Danish Stroke Collaboration Symposium 2016

16 - 17 June 2016

Eduard Bierman Auditorium
Lakeside Lecture Theatres, Aarhus University
&
Auditorium B, Aarhus University Hospital, Skejby

Scientific Organizing:

Kim Ryun Drasbek
Center of Functionally Integrative Neuroscience (CFIN)
Aarhus University
ryun@cfin.au.dk

Kate Lykke Lambertsen
Department of Neurobiology Research, Institute of Molecular Medicine, University of Southern Denmark
klambertsen@health.sdu.dk

Bettina Hjelm Clausen
Department of Neurobiology Research, Institute of Molecular Medicine, University of Southern Denmark
bclausen@health.sdu.dk

Vibeke Bay
Center of Functionally Integrative Neuroscience (CFIN)
Aarhus University
vibeke.bay@cfin.au.dk

PROGRAM AT A GLANCE ...

THURSDAY 16 JUNE 2016
Eduard Bierman Auditorium, Lakeside Lecture Theatres, Aarhus University

Talks by:

- Kate Lykke Lambertsen,
  Department of Neurobiology Research, SDU
  Microglial-macrophage TNF and neuroinflammation

- Anders Bach
  Department of Drug Design and Pharmacology, KU
  Targeting Oxidative Stress in Stroke

- Kim Ryun Drasbek
  Center of Functionally Integrative Neuroscience, AU
  Profiling extracellular vesicles and miRNA in plasma

- Zindy Raida
  Scanbur
  How to pick the right animal-model for your research

- **Keynote lecture: Grethe Andersen**
  Danish Stroke Center, Dept. of Neurology, AUH
  Modern Stroke diagnostics and treatment. New direction for stroke research

FRIDAY 17 JUNE 2016
Auditorium B, Aarhus University Hospital, Entrance 6

Talks by:

- Anne Nielsen
  Center of Functionally Integrative Neuroscience, AU
  Deep learning: Utilizing the potential in data bases to predict final outcome of acute stroke

- Bettina Hjelm Clausen
  Department of Neurobiology Research, SDU
  Cell therapy centered on IL-1Ra is neuroprotective in experimental stroke

- Jens Nyengaard
  Stereology and Electron Microscopy Laboratory, AU
  Structural characterization of brain after experimental stroke

THURSDAY 16 JUNE 2016

Eduard Bierman auditorium, Lakeside Lecture Theatres, Aarhus University

14.30 – 14.50	Registration and coffee
14.50 - 15.00	Welcome
15.00 – 16.30	Session 1 (Chair: Torben Moos, AAU)
15.00 – 15.20	**Kate Lykke Lambertsen**, Department of Neurobiology Research, IMM, SDU & Department of Neurology, OUH *Microglial-macrophage TNF and neuroinflammation*
15.25 – 15.45	**Anders Bach**, Department of Drug Design and Pharmacology, KU *Targeting Oxidative Stress in Stroke*
15.50 – 16.10	**Kim Ryun Drasbek**, Center of Functionally Integrative Neuroscience, AU *Profiling extracellular vesicles and miRNA in plasma*
16.15 – 16.25	**Zindy Raida**, Scanbur *How to pick the right animal-model for your research*
16.30 – 17.00	Break
17.00 - 17.45	Keynote lecture (Chair: Kim Ryun Drasbek, AU) **Grethe Andersen**, Danish Stroke Center, Dept. of Neurology, AUH *Modern Stroke diagnostics and treatment.* *New direction for stroke research*

19.00	**Symposium dinner** Venue: Restaurant Komfur Guldsmedgade 38-40 Phone: +45 86 12 33 90 restaurant komfur

ABSTRACTS - THURSDAY 16 JUNE 2016

Kate Lykke Lambertsen
Department of Neurobiology Research, IMM, SDU & Department of Neurology, OUH
Microglial-macrophage TNF and neuroinflammation

Inflammation is a hallmark of acute trauma to the CNS. The tumor necrosis factor (TNF) signaling cascade modulates tissue injury in experimental stroke and spinal cord injury and is therefore a potential target in future therapies. We have studied the action and the cellular expression of TNF in focal cerebral ischemia and spinal cord injury in mice. We find a neuroprotective effect of microglial-derived transmembrane-TNF, but not soluble-TNF nor macrophage-derived TNF, in several different transgenic and chimeric mouse strains. We also report that selectively blocking soluble-TNF, using XPro1595, is associated with neuroprotection after spinal cord injury and improved functional outcome after both experimental stroke and spinal cord injury. All together, this talk will focus on the function of microglia, and TNF signaling in cerebral ischemia and spinal cord injury.

Anders Bach
Department of Drug Design and Pharmacology, KU
Targeting Oxidative Stress in Stroke

Recently, the Bach Group was started with the aim of establishing a drug discovery platform and applying it for finding new small-molecule inhibitors of CNS targets related to ischemic stroke. In this presentation, I will describe general pharmacological strategies for inhibiting oxidative stress, which play a crucial role in mediating severe toxicity in the acute phase of stroke, and initiating and contributing to late-stage apoptosis and inflammation. Specifically, I will discuss the targets we currently focus on (Keap1, NADPH oxidase, and PSD-95) and our approach to drug discovery, which comprises fragment-based strategies and multi-target inhibitors. Recent results related to our most advanced target, Keap1, will be presented.

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ABSTRACTS - THURSDAY 16 JUNE 2016

Kim Ryun Drasbek
Center of Functionally Integrative Neuroscience, AU
Profiling extracellular vesicles and miRNA in plasma

The role of extracellular vesicles (EVs) in distant cell-to-cell signaling is currently being explored for a number of circumstances and diseases. EVs (incudes exosomes, microparticles, and microvesicles) are secreted by many different cell types and by separate pathways. This influences the surface of the EVs, which might direct the EVs to specific target cells and areas. As the content of in vitro cell-derived EVs can be controlled, and naturally in vivo secreted EVs can be filled with engineered content, EVs holds the potential as natural vehicles for drug delivery in personalized medicine. An overview of some of the numerous methods developed to isolate these EVs will be given as well as insights in the profiling of EVs.

Even though changes in EV number have been correlated with beneficial effects following treatment, the content of the EVs could also prove to be important in their signaling capabilities. Especially the high content of distinct microRNAs (miRNAs) are interesting as miRNAs posttranscriptionally regulates the translation of over 50% of all cellular mRNAs to proteins. These short 22 nucleotide long RNA molecules controls mRNA translation by either blocking protein synthesis or mediating degradation of the mRNA. Profiling the content of the substantial number of miRNAs in EVs takes advantage of the great advances in sequencing and/or chip technologies coupled with bioinformatics tools.

Taken together EVs and miRNA could be a central part of the signaling pathway underlying the protective effects of remote ischemic conditioning in stroke.

Zindy Raida
Scanbur
How to pick the right animal-model for your research

To pick the right animal model for your research is important to ensure data validity and reproducibility.

I will give you a quick introduction into the most important considerations you should make before choosing your animal model and also introduce you to the most common mistakes and their possible impact.

ABSTRACTS - THURSDAY 16 JUNE 2016

Grethe Andersen
Danish Stroke Center, Dept. of Neurology, AUH
Modern Stroke diagnostics and treatment. New direction for stroke research

Modern stroke diagnostics and treatment has changed the prognosis for acute ischemic stroke dramatically. In this new revascularization era it has become important to investigate neuroprotection in a timely fashion and in combination with r-tPA or endovascular treatment. Diagnostic MR is increasingly used and infarct growth or tissue salvage is important surrogate measures to prove the potential of neuroprotection and control for the influence of heterogeneous stroke types. To maximize brain tissue salvage also pre-hospital stroke symptom registration and organization is imperative in order to use transport times efficient and start neuroprotective trials as soon as possible. Examples from a per-conditioning trial in acute stroke and a register based hypothesis generating study of SSRI treatment before, during and after acute stroke will be discussed.

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FRIDAY 17 JUNE 2016

Auditorium B, Aarhus University Hospital, Entrance 6

13.30 – 14.40	Session 2 (Chair: Kate Lykke Lambertsen, SDU)
13.30 – 13.50	**Anne Nielsen**, Center of Functionally Integrative Neuroscience, AU *Deep learning: Utilizing the potential in data bases to predict final outcome of acute stroke*
13.55 – 14.15	**Bettina Hjelm Clausen**, Department of Neurobiology Research, SDU *Cell therapy centered on IL-1Ra is neuroprotective in experimental stroke*
14.20 – 14.40	**Jens Nyengaard**, Stereology and Electron Microscopy Laboratory, Centre for Stochastic Geometry and Advanced Bioimaging, AU *Structural characterization of brain after experimental stroke*

ABSTRACTS - FRIDAY 17 JUNE 2016

Anne Nielsen
Center of Functionally Integrative Neuroscience, AU
Deep learning: Utilizing the potential in data bases to predict final outcome of acute stroke

Acute ischemic stroke is one of the major diseases responsible for severe disability and death. Brain tissue tolerates ischemia quite poorly and rapid reperfusion through endovascular and/or thrombolytic treatment is thus of utmost importance for good outcome. The decision to treat is today based on images of the brain obtained from either computed tomography (CT) or magnetic resonance imaging (MRI). Naturally, there have been many attempts to automate the treatment decision based on identifying features in the images using so-called morphological methods or logistic regression based algorithms. So far with only limited success and clinical adaptation.

In recent years a technique known as 'deep learning' has become popular and widely used. Especially a branch called artificial neural networks is now a technique with extensive application in both science and everyday life, used extensively by companies such as Google, Facebook, Netflix, etc. An artificial neural network works by mimicking the learning mechanisms of the human brain, which – like the human brain – makes it ideal for image classification and segmentation.

The talk will focus on recent work, where predicting stroke final outcome using artificial neural networks in conjunction with a MRI-based database of previous patients has been pursued. I will give a brief introduction to the neural network technique and put some focus on the perhaps most important steps: Training and test. In addition, preliminary results will be presented, which show significant improvement of performance over current state-of-the-art methodology. The neural network technique has shown the making of an important support-decision tool in neuroscience and medical science in general.

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ABSTRACTS - FRIDAY 17 JUNE 2016

Bettina Hjelm Clausen
Institute of Molecular Medicine, Department of Neurobiology Research, University of Southern Denmark, Odense
Cell therapy centered on IL-1Ra is neuroprotective in experimental stroke

Cell-based therapies are emerging as new promising treatments in stroke. However, their functional mechanism and therapeutic potential during early infarct maturation has so far received little attention. Here, we asked if cell-based delivery of the interleukin-1 receptor antagonist (IL-1Ra), a known neuroprotectant in stroke, can promote neuroprotection. First we show by the use of IL-1Ra-overexpressing and IL-1Ra-deficient mice that IL-1Ra is neuroprotective in stroke. Characterization of the cellular and spatiotemporal production of IL-1Ra and IL-1α/β identifies microglia, not infiltrating leukocytes, as the major sources of IL-1Ra after pMCAo. Reconstitution of whole body irradiated mice with IL-1Ra-producing bone marrow cells is associated with neuroprotection and recruitment of IL-1Ra-producing leukocytes after pMCAo. Neuroprotection is also achieved by therapeutic injection of IL-1Ra-producing bone marrow cells 30 min after stroke onset, additionally improving the functional outcome. The IL-1Ra-producing bone marrow cells increased the number of IL-1Ra-producing microglia and reduce the availability of IL-1 . The importance of these results is underlined by demonstration of IL-1Ra-producing cells in the human ischemic cortex. Combined, our results attribute distinct neuroprotective or neurotoxic functions to segregated subsets of microglia and suggest that treatment strategies increasing the production of IL-1Ra by leukocytes or microglia may also be neuroprotective.

Jens Nyengaard
Stereology and Electron Microscopy Laboratory, Centre for Stochastic Geometry and Advanced Bioimaging, AU
Structural characterization of brain after experimental stroke

The brain has a high glucose-dependent metabolism and is therefore very sensitive to injury. Brief episodes of oxygen deprivation or compromised blood flow may result in irreversible neuronal and glial cell damage. Both ischemic and hemorrhagic stroke may result in structural brain damage which may be quantified both at the macroscopic and microscopic level.

The presentation will show a battery of quantitative structural methods which can be used to assess the damage in the brain: Volume of the infarcted region may be estimated by the Cavalieri estimator and 2D nucleator. Neuronal and glial cell numbers may be estimated by the optical fractionator. Length and surface of blood vessels may be estimated by global spatial sampling and the Fakir method, respectively. Length and complexity of neuronal dendritic tree or astrocyte processes may be estimated after 3D reconstruction in thick (200 µm) sections and evaluated by specialized software.

Participants at
Danish Stroke Collaboration Symposium 2016

Name	Affiliation	E-mail
Anders Bach	Faculty of Health and Medical Sciences Department of Drug Design and Pharmacology University of Copenhagen	anders.bach@sund.ku.dk
Anne Nielsen	CFIN, Aarhus University	anne@cfin.au.dk
Badam Shafaq	Hammel Neurorehabilitation and Research Center	badashaf@rm.dk
Barbara Blicher Thomsen	Department of Veterinary Clinical and Animal Sciences, University of Copenhagen	blicher@sund.ku.dk
Bettina Hjelm Clausen	Department of Neurobiology Research, Institute of Molecular Medicine, University of Southern Denmark	bclausen@health.sdu.dk
Claus Z. Simonsen	Dept. of Neurology, Aarhus University Hospital	clausimo@rm.dk
Grethe Andersen	Dept. of Neurology, Aarhus University Hospital	greander@rm.dk
Hanne Gredal	Department of Veterinary Clinical and Animal Sciences, University of Copenhagen	hbg@sund.ku.dk
Jane Fuglsang	Nordic Biosite	jane.fuglsang@nordicbiosite.com
Jens R Nyengaard	Aarhus University	jrnyengaard@clin.au.dk
Jesper Just	CFIN, Aarhus University	jesperj@cfin.au.dk
Kate Lambertsen	Department of Neurobiology Research, Institute of Molecular Medicine, University of Southern Denmark	klambertsen@health.sdu.dk
Kim Ryun Drasbek	CFIN, Aarhus University	ryun@cfin.au.dk
Kristian Sandberg	Hammel Neurorehabilitation and Research Center, Aarhus University Hospital	krissand@rm.dk
Lisa Juul Routhe	Aalborg University	ljr@hst.aau.dk
Maryam Ardalan	CFIN, Aarhus University	maryam.ardalan@clin.au.dk
Mette Sloth	CFIN, Aarhus University	mettesloth89@yahoo.dk
Michael Andreasen	Hammel Neurorehabilitation and Research Center	
Minna C. Lund	Department of Neurobiology Research, Institute of Molecular Medicine, University of Southern Denmark	milu@sdu.dk
Minna Yli-Karjanmaa	Department of Neurobiology Research, Institute of Molecular Medicine, University of Southern Denmark	myli@health.sdu.dk
Rolf Blauenfeldt	Dept. of Neurology, Aarhus University Hospital	rolfblau@rm.dk
Sidsel Hastrup	Dept. of Neurology, Aarhus University Hospital	sidshast@rm.dk
Simon Flæng	Department of Neurobiology Research, Institute of Molecular Medicine, University of Southern Denmark	sflaeng@health.sdu.dk
Susanne Smith Christensen	CFIN, Aarhus University	susanne@cfin.au.dk
Thorbjørn Engedal	CFIN, Aarhus University	tsengedal@gmail.com
Torben Moos	Department of Health Science and Technology, Aalborg University	tmoos@hst.aau.dk
Tristan Hollyer	CFIN, Aarhus University	tristan@cfin.au.dk
Ulla Laursen	Nordic Biosite	ulla.laursen@nordicbiosite.com
Vibeke Bay	CFIN, Aarhus University	vibeke@cfin.au.dk
Zindy Raida	Scanbur	zindy.raida@scanbur.eu

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