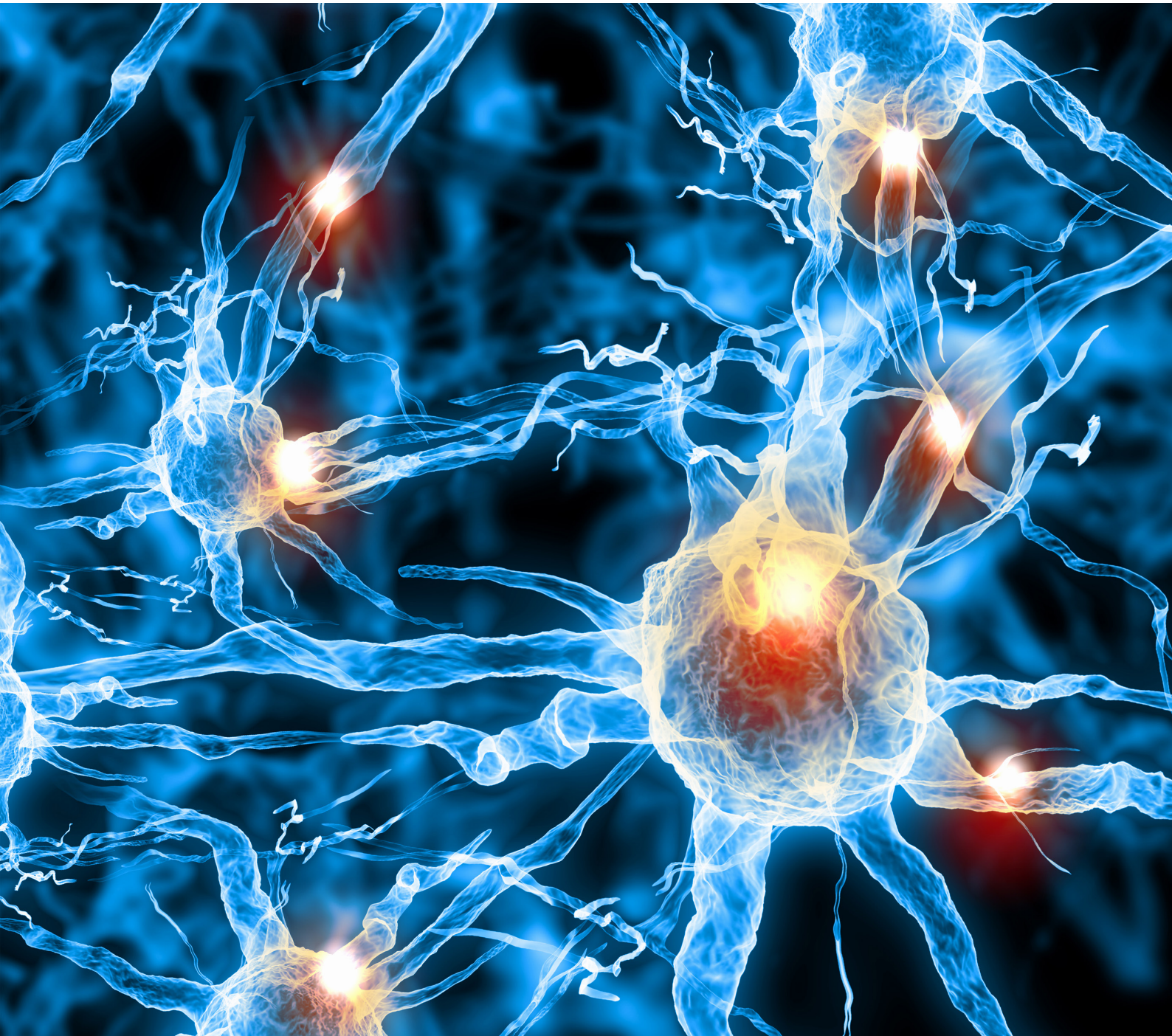
DANDRITE

Danish Research Institute of Translational Neuroscience
Nordic EMBL Partnership for Molecular Medicine

ANNUAL REPORT 2014



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WORDS FROM THE DIRECTOR

It is with our great pleasure to present the second annual report from DANDRITE - the Danish Research Institute of Translational Neuroscience, which is also the Danish node of the Nordic-EMBL Partnership for Molecular Medicine. Headlines of 2014: expanding research, successful recruitment and start of two new group leaders, growth in the groups and many new faces at DANDRITE, launch of the DARE program for collaborative research, addition of team leader and affiliated researcher programs, launch of joint DANDRITE seminar series, and a first assembly of the scientific advisory board.

SECOND YEAR OF DANDRITE

The neuroscience of DANDRITE is thriving and expanding with the growing team of group leaders (see below) and the initiation of many new PhD and postdoc programs. As can be seen from our report the groups cover very exciting research ranging from the structure, function and genetic make-up of protein complexes in brain to circuit neuroscience, behavior and disease biology studied in model organisms and man - "from atomic to anatomic" we like to say. The large width of the DANDRITE research program, which is yet also of a focused nature with deep expertise at all levels, offers a wealth of opportunities for collaborations with academia, clinical research and industry, and the DANDRITE Associated Research (DARE) initiative was therefore launched to lower the barrier for ambitious, new collaborations to flourish.

Photo: Lars Kruse

This also called our attention to the organizational structure of DANDRITE, which has been consolidated and augmented for optimal synergy of research and infrastructure to develop, and the training and career development of young researchers to be strengthened. DANDRITE group leaders have furthermore initiated departmental seminar series and joint seminar series with other research communities and named seminar series at Aarhus University, such as the Kjeldgaard lectures of Molecular Biology and Genetics, the iNANO distinguished lectures, the Aarhus University Hospital, NeuroCampus Aarhus, MEMBRANES, and iPSYCH.

Growing as an organization DANDRITE has defined two levels of associations for other research groups at Aarhus University, namely as Team Leaders for independent researchers in non-tenured positions, and as Affiliated Researchers for tenured researchers (see section ACADEMIC ORGANIZATION page 26).

With a steadily increasing number of groups and young researchers associated with DANDRITE, Internal Meetings have been launched every second week based on project presentations to strengthen internal communications and the free exchange of ideas, discussions and expertise. Furthermore, our communications through dandrite.au.dk and newsletters are circulated to many communities in Denmark and abroad, and we support many levels of popular communications and outreach.

December 2nd, 2014	DANDRITE open symposium "New Frontiers in Molecular and Translational Neuroscience", featuring lectures by four invited candidates for a group leader position, and with EMBL and Nordic-EMBL Partnership members among attendees (see below).
November 27th, 2014	Seminar by Senior Scientist Nikolai Engedal from the Centre for Molecular Medicine Norway - NCMM of the Nordic EMBL Partnership for Molecular Medicine: "Deciphering how calcium and ER stress responses affect autophagy in prostate cancer cells".
September 15th, 2014 to January 15th, 2015	Joint hiring process for group leaders at all four nodes of the Nordic EMBL Partnership for Molecular Medicine (NMMN). DANDRITE recruitment of the fifth and final group leader. The following professors from NMMN/EMBL participated in the assessments and interview process: For DANDRITE, Aarhus University: Director Prof. Poul Nissen, Professor Poul Henning Jensen, and Professor Anders Nykjær. For EMBL: Dr. Nassos Typas, EMBL Heidelberg, and Dr. Henning Hermjakob, EMBL-EBI Hinxton. For MIMS, University of Umeå: Professor Maria Fällman, Professor Sun Nyunt Wai. For NCMM, University of Oslo: Director, prof. Kjetil Taskén. Proffessor Hilde Nilsen. For FIMM, University of Helsinki: Director, professor Olli Kallioniemi research director Dr. Janna Saarela.
August 26th-28th, 2014	Nordic EMBL Partnership for Molecular Medicine: Annual meeting 2014. 25 PhD students, postdocs, professors and technical and administrative staff from DANDRITE participated among a total of 120 participants.
July 2nd-3rd, 2014	EMBO-EMBL Anniversary Science and Policy Meeting. The meeting was attended by directors and chief administrators of all four nodes of the Nordic-EMBL Partnership, executive board member and dean Allan Flyvbjerg (AU Health Sciences), and Danish EMBL representative Troels Rasmussen (Danish Agency for Research and Innovation). Business meeting of the partnership was arranged.
November 5th, 2013 to March 5th, 2014	Hiring process for two group leaders at DANDRITE (third and fourth). The following professors from NMMN/EMBL participated in the assessments and interview process: For DANDRITE, Aarhus University: Director, professor Poul Nissen, Professor Anders Nykjær, Professor Poul Henning Jensen, Head of department Erik Østergaard Jensen (Dept. of Molecular Biology and Genetics), and Head of department Thomas G. Jensen (Dept. of Biomedicine). For EMBL: Dr. Cornelius Gross and Dr. Paul Heppenstall, EMBL-Monterotondo. For NCMM: Professor Erlend Nagelhus, For MIMS: Professor Åke Forsberg. For FIMM: Professor Eero Castren.

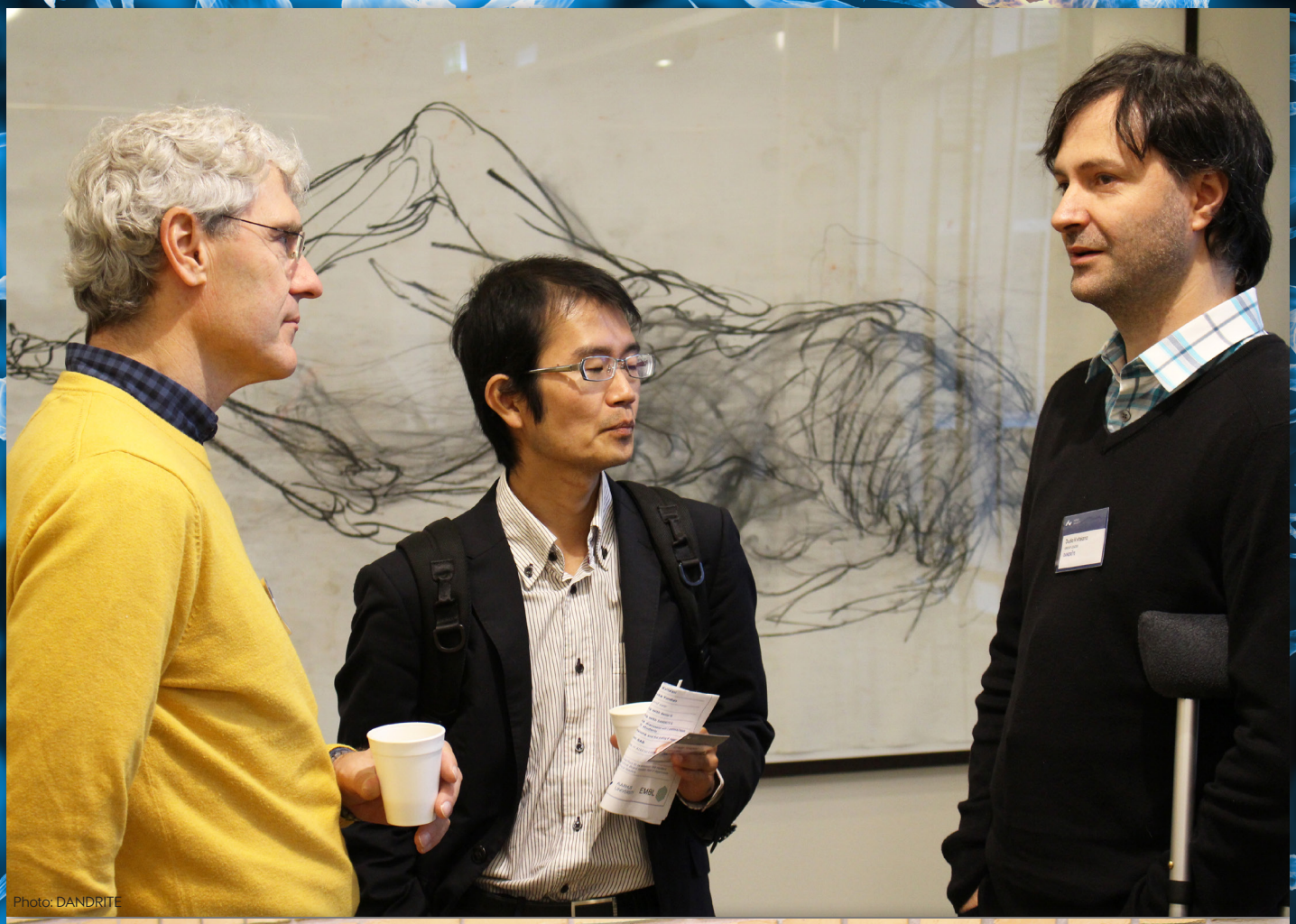


Photo: DANDRITE

Photo: DANDRITE

VISITORS, GUESTS & SEMINARS

December

- Visiting PhD student **Friederike Degenhardt,** TU Dortmund University, Germany, Hosted by Nissen lab (3 months).
- Visiting scholar student **Matthijs Wopke de Boer,** Hosted by Philipsborn lab (2 months).
- Visiting PhD student, **Sarah van Veen**, University of Leuven, Belgium, Hosted by Nissen lab (10 days).
- Visiting PhD students: **Maarten Rotman** and **Gangadaar Thotakura**, Mayo Clinic, US, Hosted by Nykjær lab (1 week).
- DANDRITE symposium "New frontiers in Molecular and Translational Neuroscience". Speakers:
    * **Andreas Zembrzycki**, Salk Institute, California, *Scale and scalability of sensory systems in the brain - Why (cortical area) size matters in development and disease.*
    * **Carsten Pfeffer**, University of California San Diego, *The Logic of Cortical Circuits*.
    * **Sadegh Nabavi**, University of California San Diego, *Can Memories be Implanted and Then Removed?*
    * **Tom Baden**, University of Tuebingen, Germany, *What the mouse eye tells the mouse brain.*

November

- DANDRITE Topical Lecture, **Nikolai Engedal**, Centre for Molecular Medicine (NCMM), Norway, *Deciphering how calcium and ER stress responses affect autophagy in prostate cancer cells.*
- DANDRITE Scientic Advisory Board meeting with DANDRITE staff, students, and Group Leaders.

- DANDRITE-DNC Joint Lecture, **Glenda Halliday**, University of New South Wales, Sydney, Australia, *Identifying the dynamics of Lewy body formation in Lewy body diseases.*

October

- DANDRITE-iPSYCH Joint Lecture, Dr. **Kristian Andersen**, The Broad Institute, Harvard/MIT, *Genomic surveillance elucidates Ebola virus origin and transmission during the 2014 outbreak.*

September

- DANDRITE-MBG Kjeldgaard Joint Lecture, Director, professor **Reinhard Jahn**, Max-Planck-Institute for Neurobiology, (city), *Molecular machines governing exocytosis of synaptic vesicles.*
- DANDRITE visiting scholar student **Amir Tayaranian Marvian**, University of Teheran, Iran, Hosted by Jensen lab (6 months).
- Visiting delegation of the neuroscience program of the Danish Institute for Studies Abroad (DIS) with 30 undergraduate students from US universities, day program hosted by DANDRITE.
- Visiting delegation of the biotechnology program of the Danish Institute for Studies Abroad (DIS) with 28 undergraduate students from US universities, day program hosted by DANDRITE.
- DANDRITE visiting scholar student **Ishita Guha Thakurta**, Hosted by Nykjær lab (4 months).

August

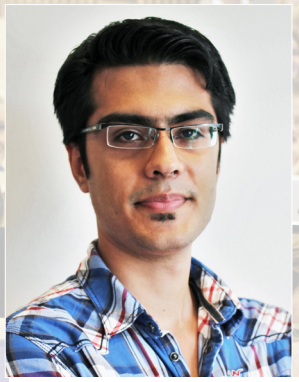
- Visiting scholar student **Mateusz Kostecki**, University of Warsaw, Poland, Hosted by von Philipsborn lab (2 months).
- Visiting PhD student **Jaroslava Geletičová**, Univ. Olumuc, Cech Republic, hosted by Nissen lab (6 months).

June-July

- DANDRITE topical seminar: Dr. **Azadeh Shahsavar**, University of Copenhagen, *Structural Insight into the Gating of a Pentameric Ligand-Gated Ion Channel, hosted by Poul Nissen.*
- 2014 Gordon Research Conference on Membrane Transport Proteins - "Structure, Function, Physiology, and Targets in Disease". Mount Snow Resort, Vermont. Conference chair: Poul Nissen

Student guest, Jaroslava Geletičová, Palacky Univ. Olomouc. Photo: DANDRITE

Research Guest Tom Baden, University of Tuebingen. Photo: DANDRITE



Student guest, Amir Tayaranian Marvian, University of Teheran, Photo: DANDRITE

May

- DANDRITE topical seminar: Dr. **Mia Pöhler**, University Hospital Erlangen, Germany, *The autophagy-lysosomal pathway in aggregation, release, and toxicity of alpha-synuclein* (host Poul Henning Jensen).
- DANDRITE-iNANO Joint Lecture, Prof. **John Johnson**, Scripps Research Institute, *Biophysical Studies of Virus Maturation: Insights into Elegantly Programmed Nano-machines.*
- Visiting Scholar student **Vesna Makovsek**, University of Ljubljani, Slovenia, Hosted by Denham lab (4 months).

January-April

- DANDRITE Symposium "New Frontiers in Molecular and Translational Neurosience". Speakers:
    * **Keisuke Yonehara**, Friedrich Miescher Institute for Biomedical Research, Basel, *Development and function of motion - sensitive circuits in the retina.*
    * **Volker Busskamp**, Harvard Medical School, Cambridge Massachussetts, *Repairing and rebuilding the human retina.*
    * **Sally Marik**, The Rockefeller University, New York, *Adult experience-dependent plasticity and the physiological role for amyloid precursor protein.*
    * **Dario Bonanomi**, The Salk Institute for Biological Studies, California, *Expanding the signaling repertoire for neuronal wiring.*
    * **Alessio Attardo**, Stanford University, California, *How does hippocampal cell biology support network information processing?*
    * **Arne Möller**, The Scripps Research Institute, California, *Nanomachines in action - Characterization of protein dynamics by high-throughput electron microscopy.*
    * **Duda Kvitsiani**, Cold Spring Harbor Laboratory, New York, *Diversity of cortical cell-types: Lessons from behavioral electrophysiology.*
    * **Judith Paridaen**, Max Planck Institute for Molecular Cell Biology and Genetics (city), *Dissecting the mechanisms of cell fate decisions in brain development: Primary cilia tip the scales?*

DANDRITE RESEARCH ACTIVITIES

Nissen Group - Structural and Functional Studies of Membrane Transporters in Brain

Photo: AU Communication

The Nissen lab investigates molecular mechanisms of membrane transport processes and biomembrane structure. Activities are mainly focused on structural biology and biochemistry, and include also collaborative studies on small-angle X-ray scattering, electron microscopy, molecular dynamics simulations, single-molecule FRET, and electrophysiology. Main subjects of research focus on P-type ATPases (ion pumps and lipid flippases) and Na+ dependent neurotransmitter and ion transporters, and include also structure based drug discovery and protein engineering.

In 2014 several studies addressed the effect of mutations, lipids and inhibitors on Na,K-ATPase and related ion pumps that consume some 40-70% of ATP turnover in the brain to maintain vital ion gradients. Na,K-ATPases also interact with the extracellular matrix, and clears potassium in the narrow, interstitial space of brain. A first report on quantitative purification of a stable lipid flippase sample was presented, which opens for structural and functional studies of these difficult-to-express proteins.

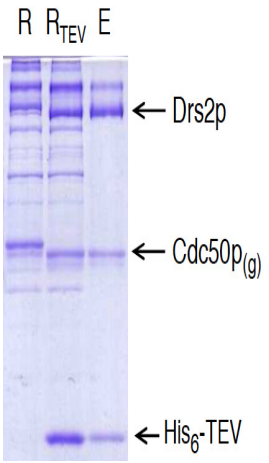


Figure: Azouaoui H et al. (2014).

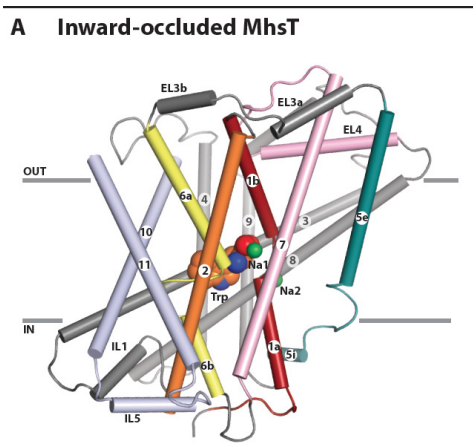


Figure: Malinauskaite L, Quick M, Reinhard L, Lyons JA, Yano H, Javitch JA, Nissen P (2014).

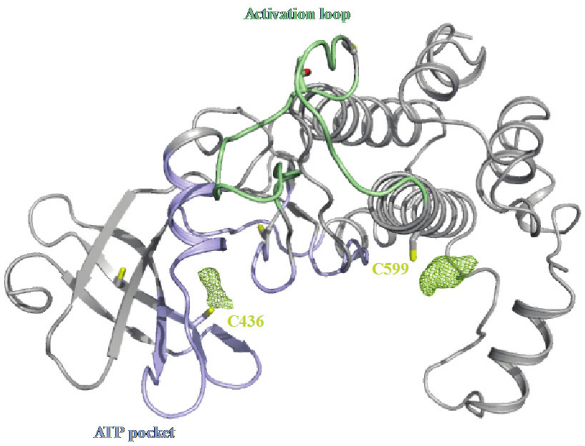


Figure: Andersen JL, Gesser B, Nissen P, Iversen L (2014).

Drug discovery

A new mechanism of allosteric inhibition of RSK/MSK kinases was pinpointed as a new strategy for drug discovery targeting e.g. cancer and neurodegenerative disorders.

Selected publications

- Andersen JL, Gesser B, Nissen P, Iversen L (2014). Methods and Tools for Identification of RSK/MSK Kinase Inhibitors. Patent application WO2014048442
- Azouaoui H *et al.* (2014). A high-yield co-expression system for the purification of an intact Drs2p-Cdc50p lipid flippase complex, critically dependent on and stabilized by phosphatidylinositol-4-phosphate. *PLoS One* 9:e112176.
- Malinauskaite L, Quick M, Reinhard L, Lyons JA, Yano H, Javitch JA, Nissen P (2014). A mechanism for intracellular release of Na+ by neurotransmitter/sodium symporters. *Nature Struct Mol Biol.* 21, 1006-12.
- Wang K, Sitsel O, Meloni G, Autzen HE, Andersson M, Klymchuk T, Nielsen AM, Rees DC, Nissen P, Gourdon P. Structure and mechanism of Zn2+-transporting P-type ATPases. *Nature* 514, 518-22.

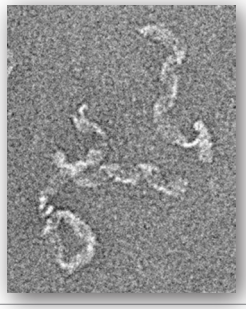
Jensen Group - Neurodegenerative disease

The Jensen group is interested in understanding how alpha-synuclein contributes to the neurodegenerative processes in Parkinson's disease, Lewy body dementia and multiple systems atrophy, which are hallmarked by the development of intracellular aggregates of alpha-synuclein. This is investigated in studies of alpha-synuclein aggregates in vitro, in cell models, transgenic animals and human tissue. The aim is to decipher how cells respond to misfolded alpha-synuclein with respect to cytotoxic and protective mechanisms that can be targeted by therapy.

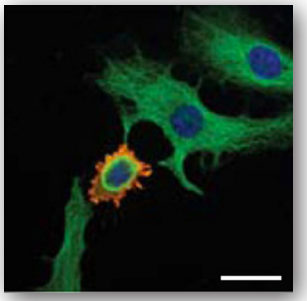
Photo: Else Magård

A large part of our current work is based on previous screens for brain proteins recognizing native and aggregated alpha-synuclein, and for kinases and gene expression changes affecting alpha-synuclein cytotoxicity. This involves extensive collaborations with experts on in vivo modeling, human brain tissue, biophysics and proteomics. Current work in the group centres on effects of alpha-synuclein on calcium regulation, neuroinflammation, and kinases regulating alpha-synuclein homeostasis. It involves generation of novel alpha-synuclein transgenic mice lines with enhances protein aggregation and establishment of the prion-like spreading models for testing disease mechanisms.

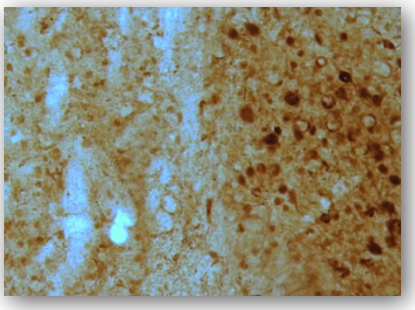
Motor disability in transgenic mouse with enhanced alpha-synuclein aggregation.
Photo: Eeva-Liisa Røssell Johansen



Structure of alpha-synuclein oligoers studied by electronmicroscopy.
Data Cristine Betzer and Arne Möller.



Excerpt from fig. 6 - C.L. Kragh et al. / Neurobiology of Disease 63 (2014) 171–183.



Alpha-synuclein hyperphosphorylation in transgenic mouse with enhanced protein aggregation.
Data: Louise Berkhoudt Lassen.

Selected publications

- Kragh *et al.* (2014) Prodegenerative IκBα expression in oligodendroglial α-synuclein models of multiple system atrophy. *Neurobiology of Disease*, Vol. 63, 01.03.2014, p. 171-183
- Rockenstein *et al.* (2014) Accumulation of oligomer-prone α-synuclein exacerbates synaptic and neuronal degeneration in vivo. *Brain.* 2014, 37:1496-513.
- Lorenzen et al. (2014) How epigallocatechin gallate can inhibit α-synuclein oligomer toxicity in vitro. J Biol Chem. 289:21299-310.
- Zondler *et al.* (2014) DJ-1 interactions with α-synuclein attenuate aggregation and cellular toxicity in models of Parkinson's disease. Cell Death Dis. 5:e1350

Photo: Private

We are interested in understanding how functionality of multi-ligand receptors is controlled. Studies from our group have demonstrated that ligand fidelity can be achieved by formation of ternary complexes between a given ligand, its multi-ligand receptor, and a specific co-receptor (Nat Rev Neurosci, 2008 and Trends Neurosci, 2012). The interactions are commonly cell-type specific or restricted to microdomains of the plasma membrane such as postsynaptic densities.

Research activities are focused towards the functional characterization of a family of structurally related mutifunctional receptors denoted sortilins. The family, which comprises sortilin, SorLA, and SorCS-1, -2, and -3, engages in cellular trafficking as well as in signalling from the plasma membrane. Expression predominates in neurons but receptors are also present in specialized cell types outside the nervous system. They bind a vast number of ligands including neurotrophic factors, APP, progranulin, and lipoproteins implying critical roles in controlling neuronal survival, differentiation, synaptic plasticity, and metabolism. Accordingly, dysfunctions of sortilins are associated with neurological, psychiatric and metabolic disorders including Alzheimer's diseases, frontotemporal-lobar dementia, ADHD, bipolar disorder, schizophrenia, and hypercholesterolemia. Using transgenic mouse models and a broad repertoire of molecular, cellular, and genetic tools it is our goal to elucidate the function of the sortilins in health and disease.

Major achievemnets

We previously reported that sortilins can team up with other receptors and their ligands to form ternary complexes; e.g. with the p75NTR receptor and proneurotrophins (proNT) to induce apoptosis (Nature, 2004 and Nat Neurosci, 2007), with TrkA, -B, and –C to stimulate trophic signalling in neurons (Nat Neurosci, 2011), and with GDNF and its receptors GFRα1 and RET to regulate GDNF signalling (Cell Rep, 2013). In 2014 we extended these observations by demonstrating that SorCS2 in conjunction with p75NTR is required for proNT-induced growth cone collapse of developing dopaminergic neurons. Ablation of *Sorcs2* in mice resulted in dopaminergic hyperinnervation of the frontal cortex, attention deficit, hyperactivity, and in a paradoxical response to amphetamine similar to that observed in patients suffering from ADHD. Contrary, in PNS glia proteolytic processing produced a two-chain SorCS2 isoform that mediated proNT-dependent Schwann cell apoptosis (Neuron, 2014). Outside the nervous system sortilin, encoded by the cardiovascular and hypercholesterolemia risk gene *Sort1*, facilitates hepatic VLDL export (Cell Metab, 2010). In two new studies we reported that sortilin also impacts on cardiovascular disease by facilitating hepatic secretion of PCSK9, a regulator of LDL receptor expression, and by affecting atherogenesis locally in the vessel wall. Sortilin deficiency resulted in impaired PCSK9 release and increased LDL receptor expression whereas in the converse situation overexpression of PCSK9 was associated with lower LDL receptor expression (Cell Metab, 2014). In a mouse models with unaltered plasma cholesterol deletion of *Sort1* inhibited development of atherosclerotic lesions by regulating local secretion of IL6 and IFNγ. Bone marrow transplantation from knockout to control mice reduced

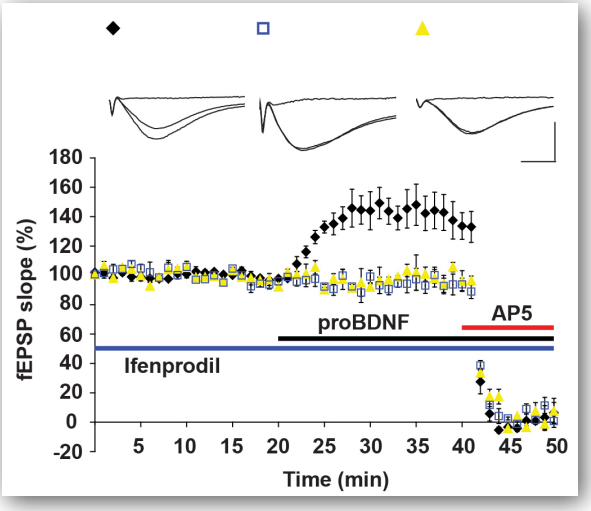
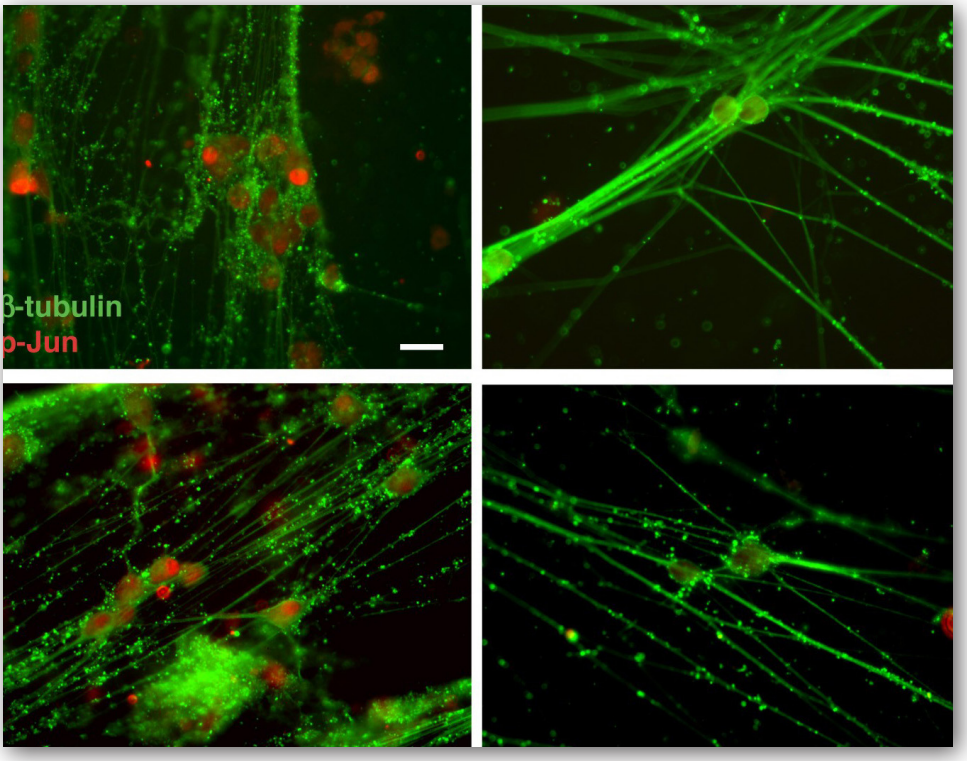


Figure: Ulrik Bølcho

macrophage infiltration and plaque formation, whereas the opposite was true when bone marrow from wildtype mice were transferred into sortilin-deficient animals (J Clin Invest, 2014). Finally SorLA, which prevent formation of amyloid plaques and Alzheimer's disease, also controls post-translational modifications (i.e. glycosylation) of APP. The binding site in SorLA was mapped to a region in which mutations are associated with both familiar and the sporadic forms of Alzheimer's disease (J Biol Chem, 2014).



Data: Nykjær lab

Selected publications

- Mortensen MB, Kjolby M, Gunnersen S, Larsen JV, Palmfeldt J, Falk E, Nykjaer A, Bentzon JF. Targeting sortilin in immune cells reduces proinflammatory cytokines and atherosclerosis. *J. Clin. Invest.* 124(12):5317-22, 2014.
- Glerup S, Olsen D, Vaegter CB, Gustafsen C, Sjoegaard SS, Hermey G, Kjolby M, Molgaard S, Ulrichsen M, Boggild S, Skeldal S, Fjorback AN, Nyengaard JR, Jacobsen J, Bender D, Bjarkam CR, Sørensen ES, Füchtbauer EM, Eichele G, Madsen P, Willnow TE, Petersen CM, and Nykjaer A. SorCS2 regulates dopaminergic wiring and is processed into an apoptotic two-chain receptor in peripheral glia. *Neuron.* 82(5):1074-87, 2014.
- Gustafsen C, Kjolby M, Nyegaard M, Mattheisen M, Lundhede J, Buttenschøn H, Mors O, Bentzon JF, Madsen P, Nykjaer A, and Glerup S. The hypercholesterolemia-risk gene SORT1 facilitates PCSK9 secretion. *Cell Metab.* 19(2):310-8, 2014.
- Lewin GR and Nykjaer A. Pro-neurotrophins, sortilin, and nociception. *Eur. J. Neurosci.* 39(3):363-74, 2014.

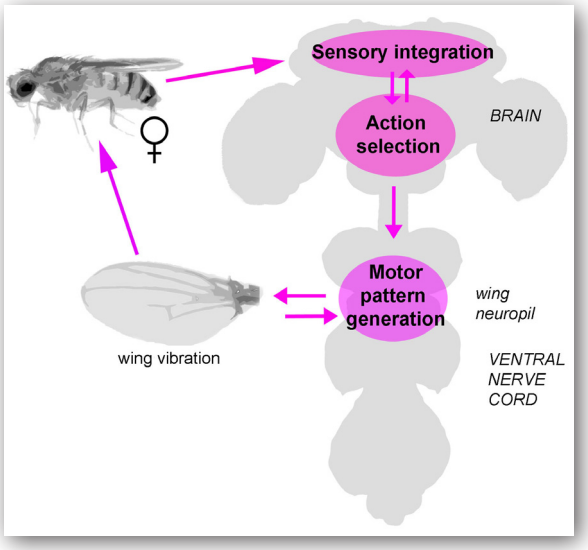
Philipsborn Group- Behavioral genetics and circuit neuroscience

We are interested in understanding how the nervous system generates and controls behavior- at the level of genes and molecules, cells and neuronal circuits. Our model system is Drosophila melanogaster, which has a relatively small and stereotyped nervous system, but displays complex and fascinating behaviors.

Photo: Else Magård

Background

By studying the neuronal circuits underlying Drosophila courtship behavior, we aim at understanding general principles of motor control and patterning as well as behavioral motivation and coordination.

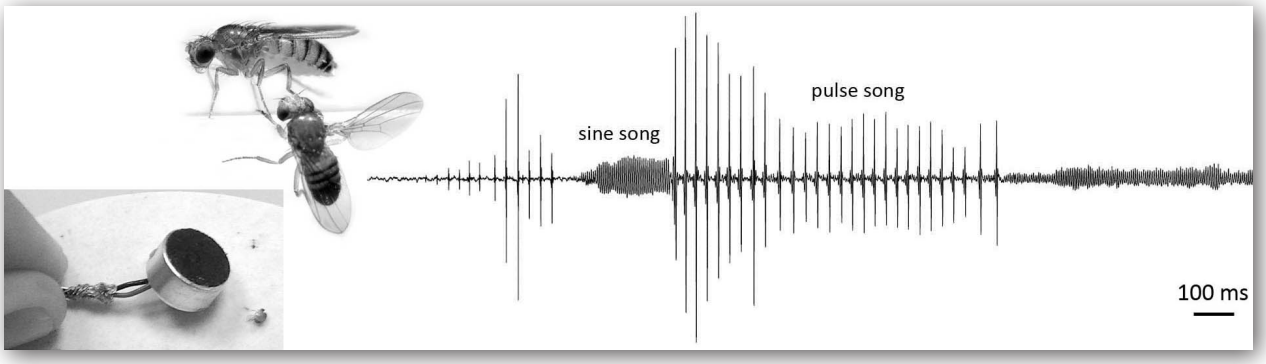


Schematic of the neuronal circuits for courtship song. Figure: Anne von Philipsborn

Drosophila male courtship is a multi-faceted behaviour including following, wing song and copulation attempts. Previously, we identified neurons and subcircuits dedicated to generation of the male courtship song, an elaborately patterned acoustic signal. Courtship circuit development depends in the male fly on expression of a sex-specific splice variant of the putative transcription factor fruitless, FruM, which is present in about 2% of the neurons in the Drosophila central nervous system. fruitless is subject to alternative splicing, generating three isoforms FruA, FruB and FruC. We have shown that FruC is unique in such that it controls the development of male specific neurons involved in pheromone processing and song behavior

Neuronal circuits for song behavior and motor control

Currently, we investigate how already described and newly identified song neurons interconnect, signal to each other and control the song pattern. We use song recording as a highly sensitive, high throughput measurement for motor

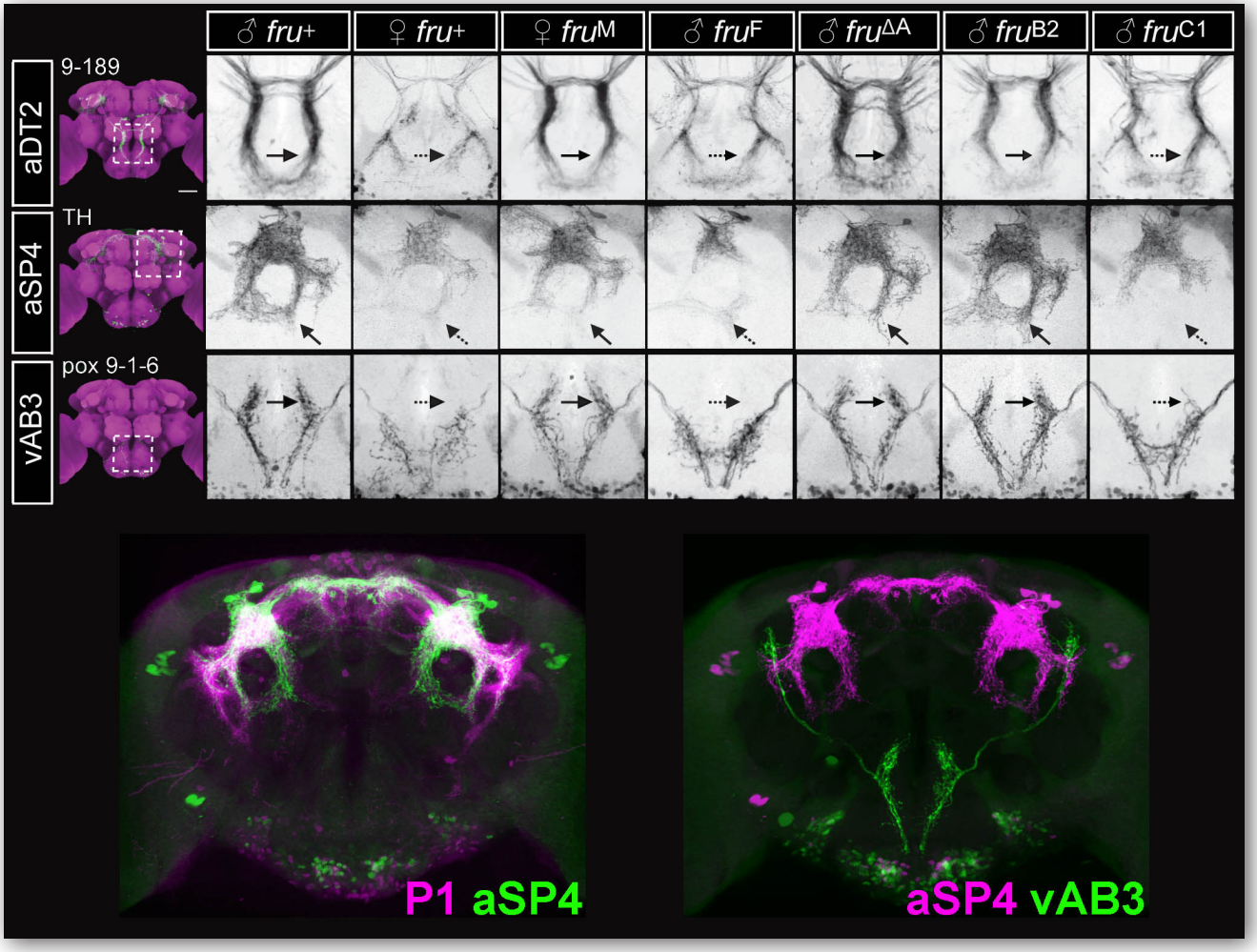


Drosophila courtship song. A male fly sings to a female by extending and vibrating one wing. Song is recorded by small microphones: the oscillogram shows sine and pulse bouts. Figure: Anne von Philipsborn

behaviour at millisecond timescale as well as genetic tools for neuronal activity imaging and thermo-/optogenetics. Simultaneously, we will scrutinize the genetic and molecular basis of circuit dynamics. We are interested in genes pivotal for computational performance and configuration of ensembles of interconnected neurons, namely, genes

encoding ion channels, membrane transporters and molecules implicated in neuromodulation.

By establishing a comprehensive model circuit for song, we want to uncover neuronal mechanisms for motor pattern generation, bi-functional motor control and behavioural switching, as well as higher-level coordination of motor output. Computational rules and basic principles of action selection and pattern generation which orchestrate Drosophila song are expected to be of general relevance for circuit neuroscience.



Fruitless^{C} controls the development of sex specific arborizations, as illustrated in the upper panel. Below the brain neuronal classes P1, aSP4 and vAB3, which require Fruitless^{C} for pheromone processing.

Figure: Modified from von Philipsborn et al (2014).

Molecular and Cellular Models for Neurological Disease in Drosophila

Fundamental mechanisms of nervous system function on the molecular, cellular and circuit level are conserved and shared across vertebrates and invertebrates.

Drosophila can serve as a convenient and genetically accessible in vivo model for analyzing the effect of pathological mutations and protein modifications on neuronal physiology. In the future, we will collaborate with other groups at DANDRITE and study for example aspects of Parkinson pathology in a Drosophila model system.

References

- von Philipsborn, A.C., Jörchel, S., Tirian, L., Demir, E., Morita, T., Stern, David L., and Dickson, Barry J. (2014). Cellular and Behavioral Functions of fruitless Isoforms in Drosophila Courtship. *Curr Biol* 24, 242-251.
- von Philipsborn, A.C., Liu, T., Yu, J.Y., Masser, C., Bidaye, S.S., and Dickson, B.J. (2011). Neuronal Control of Drosophila Courtship Song. *Neuron* 69, 509-522.

Denham Group - Stem Cells

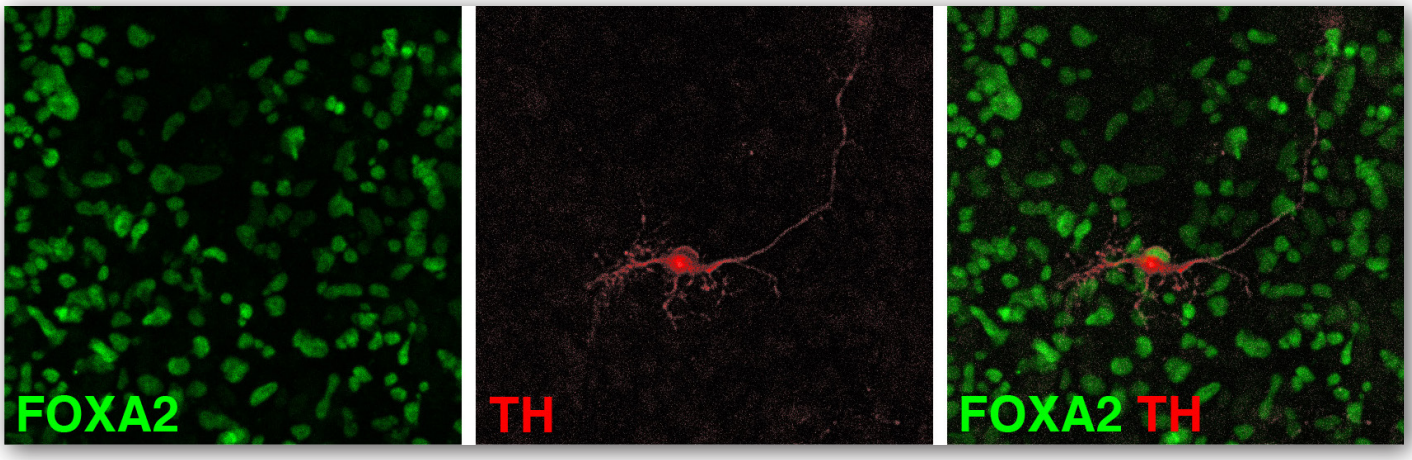
Photo: Melbourne University

Our laboratory is interested in understanding how the nervous system develops and the processes involved in neurodegeneration. We use human embryonic stem (ES) cells and induced pluripotent stem (iPS) cells to study the signalling pathways required for their differentiation into precise neural progenitor cell types [1,2]. In particular, our group is interested in the specification of mesencephalic dopaminergic neurons, the major cell type affected in Parkinson's disease.

The objective is to develop in vitro models for studying neural development and disease processes and to identify early cellular changes that underlie the onset of neurodegenerative diseases such as Parkinson's disease. Furthermore, we are also interested in how different neural progenitor subtypes survive and function after transplantation in an adult rodent brain [1]. Our overall goals are to develop potential new treatment strategies for neurodegenerative disorders.

Background and Future Plans

Pluripotent stem cell biology is one of the most rapidly advancing areas of medical research. The advancements are both in the types of cells being generated and their application for research and clinical purposes. The reprogramming of somatic cells into iPS cells has further accelerated this progress with new opportunities now available to derive iPS cells from patients with familial forms of neurological disorders. Our group aims to generate iPS cells from patient fibroblasts, which carry a known Parkinsonian mutation. Using homologous recombination techniques we intent to induce or correct mutations in the pluripotent stem cells and then use these cell lines to study the early disease processes that lead to Parkinson's disease.



TH/FOXA2 unpublished data. Photo: Mark Denham

Recently our group also show that dual inhibition of the GSK3β and activin/nodal pathways by small molecules differentiate human pluripotent stem cells (hPSCs) directly into a caudal progenitor cells (CNPs) [1]. Exposure of CNPs to BMP2/4, sonic hedgehog or FGF2 signalling, efficiently directs their fate to neural crest/roof plate cells, floor plate cells, and caudally-specified neuroepithelial cells, respectively. Our studies are the first to identify a multipotent neural progenitor derived from hPSCs, that is the precursor for major neural lineages of the embryonic caudal neural tube.

References

- Denham M, Hasagawi K, Zhang D, Hough S, Menheniott T, Leung J, Rollo B, Newgreen D, Pera M, Dottori M. Identification of a multipotent neural progenitors that give rise to the central and peripheral nervous system. *Stem Cells* 2015 (In press).
- Denham M, Bye C, Leung J, Conley B, Thompson L, Dottori M. GSK3β and Activin/Nodal Inhibition in Human Embryonic Stem Cells induces a Pre-neuroepithelial State that is required for Specification to a Floor Plate Cell Lineage. *Stem Cells* 2012.
- Denham M, Parish C, Leaw B, Wright J, Reid C, Petrou S, Dottori M, Thompson L. Neurons derived from human embryonic stem cells extend long-distance axonal projections through growth along host white matter tracts after intra-cerebral transplantation. *Frontiers in Cellular Neuroscience*. 6(11) 2012.


Photo: DANDRITE


Photo: DANDRITE


Photo: DANDRITE

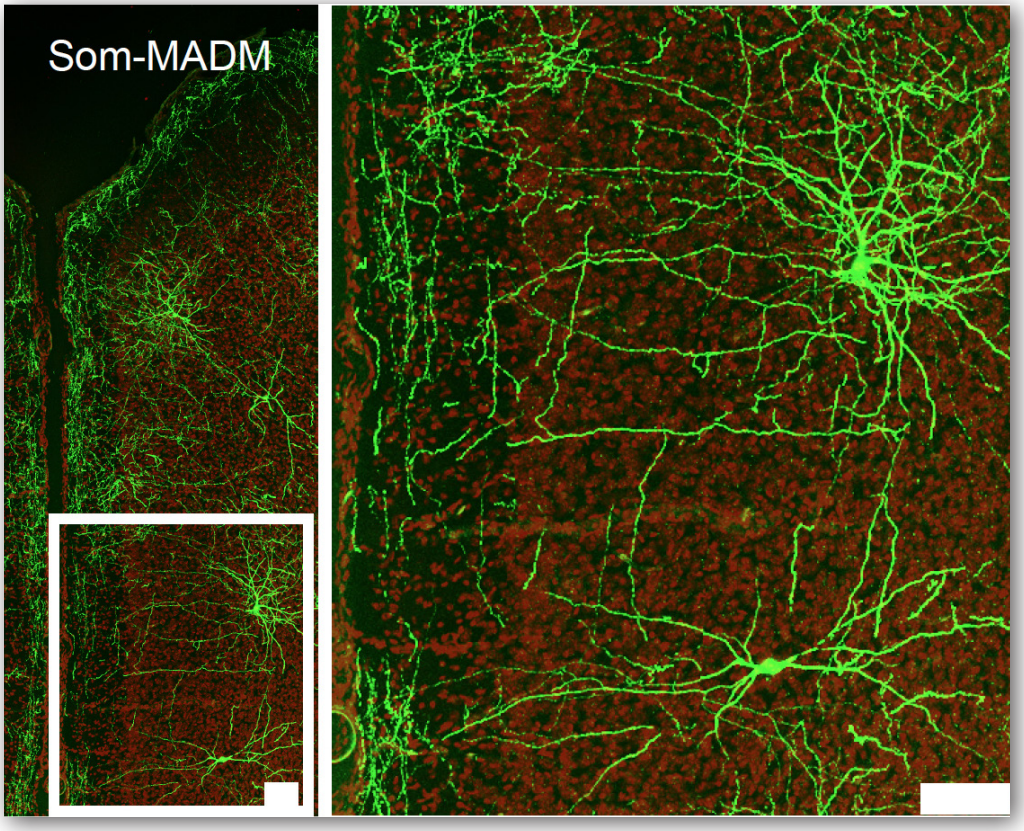

Photo: Fabia Febbraro

Kvitsiani group - Neuronal circuits and molecular basis of effort based decision-making

Photo: Private

We investigate genetic and neural circuit mechanisms underlying effort based decision-making in flies, rodents and humans. The aim of our research is to build predictive and quantitative models of behavior that will help us generate testable hypothesis underlying mechanisms of decision making. The methods used include molecular genetics, psychophysics, behavioral electrophysiology and optogenetics.

We form our research program by asking a very simple question: why do animals and humans assign greater value to objects obtained by bigger effort? Our aim is to understand biology of effort based decisions on multiple levels: from molecules to circuits. Using reverse genetic screens in combination with effort based behavioral tasks in fruit flies we hope to uncover molecular basis of it. Using extracellular electrophysiology and cell-type specific recordings in rodents we plan to identify circuit level computations in mouse brain that integrates effort into value based decisions. Once relevant neural circuits are identified we will use optogenetic perturbations in behaving rodents to establish causality between neural activity and behavior. Another



Somatostatin interneurons sparsely labeled in Medial Prefrontal Cortex of mice. Right panel shows higher magnification image of a region in white rectangle. Somatostatin interneurons target distal dendrites of pyramidal neurons. One can see axonal processes of Somatostatin interneurons targeting upper layers in prefrontal cortex.
Figure: Kvitsiani D et al. Nature 2013.

focus of research will be to test how humans behave in an effort based decision tasks and see if behavioral diversity can be explained by genetic make-up of individuals. Overall our long term goal is to use ecology inspired quantitative behavioral models to guide and sharpen scientific questions.
Previously we have used optogenetic assisted electrophysiological tagging of extracellular spikes to record genetically defined cell-types in freely behaving mice (Fig a,b). We plan to build on this experience and try to dissect the circuit

dynamics in behaving animals by monitoring activity of specific cell-types in prefrontal areas of mouse neocortex. Mice will be trained on effort based decision-making task and will be given a free choice among alternative rewards. We will measure choice probability/value as a function of task difficulty. This will allow us to build psychometric curves and identify hidden variables that link effort with value. Next we will look for circuit mechanisms of effort integration into value based choice. Finally optogenetic activation and inactivation experiments will test on a trial by trial basis what groups of neurons mediate these behaviors. In parallel to these experiments we will set up effort based behavioral assays in flies. Flies will be given rewards at arbitrary locations as a function of travel time and/or difficulty. We hope that genetic screen using RNAi library will identify specific molecules that measure effort. We also hope that these studies in flies and in rodents will synergize and identification of key conserved molecular players from flies will help us identify critical circuit elements in mice.

Finally we also would like to test human subject on similar behavioral tasks. Our goal is to see if genetic make up of individuals can account for behavioral performance of our test subjects.

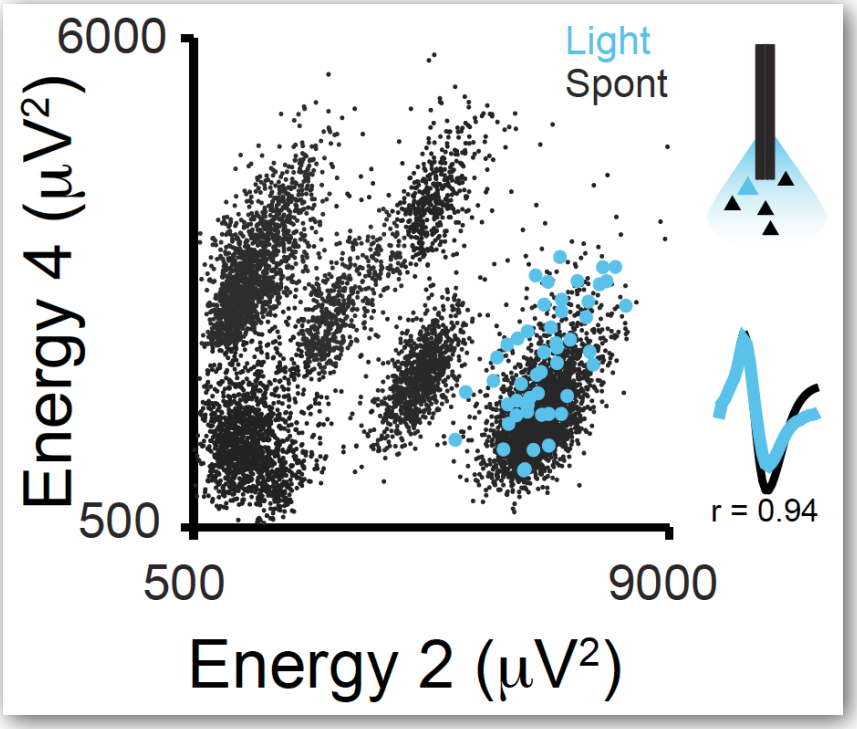


Illustration of optical tagging method. Identification of cell-types in extracellular recordings using targeted expression of Channelrhodopsin2 (ChR2) molecule in genetically defined neurons (blue cells).
Figure: Duda Kvitsiani.

References:

- Kvitsiani D*, Ranade S*, Hangya B, Taniguchi H, Huan Kepecs A. Distinct behavioural correlates and network interactions of two interneuron classes in mouse prefrontal cortex. *Nature*. 2012. June 20; 498(7454): 363-6. * These authors contributed equally.
- Taniguchi H, He M, Wu P, Kim S, Paik R, Sugino K, Kvitsiani D, Fu Y, Lu J, Lin Y, Miyoshi G, Shima Y, Fishell G, Nelson SB, Huang ZJ. A resource of Cre driver lines for genetic targeting of GABAergic neurons in cerebral cortex. *Neuron*. 2011 Sep 22; 71(6): 995-1013.
- Stockinger P*, Kvitsiani D*, Rotkopf S, Tirian L, Dickson BJ. Neural circuitry that governs Drosophila male courtship behaviour. *Cell.* 2005 Jun 3;121(5): 664-6. * These authors contributed equally.

Yonehara group - Structure, function and development of neural circuits in visual system

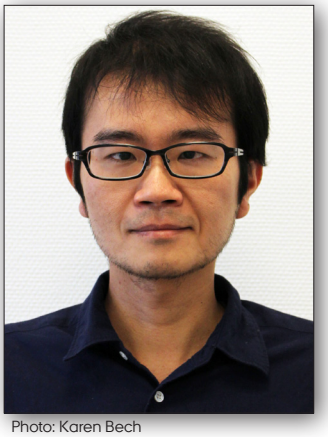


Photo: Karen Bech

The Yonehara group investigates the structure, function and development of neural circuits in the visual system. We are interested in the role of different cell types in neuronal circuits and the genetic and molecular mechanisms of how those circuits are assembled during development. The methods used include two-photon imaging, electrophysiology, optogenetics, trans-synaptic virus, genetic labeling, molecular biology, genomics and behavioral analysis.

Our research is based on the central hypothesis that functionally important neuronal circuit motifs are repeatedly used across various brain regions and species, and therefore identifying and understanding the structure and function of such motifs could give insights into the functional organisation of the brain. The mouse visual motion circuits, particularly the retina and its direct brain target the superior colliculus, provides us with an approachable substrate to work towards this goal, given its functionally and genetically well-defined cell types, multi-layered organization and tractable visually-guided behaviors. Two key organising principles that characterize not only the visual motion circuits of mammals and insects, but also other neuronal systems, are 1) parallel processing and 2) asymmetry of neuronal connectivity. We have focused, and will continue to focus, on questions relevant to these organising principles (Yonehara et al., Nature, 2011; Yonehara et al., Neuron, 2013).

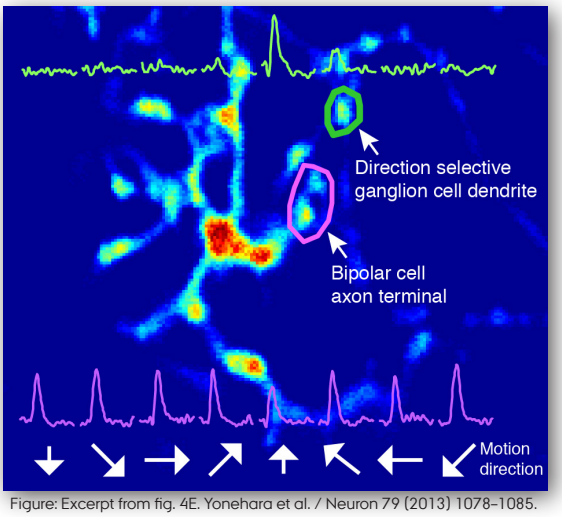


Figure: Excerpt from fig. 4E. Yonehara et al. / Neuron 79 (2013) 1078–1085.

The research plan is firstly to identify a computation performed by a given neuronal circuit comprising distinct cell types in the adult brain. Secondly, to investigate how the computation is performed by linking the activity and synaptic connectivity of individual cell types in the circuit to the computation that the circuit achieves. Thirdly, to examine the role of individual cell types in transforming the sensory input into output innate behavior or eye movement control. Finally, to study the genetic mechanisms by which the elementary circuit motifs are assembled, and how its dysfunction can result in disease. Ultimately, by these experiments we aim to link genes to behavior. We will also develop new genetic and viral technologies that facilitate probing circuit function in healthy and diseased systems.

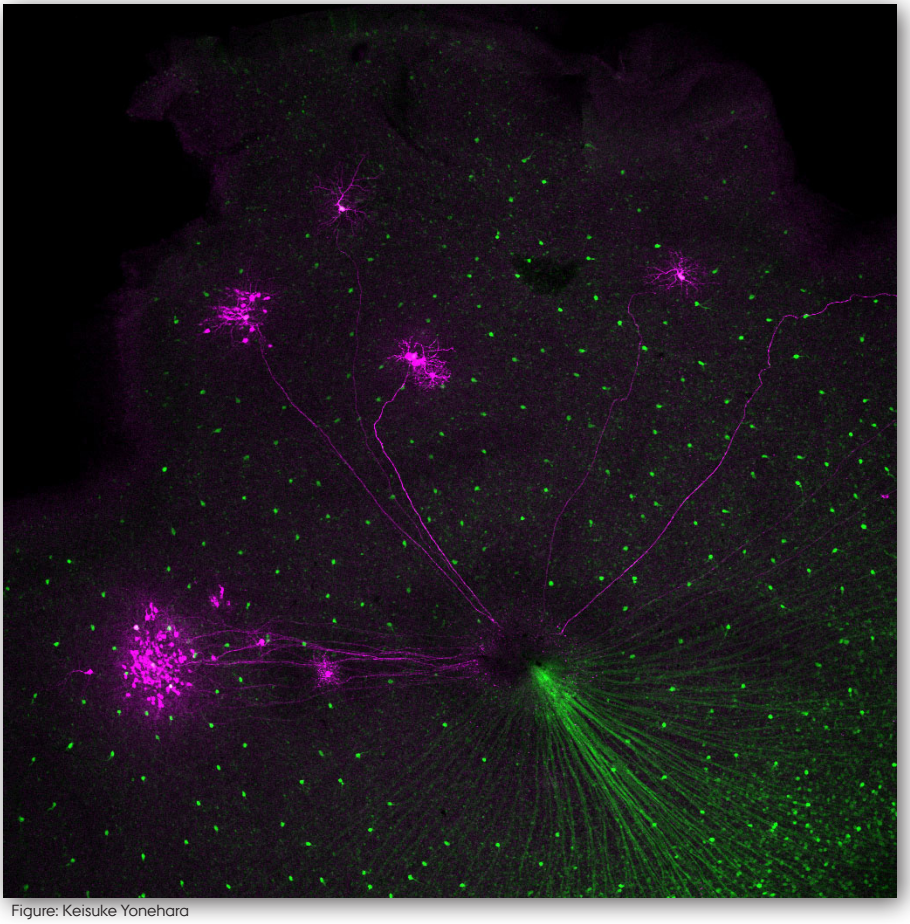


Figure: Keisuke Yonehara

References

- Yonehara K*, Farrow K*, Ghanem A, Hillier D, Balint K, Teixeira M, Jüttner J, Noda M, Neve RL, Conzelmann KK, Roska B (2013). The first stage of cardinal direction selectivity is localized to the dendrites of retinal ganglion cells. *Neuron* 79: 1078-1085. *equally contributed.
- Farrow K, Teixeira M, Szikra T, Viney TJ, Balint K, Yonehara K , Roska B (2013). Ambient illumination toggles a neuronal circuit switch in the retina and visual perception at cone threshold. *Neuron* 78: 325-338.
- Di Meglio T, Kratochwil CF, Vilain N, Loche A, Vitobello A, Yonehara K , Hrycaj SM, Roska B, Peters, AH, Eichmann A, Wellik D, Ducret S, Rijli FM (2013). Ezh2 orchestrates topographic migration and connectivity of mouse precerebellar neurons. *Science* 339: 204-207.
- Yonehara K, Balint K, Noda M, Nagel G, Bamberg E, Roska B (2011). Spatially asymmetric reorganization of inhibition establishes a motion-sensitive circuit. *Nature* 469: 407-410.

Arne Möller Team - Electron Microscopy: A direct view on Macromolecular machines

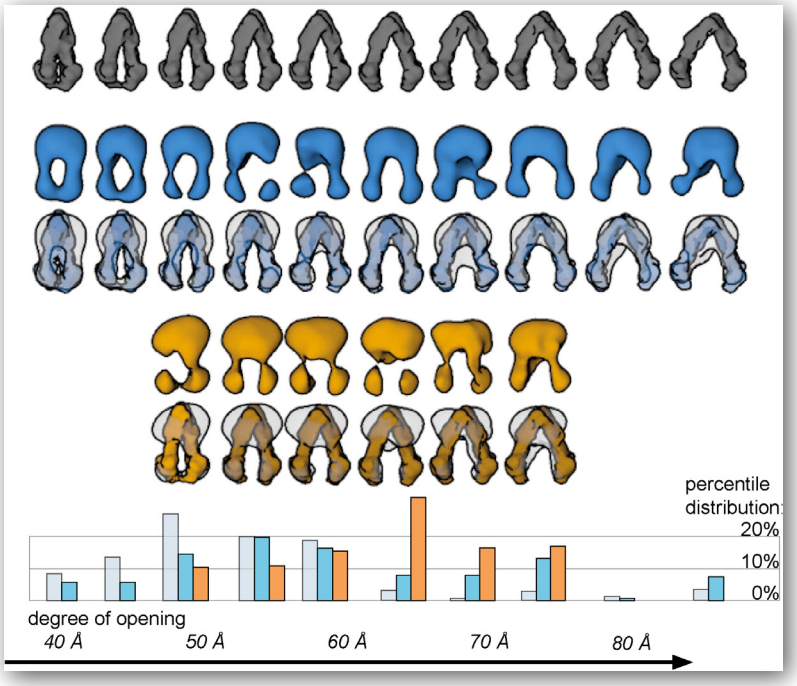
Photo: Lisbeth Heilesen

We use 3D cryo Electron Microscopy (cryo-EM) to determine the structure of macromolecular machines. Cryo-EM can be referred to as “bridge to the cell”, as it is uniquely suited to image a large array of protein complexes in a quasi-native environment. EM is a direct imaging method that literally allows us to “see” the proteins that we are investigating.

In Arne Möller Laboratory we focuson 3D structures of dynamic protein complexes that exert major conformational changes and are involved in intra cellular and transmembrane transport, protein trafficking and regulation. The majority of our targets are membrane proteins that translocate cargo through the lipid bilayer. Another important target are Sortilins, membrane protein receptors that are key players in many neurological disorders. Sortilin interacts with a large array of binding partners; each of which specifically alters the function of the protein. We want to determine their 3D structures to characterize the modes of binding. This information is crucial to fully understand these fundamental molecular machines and to develop strategies for the development of site-specific therapeutics.

The lab is also actively pursing method development, which includes software protocols for streamlined EM-imaging and analysis as well as optimization of sample preparation. In collaboration with the CDNA center at iNANO we have now started to utilize specifically engineered RNA/DNA scaffolds as markers for proteins that would otherwise not be detectable by cryo-EM. The lab is also actively engaged in numerous collaborations and the dissemination of this technology to other researchers at DANDRITE and AU.

In collaboration with the iNANO center we have now established a state of the art cryo-EM facility, which will also be accessible to scientists outside AU. In the future this setup will enable us to target a plethora of interesting biological questions.



Typical EM-image of the bacterial transmembrane transport protein, MsbA. Data analysis and image processing led to a 3D representation of the entire conformational spectrum of this highly dynamic molecular machine and its mammalian homologue P-glycoprotein.

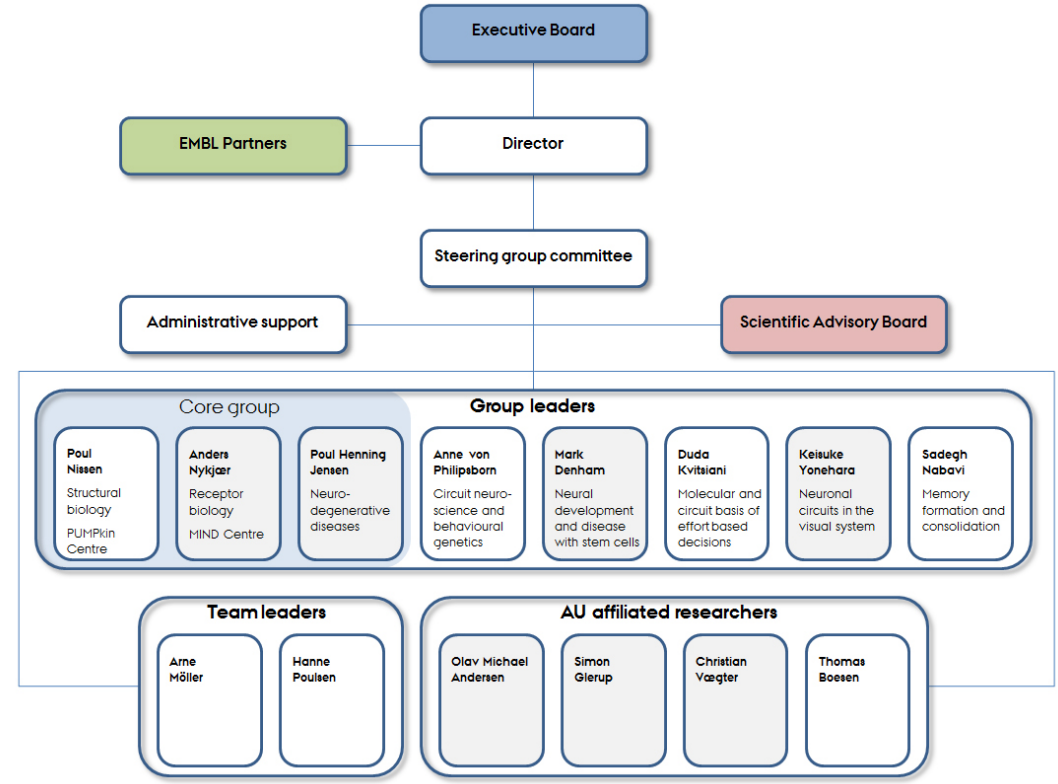
Figure from: Moeller, A., Lee, S. C., Tao, H., Speir, J. A., Chang, G., Urbatsch, I. L., ... Zhang, Q. (2015). Distinct Conformational Spectrum of Homologous Multidrug ABC Transporters. Structure.

References

- Bhabha, G., Cheng, H.-C., Zhang, N., Moeller, A., Liao, M., Speir, J. a., Vale, R. D. (2014). Allosteric communication in the Dynein motor domain. *Cell*, 159(4).

DANDRITE ORGANIZATION STRUCTURE

DANDRITE is hosted by Aarhus University (AU) and placed at two faculties and two departments: Department of Biomedicine (Faculty of Health) and Department of Molecular Biology and Genetics (Faculty of Science and Technology).
DANDRITE is organized with a 3 three-tier management structure consisting of an Executive Board, a Director, and a Steering Committee and is supported by Scientifc Advisory Board.



Graphic: Karen Bech

EXECUTIVE BOARD

- Chair, Professor David Brooks, Department of Clinical Medicine, Aarhus University and Aarhus University Hospital-Danish Neuroscience Center.
- Dean Niels Christian Nielsen, Faculty of Science and Technology
- Dean Allan Flyvbjerg, Faculty of Health Sciences
- Director, Professor Poul Nissen, DANDRITE
- Professor Anders Nykjær, DANDRITE
- Professor Poul Henning Jensen, DANDRITE
- Director of Research Anne-Marie Engel, Lundbeck Foundation (non-voting)
- Administrative support by Chief Administrative officer Else Magård, DANDRITE.

DIRECTOR

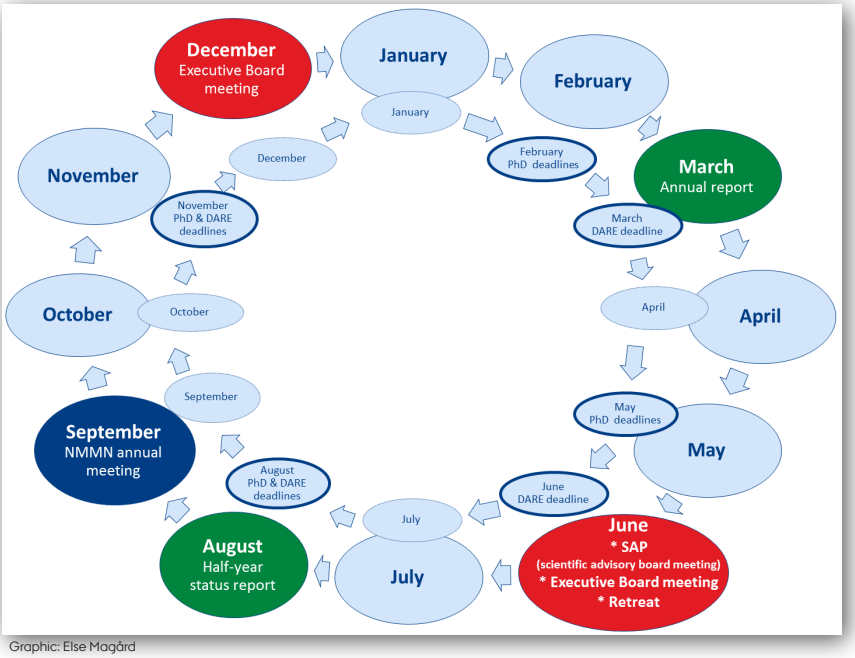
On March 5th, 2014 the Executive Board appointed founding Director Professor Poul Nissen as director of DANDRITE for a term of four years.

STEERING COMMITTEE

The steering committee consists of the director, the core group leaders and two representatives of the group leaders (2 year terms). The steering committee is responsible for strategic developments of research, the planning and coordination of activities, and the distribution of running budget. The steering committee will also be overseeing public dissemination and outreach of DANDRITE research and activities.

The steering committee meetings take place weekly, Mondays 10AM-11AM, and in 2014 it consisted of the follwing members:

DANDRITE Annual Wheel Graphic: Else Magård



Graphic: Else Magård

- Professor Poul Nissen, Director
- Professor Anders Nykjær
- Professor Poul Henning Jensen
- Group Leader Anne Von Philipsborn
- Group Leader Mark Denham
- Chief Administrative Officer, Else Magård
- Communications Assistant & Director PA, Karen Bech

Monthly Extended Business Meeting

Participants in addition to the DANDRITE Steering committee are:

- All DANDRITE group leaders
- All DANDRITE Team leaders
- Affiliated Researcher spokesperson (Associate professor Christian B. Vægter)
- Postdoc spokesperson (Dr. Niels Wellner)
- PhD student spokesperson (Alyssa Huebner)
- Technician spokesperson (Lotte T. Pedersen)

Monthly coordination Meeting

A monthly meeting of the DANDRITE core Group Leaders and chief administrator with the two department heads (Thomas G. Jensen, Department of Biomedicine and Erik Østergaard Jensen, Department of Molecular Biology and Genetics) for coordination of activities, teaching and infrastructural matters

Young Investigator forum of the Nordic EMBL Partnership

The forum plans a Pre-meeting for the Young Investigators at the 6th Annual Meeting of the Nordic-EMBL Partnership for Molecular Medicine, organized in 2015 by DANDRITE in Aarhus. The forum consists of.

- Postdoc Florian Hilbers
- Postdoc Joseph Lyons
- Postdoc Alessia Arduin
- PhD student Jakob Ulstrup
- PhD student Sigrid Thirup Larsen

Student and Postdoc Network

Students and postdocs organize monthly meetings with scientific presentations and social interactions.

Network for technicians

Meet on *ad hoc* basis.

DANDRITE Seminar committee

- Group Leader Anne von Philipsborn
- Team Leader Hanne Poulsen
- Postdoc Mads Fuglsang Kjølby
- Postdoc Louise Berkhoudt Lassen
- PhD student Alyssa Huebner
- Communications assistent Karen Bech

Social event committee

- Communications assistent Karen Bech
- Postdoc Florian Hilbers
- Postdoc Niels Wellner

Photo: Karen Bech

Administrative organization

DANDRITE research encompasses interdisciplinary and translational activties, and the administrative matters cross organizational borders. The goal of the DANDRITE administration is to cater for all needs connected to DANDRITE activities and to facilitate administrative procedures. AU administrational units assist from the following offices: Research and Talent, Finance and Planning, Human Resources, Studies Administration, Communication, IT, and Knowledge Exchange. Furthermore, AU administration centers at Faculty of Health and at Faculty of Science & Technology assist.

SCIENTIFIC ADVISORY BOARD AND MEETING

TThe scientific advisory board will convene annually and provide independent advice on scientific and strategic matters, and evaluations of achievements and allocations. SAB members are international, highly reputed researchers. First advisory board meeting took place November 6, 2014, and the next will take place in June 2016 and then annually. DANDRITE's scientific advisory board (SAB) members are:

- Professor Moses Chao, New York University (NYU)
- Professor Kathleen Sweadner, Harvard Medical School
- Professor Mart Saarma, University of Helsinki
- Professor Glenda Halliday, Neuroscience Research Australia (NeuRA)
- Director Matthias Wilmanns, EMBL Hamburg
- Div. Director Jan Egebjerg, Lundbeck
- Professor Rüdiger Klein, Max-Planck-Institute of Neurobiology
- Professor Carl Petersen, École polytechnique fédérale de Lausanne EPFL

Photo: Susanne Schousboe Sjøgaard

Excerpts from the 2014 SAB report include:

..."As DANDRITRE does not have the structure of a classical University department, it can be viewed as an experimental platform for new administrative and organizational ideas. The experiment during the first year has worked very well. From the very beginning, DANDRITE has the goal to serve as a generator for new initiatives in neuroscience, and an introducer of technologies new to Denmark."....

...."DANDRITE has had a very good start and has done an excellent job in recruiting four outstanding young group leaders. Their recruitment significantly strengthens the institute and brings a series of new technologies and know-how to the institute, and also to the neuroscience community in Aarhus and in Denmark."....

....."The initial success of DANDRITE is based on 1) rigorous focus on scientific excellence, which is maintained by careful selection of the research groups and regular external review, 2) strong scientific leadership with the vision to address key scientific questions that have the potential to bring major innovations in the field of neuroscience, and 3) an exceptionally flexible and flat administrative structure that enables the Institute to identify and invest in the most innovative and promising science. These principles are essential to build and maintain world class science and technology, as well as for teaching of neuroscience, and should be strongly supported and potentially extended in Aarhus University."....

Photo: DANDRITE


Photo: DANDRITE

ACADEMIC ORGANIZATION

DANDRITE associates other research groups through three different instruments:

i) Team Leaders (TL)

ii) Affiliated Researchers (AFR)

iii) DANDRITE Associate Research (DARE) investigators.

Requests for TL or AFR status are approved by the DANDRITE steering committee, which also approves DARE applications on the basis of a peer-review.

DANDRITE Team leaders (TL):

A maximum of 4 TL can be associated to DANDRITE and support infrastructural or research-oriented strategies in DANDRITE.

- A TL holds a non-tenured junior group leader position/assistant professorship at Aarhus University (AU).
- The appointment as DANDRITE TL is for 3 years with possible extension for a total of maximum 6 years.
- DANDRITE TL status is concluded earlier if a permanent position at associate professor level is obtained.
- Salaries and general running expenses are not funded by DANDRITE, but seed funding can be provided, and specific equipment and project expenses can be financed by DANDRITE as strategic investments.
- TLs have access to the DANDRITE infrastructure (expertise and equipment) and administrative support on similar terms as group leaders.
- TLs participate in the monthly Extended Business Meetings and internal activities at DANDRITE
- TLs qualify as internal DANDRITE applicants for DARE proposals. In addition to the general criteria for DARE programs. TL applications for DARE will be evaluated on their strategic value to DANDRITE.

DANDRITE affiliated researchers (AFR):

Photo: Karen Bech

Typically AU researchers with permanent/senior positions that are tightly associated to DANDRITE core-GL for mutual benefits on research aims (e.g. through joint grants/research centers, shared laboratories). The affiliation can also support strategic structures of AU departments and infrastructures.

- AFR are associated to DANDRITE via a core-GL and have qualifications at associated professor level or higher.
- For projects associated with DANDRITE, AFR have access to DANDRITE research infrastructures (expertise and equipment) on similar terms as group leaders.
- AFR take part in internal DANDRITE activities.
- AFR are represented by a spokesperson at the monthly Extended Business Meetings.
- AFR have access to DARE programs through a core-GL as the formal applicant and grant holder. AFR cannot be external partners of a DARE project.
- AFR can represent DANDRITE on collaborative initiatives, such as international networks.

DANDRITE Associate Research Program investigators - (DARE)

DARE Investigators are external collaborators with a DANDRITE GL/TL on a DARE project

DARE Investigators have qualifications at associated professor level or higher and are normally employed at a Danish research institution or company.

DARE Investigators do not participate in the regular internal DANDRITE activities.

DARE Investigators are invited to DANDRITE symposia and other larger scientific events.
Depending on the type of project the formal duration of a DARE investigator status is as follows.

- PhD projects: 4 years
- Postdoc projects: 3 years
- Equipment: 3 years

Photo: Susanne Schousboe Sjøgaard

PERSONNEL

A major, initial goal of DANDRITE has been to recruit five outstanding young group leaders in 2 or 3 campaigns following the EMBL model and finishing spring 2015.
First group leaders were recruited after interviews and contract negotiations concluding in September 2013. Group Leader Mark Denham started his contract on December 1, 2013 and Group leader Anne von Philipsborn on January 1, 2014.

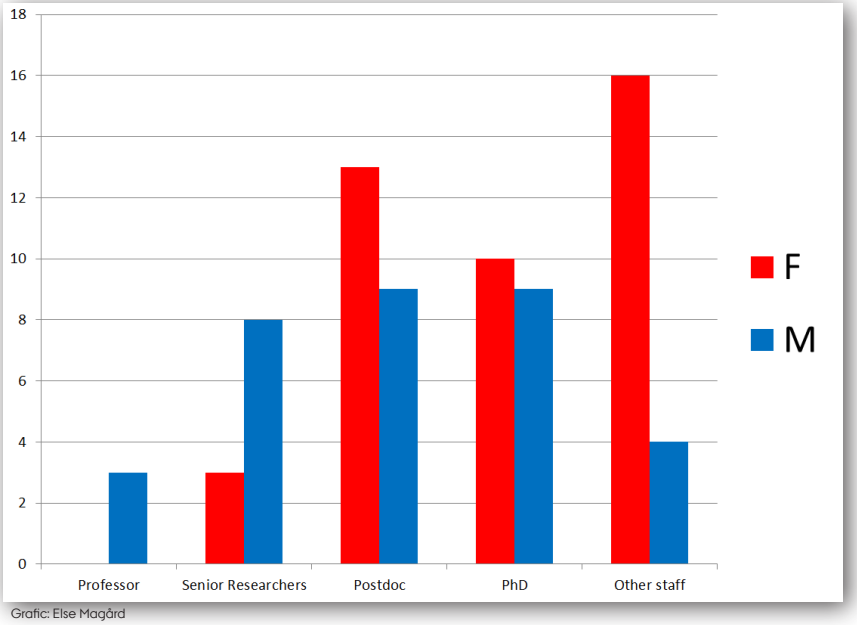
Count and percentages of personnel employed and affiliated during 2014 grouped by appointment category and gender.

DANDRTIE Personnel 2014

DANDRTIE Personnel 2014	Female	Male	Total	% Personel categori
Professor	0	3	3	4
Senior Researchers	3	8	11	15
Postdoc	13	9	22	29
PhD	10	9	19	25
Other staff (lab.tech., Research Assist., and administration)	16	4	20	27
Grand Total	42	33	75	100
% Male / Female	56	44	100	

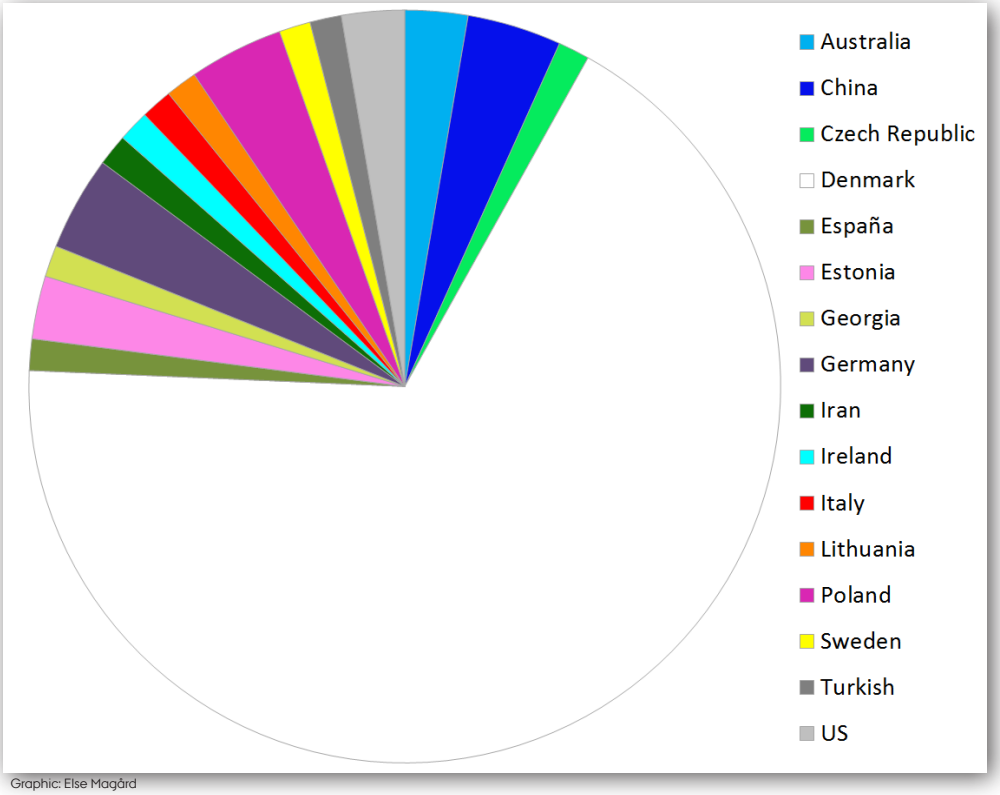
Graphic: Else Magård

Graphic representation of personnel employed and affiliated during 2014 grouped by appointment category and gender.



Grafic: Else Magård

Graphic representation of personnel employed and affiliated during 2014 grouped by nationality.



Graphic: Else Magård

PERSONNEL LIST

Denham Group
Alyssa Huebner
Mark Denham
Muwan Chen
Susanne Hvolbøl Buchholdt

Kvitsiani Group
Duda Kvitsiani
Joshua Sanders

Möller Laboratory
Arne Møller

Nissen Group
Alessia Arduin
Aljona Kotsubei
Anna Marie Nielsen
Anne-Marie Lund Winther
Antoni Kowalski
Azadeh Shahsavar
Christine Juul Fælled Nielsen
Dorota Focht
Florian Hilbers
Franciszek Fijalkowski
Hanne Poulsen
Ingrid Dach
Jacob Lauwring Andersen
Jakob Ulstrup
Jonas Lindholt Gregersen
Joseph Lyons
Kaituo Wang
Khaled Taj
Lina Malinauskaite
Lotte Thue Pedersen
Magnus Kjærgaard
Mette Laursen
Miriam-Rose Ash
Oleg Sitsel
Peter Aasted Paulsen
Pontus Gourdon
Poul Nissen
Rasmus Pihl
Sigrid Thirup Larsen
Thomas Boesen

Nykjær Group
Anders Nykjær
Anja Aagaard D. Pedersen
Anne Kerstine Thomassen
Benedicte Vestergaard Jensen
Ditte Olsen
Hande Login
Ditte Olsen
Hande Login
Karen Marie Pedersen
Mads Fuglsang Kjølby
Mette Singers Johansen
Niels Sanderhoff Degn
Niels Wellner
Pernille Thomasen
Peter Lund Ovesen
Susanne Schousboe Sjøgaard
Ulrik Bølcho

Nykjær Group (Christian Vægter)
Christian Bjerggaard Vægter
Debbie Winther Lemming
Lone Tjener Pallesen
Maj Ulrichsen
Mette Richner

Nykjær Group (Olav Andersen)
Olav Michael Andersen
Annemarie Svane Aavild Poulsen
Arnela Mehmedbasic
Sandra Bonnesen

Nykjær Group (Simon Glerup)
Simon Glerup Pedersen
Simon Mølgaard Jensen

Philipsborn Group
Anne von Philipsborn
Begoña López Arias
Louise Lykkemark Christensen

Administration
Else Magård
Karen Bech

NEW FACES 2014

Laboratory technician Mette Singers Johansen

Research assistant Niels Sanderhoff Degn

PA for Professor Anders Nykjær, Susanne S. Sjøgaard

Postdoc Muwan Chen

Postdoc Joshua Sanders

Postdoc Florian Hilbers

Postdoc Christine Betzer

Postdoc Antoni Kowalski

Postdoc Begoña López Arias

Postdoc Niels Wellner

Group leader Keisuke Yonehara

Postdoc Alessia Arduin

Postdoc Azadeh Shahsavar

PhD student Alyssa Huebner

Postdoc Ingrid Dach

Team Leader Arne Möller

Postdoc Hande Login

PhD student Jakob Ulstrup

PhD student Annemarie Svane Aavild Poulsen

Group Leader Duda Kvitsiani

Postdoc Magnus Kjaergaard

PRICES & AWARDS

December	Master student Milena Laban received Novo Scholarship granted by Novo Nordisk Foundation and Novozymes.
November	PhD student Jakob Ulstrup received Best Poster Price at CoLuAa meeting.
October	Postdoc Joseph Lyons received postdoctoral fellowship granted by the Lundbeck Foundation. Grant amount: 0.7 million DKK.
September	Postdoc Nelson Ferreira received postdoctoral fellowship granted by the Lundbeck Foundation. Grant amount: DKK 2.1 million.

The winners of the Poster Performance Awards 2014 together with the Poster Committee (from the left): Tea Pemovska (FIMM), Mark Denham (DANDRITE), Tero Aittokallio (FIMM), Felipe Cava (MIMS), Oleg Sitsel (DANDRITE), Harri Itkonen (NCMM), Judith Staerk (NCMM), Pedro Lopes (MIMS). Photo: MIMS.

	Core Group Leader Anders Nykjær appointed Professor of Neuroscience at Mayo Medical School, Mayo Clinic Florida.
	Group leader Keisuke Yonehara received The Max. M. Burger Prize for "Outstanding publication" granted by Friedrich Miescher Institute (FMI).
	Team leader Arne Möller received MOBILEX grant granted by the the Danish Council for Independent Research. Grant amount: DKK 2.5 million. Project title: Engineered DNA/RNA Nano-Assemblies Enable High Throughput Characterization Of Protein Complexes.
	Postdoc Magnus Kjærgaard received postdoctoral fellowship granted by the Lundbeck Foundation. Grant amount: DKK 1.4 million.
	PhD student Oleg Sitsel received Poster Performance Awards 2014 at Nordic Molecular Medicine Network Meeting 2014 Umeå.
	Postdoc Mette Laursen postdoctoral fellowship granted by the Danish Council for Independent Research. Project title: Structural and Functional Studies of Acyl Coenzyme A Carboxylase Complexes from Mycobacterium tuberculosis. Grant amount: DKK 2.1 million.

GRANTS RECEIVED

December	Group leader Mark Denham as partner of the Strategic research centre: "BrainStem" funded by "Innovationsfonden". BrainStem is a collaboration between University of Copenhagen, Aarhus University, Lund University, University of Southern Denmark, Lundbeck A/S and Bioneer A/S. Grant amount (total): DKK 25 million.
	Group leader Keisuke Yonehara received "ERC Starting Grant", granted by Horizon 2020, The European Research Council. Grant amount: EUR 1.5 million.
September	Group leader Keisuke Yonehara received The Max. M. Burger Prize for "Outstanding publication" granted by Friedrich Miescher Institute (FMI).

INVITED TALKS GIVEN

December	Core Group Leader Anders Nykjær. Title: Sortilin receptors in psychiatric disorders. Given at Yale University, USA.
November	Core Group Leader Poul Henning Jensen. Title: Pathogenesis. Given at Global Multiple System Atrophy (MSA) Research Roadmap Meeting, Las Vegas, USA.
	Core Group Leader Poul Nissen. Title: Transport of sodium in and out of the cell. Given at Barcelona BioMed Conference: Transporters and other Molecular Machines.
October	Core Group Leader Poul Henning Jensen.Title: "Calcium dysregulation in Parkinson disease". Given at Workshop: Systematic Curation of Molecular Pathways implicated in Parkinson's disease, Luxembourg.
	Core Group Leader Poul Nissen. Keynote Title: ESS Foundation Stone Ceremony and Science Symposium taking place in Lund, Sweden.
September	Core Group Leader Poul Nissen. Title: IUBMB Lecture. Given at 2014 Year of Crystallography Symposium, Oieras Portugal.
	Core Group Leader Poul Nissen. Title: Membrane Protein Crystallization. Given at 15th International Conference on the Crystallization of Biological Macromolecules, Hamburg.
August	Core Group Leader Poul Henning Jensen: Title: "Lets (not) do the twist with alpha-synuclein". Given at The Nordic EMBL partnership for Molecular Medicine 5th Network Meeting, 2014, Umeå University, Sweden.
	Group Leader Anne von Philipsborn. Title: Neuronal circuits for Drosophila courtship song. Given at The Nordic EMBL partnership for Molecular Medicine 5th Network Meeting, 2014, Umeå University, Sweden.
	Group Leader Mark Denham. Title: Re-creating the nervous system in a dish with human pluripotent stem cells. Given at The Nordic EMBL partnership for Molecular Medicine 5th Network Meeting, 2014, Umeå University, Sweden.
	Core Group Leader Poul Nissen. Title: Structure of P-type ATPases. Given at ASBMB symposium: NaK-ATPase and related Transport ATPases, Lunteren, Holland.
	Core Group Leader Poul Nissen. Title: Oswalt Colloquium: The Future of Membrane Protein Research. Given at Max Planck Institut for Biophysics, Frankfurt.
June	Core Group Leader Anders Nykjær. Title: Sortilin receptors in neuronal plasticity and psychiatric disorders. Given at Mayo Clinic Seminars, FL, USA.
	Core Group Leader Poul Nissen. Title: GRC Biopolymers. Given at Salve Regina University, Rhode Island, US.
May	Core Group Leader Poul Nissen. Title: EMBO lecture, Channels and transporters. Given at Erice, Itlay
	Core Group Leader Poul Nissen. Title: MicroMAX and MedMAX - An introduction to opportunities for biomedical sciences at MAX IV, Lund, Sweden.
April	Core Group Leader Poul Henning Jensen: Title: Challenges in investigating pathogenic protein structures in brain tissue. Given at Satellite Seminar and Chinese Human Brain Banking Workshop on Standardized Operation, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China.
	Core Group Leader Poul Henning Jensen: Title: Disease modeling and brain banks - how to discover the unknown and validate the known. Given at International Workshop on Human Brain Banking in China, Central South University, Xiangya School of Medicine, Changsha, Hunan, China
March	Core Group Leader Anders Nykjær. Title: Vps10p-domain receptor family (Sortilins). Groningen Neuroscience Lecture. . Given at Aarhus University and Aarhus University Hospital.
	Core Group Leader Poul Nissen. Title: Non-stoichiometric relations in biology - and the law of mass action. Given at Waage-Guldberg 150 years anniversary symposium on the law of mass action, Oslo, Norway.
	Core Group Leader Poul Nissen. Title: New Structures and Functional Insight of the Neurotransmitter-Sodium Symporters. Given at GRC Ligand Recognition and Molecular Gating, California, US.
January	Core Group Leader Poul Nissen. Title: 2014 Year of Crystallography Symposium, University of Copenhagen.

PUBLICATIONS AND PATENTS

Publications

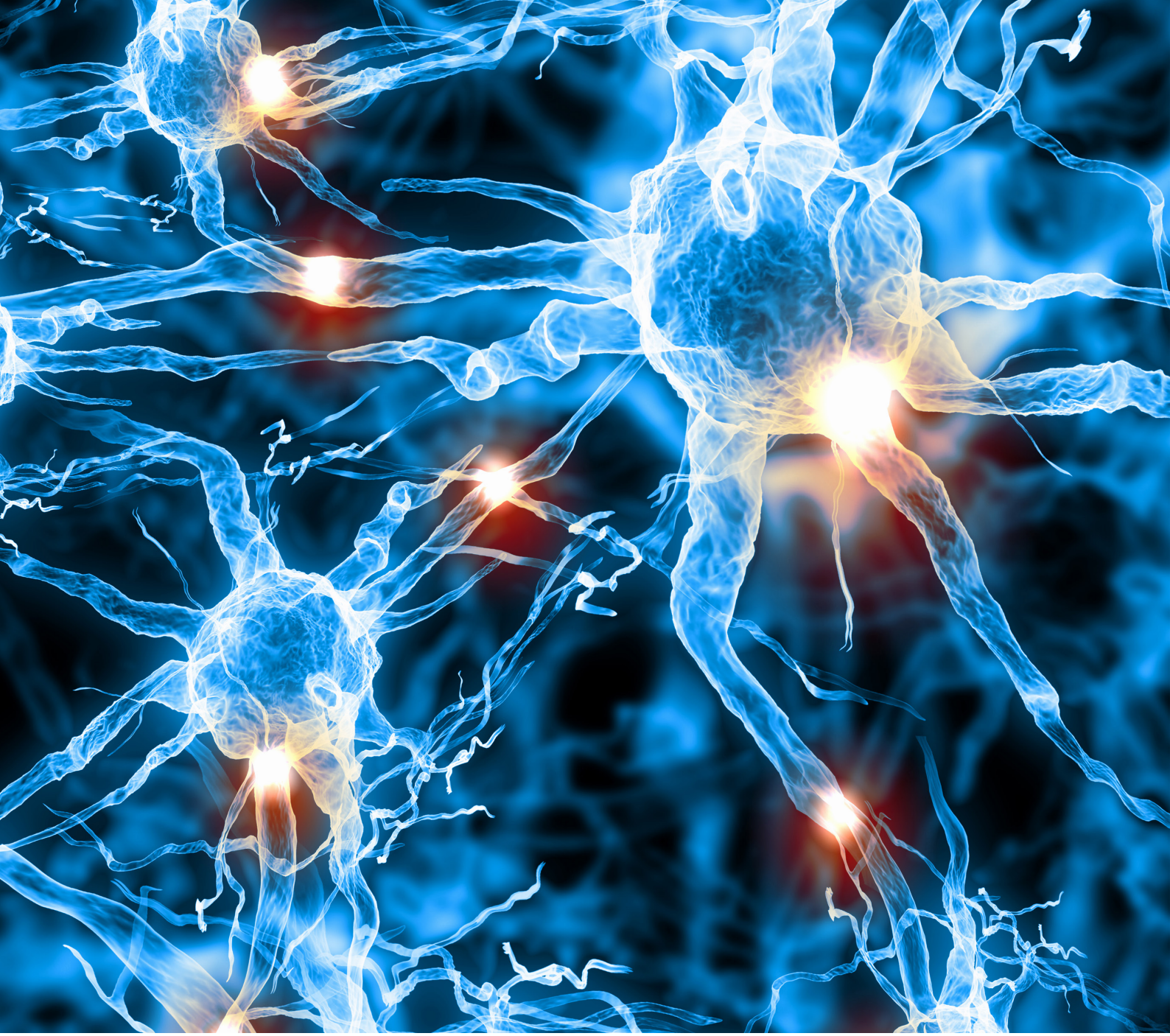
1. Copper-transporting P-type ATPases use a unique ion-release pathway. Andersson M, Mattle D, Sitsel O, Klymchuk T, Nielsen AM, Møller LB, White SH, Nissen P, Gourdon P (2014) Nature Structural and Molecular Biology 21. doi: 10.1038/nsmb.2721
2. Transport Pathway in Cu+ P-Type ATPases. Andersson M, Mattle D, Sitsel O, Nielsen AM, Lindahl E, White SH, Nissen P, Gourdon P (2014) Biophysical Journal 106(2). doi: 10.1016/j.bpj.2013.11.2406
3. A high-yield co-expression system for the purification of an intact drs2p-cdc50p lipid flippase complex, critically dependent on and stabilized by phosphatidylinositol-4-phosphate. Azouaoui H, Montigny C, Ash MR, Fijalkowski F, Jacquot A, Grønberg C, López-Marqués RL, Palmgren MG, Garrigos M, le Maire M, Decottignies P, Gourdon P, Nissen P, Champeil P, Lenoir G (2014) PloS One 9(11). doi: 10.1371/journal.pone.0112176
4. Inhibition of Ubiquitin Proteasome System Rescues the Defective Sarco(endo)plasmic Reticulum Ca2+-ATPase (SERCA1) Protein Causing Chianina Cattle Pseudomyotonia. Bianchini E, Testoni S, Gentile A, Calì T, Ottolini D, Villa A, Brini M, Betto R, Mascarello F, Sandonà D, Sacchetto R, Nissen P (2014) Journal of Biological Chemistry 289(48). doi: 10.1074/jbc.M114.576157
5. Functional characterization of Friedreich ataxia iPS-derived neuronal progenitors and their integration in the adult brain. Bird MJ, Needham K, Frazier AE, van Rooijen J, Leung J, Hough S, Denham M, Thornton ME, Parish CL, Nayagam BA, Pera M, Thorburn DR, Thompson LH, Dottori M (2014) PLoS One 9(7). doi: 10.1371/journal.pone.0101718
6. Sorting receptor sortilin-a culprit in cardiovascular and neurological diseases. Carlo AS, Nykjaer A, Willnow TE (2014) Journal of Molecular Medicine 92(9). doi: 10.1007/s00109-014-1152-3
7. Getting closer to the function of the postsynaptic receptor SORCS3 in synaptic transmission and synaptic plasticity. Christiansen GB, Breiderhoff T, Nykjær A, Jensen K, Willnow T, Holm MM (2014) Abstract from 9th FENS forum of neuroscience, Milan, Italy.
8. Comparing crystal structures of Ca2+-ATPase in the presence of different lipids. Drachmann ND, Olesen C, Møller JV, Guo Z, Bublitz M, Nissen P (2014) FEBS Journal 281(18). doi: 10.1111/febs.12957
9. Sortilins in neurotrophic factor signaling. Glerup S, Nykjaer A, Vægter CB (2014) Handbook of Experimental Pharmacology 220. doi: 10.1007/978-3-642-45106-5_7
10. SorCS2 Regulates Dopaminergic Wiring and Is Processed into an Apoptotic Two-Chain Receptor in Peripheral Glia. Glerup S, Olsen D, Vægter CB, Gustafsen C, Sjøgaard S, Hermey G, Kjølby MF, Jensen SM, Ulrichsen M, Hansen SB, Skeldal S, Fjorback AN, Nyengaard JR, Jacobsen J, Bender D, Bjarkam CR, Sørensen ES, Füchtbauer EM, Eichele G, Madsen P, Willnow T, Petersen CM, Nykjær A (2014) Neuron 82(5). doi: 10.1016/j.neuron.2014.04.022
11. The Hypercholesterolemia-Risk Gene SORT1 Facilitates PCSK9 Secretion. Gustafsen C, Kjolby M, Nyegaard M, Mattheisen M, Lundhede J, Buttenschøn H, Mors O, Bentzon JF, Madsen P, Nykjaer A, Glerup S (2014) Cell Metabolism 19(2). doi: 10.1016/j.cmet.2013
12. Crystals of Na(+)/K(+)-ATPase with bound cisplatin. Huliciak M, Reinhard L, Laursen M, Fedosova N, Nissen P, Kubala M (2014) Biochemical Pharmacology 92 (3). doi: 10.1016/j.bcp.2014.08.029
13. Pro-neurotrophins, sortilin, and nociception. Lewin GR, Nykjaer A (2014) The European journal of neuroscience 39(3). doi: 10.1111/ejn.12466
14. Prodegenerative IκBα expression in oligodendroglial α-synuclein models of multiple system atrophy. Kragh CL,

Gysbers AM, Rockenstein E, Murphy K, Halliday GM, Masliah E, Jensen PH (2014) Neurobiology of Disease. 63. doi: 10.1016/j.nbd.2013.12.002

15. Alpha synuclein in Parkinson's disease: Handbook of Neurotoxicity. Kragh CL, Romero-Ramos M, Hallida GM, Jensen PH (2014) Springer Science+Business Media B.V. doi: 10.1007/978-1-4614-5836-4_14
16. How epigallocatechin gallate can inhibit α-synuclein oligomer toxicity in vitro. Lorenzen N, Nielsen SB, Yoshimura Y, Vad BS, Andersen CB, Betzer C, Kaspersen JD, Christiansen G, Pedersen JS, Jensen PH, Mulder FAA, Otzen DE (2014) Journal of Biological Chemistry 289(31). doi: 10.1074/jbc.M114.554667
17. A mechanism for intracellular release of Na(+) by neurotransmitter/sodium symporters. Malinauskaite L, Quick M, Reinhard L, Lyons JA, Yano H, Javitch JA, Nissen P (2014) Nature Structural and Molecular Biology, 21(11). doi: 10.1038/nsmb.2894
18. S-Palmitoylation and S-Oleoylation of Rabbit and Pig Sarcolipin. Montigny C, Decottignies P, le Maréchal P, Capy P, Bublitz M, Olesen C, Møller JV, le Maire M, Nissen P (2014) Journal of Biological Chemistry 289. doi: 10.1074/jbc.M114.590307
19. Targeting sortilin in immune cells reduces proinflammatory cytokines and atherosclerosis. Mortensen MB, Kjolby M, Gunnersen S, Larsen JV, Palmfeldt J, Falk E, Nykjaer A, Bentzon JF (2014) Journal of Clinical Investigation. doi: 10.1172/JCI76002
20. How do we show molecules and how they move?. Nissen P (2014) Biozoom 3.
21. Brian Clark has died - marking the end of an era : Professor Brian Frederic Carl Clark, founder of Structural Biology Research at Aarhus University, died on Monday, October 6, 2014. Aged 78 years. Nissen P, Heilesen L (2014) IUBMB Life 66(10). doi: 10.1002/iub.1325
22. Initiating Heavy-atom Based Phasing by Multi-Dimensional Molecular Replacement. Pedersen BP, Gourdon P, Liu X, Lykkegaard KJ, Nissen P (2014) arXiv 1403.7484.

Patents

- Methods and tools for identification of rsk/msk kinase inhibitors. Andersen JL (Opfinder), Nissen P (Opfinder), Iversen L (Opfinder), Gesser B (Opfinder). IPC nr.: C12N15/62; C12N9/12; C30B29/58; G06F19/16. Patentnummer: WO2014048442 (A1). apr. 03, 2014.



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