydopamine (6-OHDA) at the tissue surface by means of a microelectrode causes a precisely localized cell death that closely resembles an *in vivo* stereotactic model. This technique introduces an internal control that accounts for variation between slices and enables a precise quantification of the cell loss due to the toxin in use. We characterized organotypic VM cultures in terms of effects of 6-OHDA toxicity and number of DAergic neurons as judged by immunofluorescence and Western blots. Our findings illustrate that this new application technique greatly improves the representativeness of organotypic cultures as a model for PD.

Special Lecture 4:
Aquaporin, water channel, in health and diseases.



Dr. Mahmood Amiry-Moghaddam, MD, PhD
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Group leader of a subgroup at the Laboratory of Molecular Neuroscience (LMN):
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Abstract:
Aquaporins are channel forming membrane proteins mediating rapid water movement across the cell membranes. The first aquaporin water channel was discovered in the red blood cells in 1992. Since then, more than 13 members of the aquaporin family have been identified. These channels are expressed in most organs such as kidney, gastrointestinal tract, lungs, skin, muscle and CNS. Many of these channels are today drug targets for future therapy. This lecture will give a general overview of some aquaporins with emphasis on the role of aquaporins brain physiology and pathology.