2016

DANDRITE ANNUAL REPORT

AARHUS UNIVERSITY

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

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Novo Nordisk Foundation, Denmark

Words from the Director

With our great pleasure, we present the 2016 annual report from DANDRITE.

2016 was a very important year at DANDRITE encompassing many important steps of implementation and consolidation of new, ambitious research programs. Molecular and cellular mechanisms of memory, decision making, motor control, brain processing in vision are examples of new fields of neuroscience introduced at DANDRITE and have also been associated with development and applications on new methods and applications of e.g. stem cells and animal models, two-photon imaging and cryo-electron microscopy to study advanced problems in neuroscience.

In 2016 DANDRITE completed the first stages of the renewal process for a second five-year period with submission of the inaugural report for the years 2013-2016 and the combined proposals for future research activities. Along with the renewal process, we hosted a Site Visit review carried out by an external Review Panel in December 2016. The Site Visit review was headed by the Lundbeckfonden and joined as well by Aarhus University and EMBL.

DANDRITE now encompasses a dynamic community of more than 115 researchers and 20+ nationalities that connects further to leading neuroscience centers across the world. DANDRITE hosted more than 50 visiting speakers and researchers and organized/co-organized several international meetings in Denmark and abroad.

Besides grand ideas and talent, excellent research also needs funding. DANDRITE has secured competitive funding that almost triples the core funding from the Lundbeckfonden and Aarhus University. DANDRITE now hosts two ERC StG programs, three other career development awards, numerous PhD and postdoc fellowships, and a range of small and larger project and equipment grants making DANDRITE not only a thriving and dynamic research environment, but also a powerful stepping stone for careers in science and research.

We hope you will enjoy a few moments to learn more about our activities on the following pages

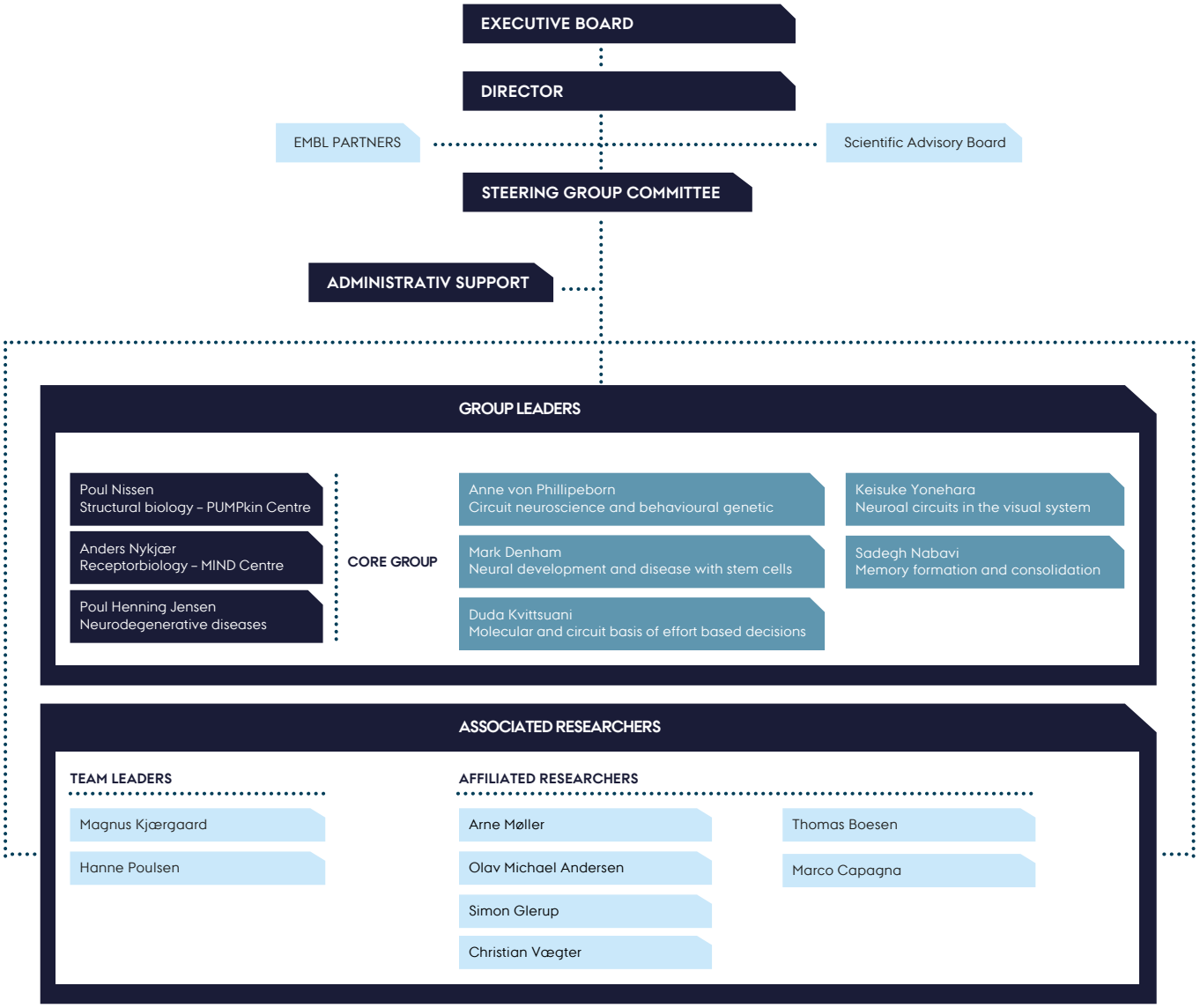
With my warmest regards,

Poul Nissen, director and core group Leader.

01 Organization Structure

Organization Structure

Governance and management of DANDRITE has a classical organization structure as illustrated with the hierarchical figure.



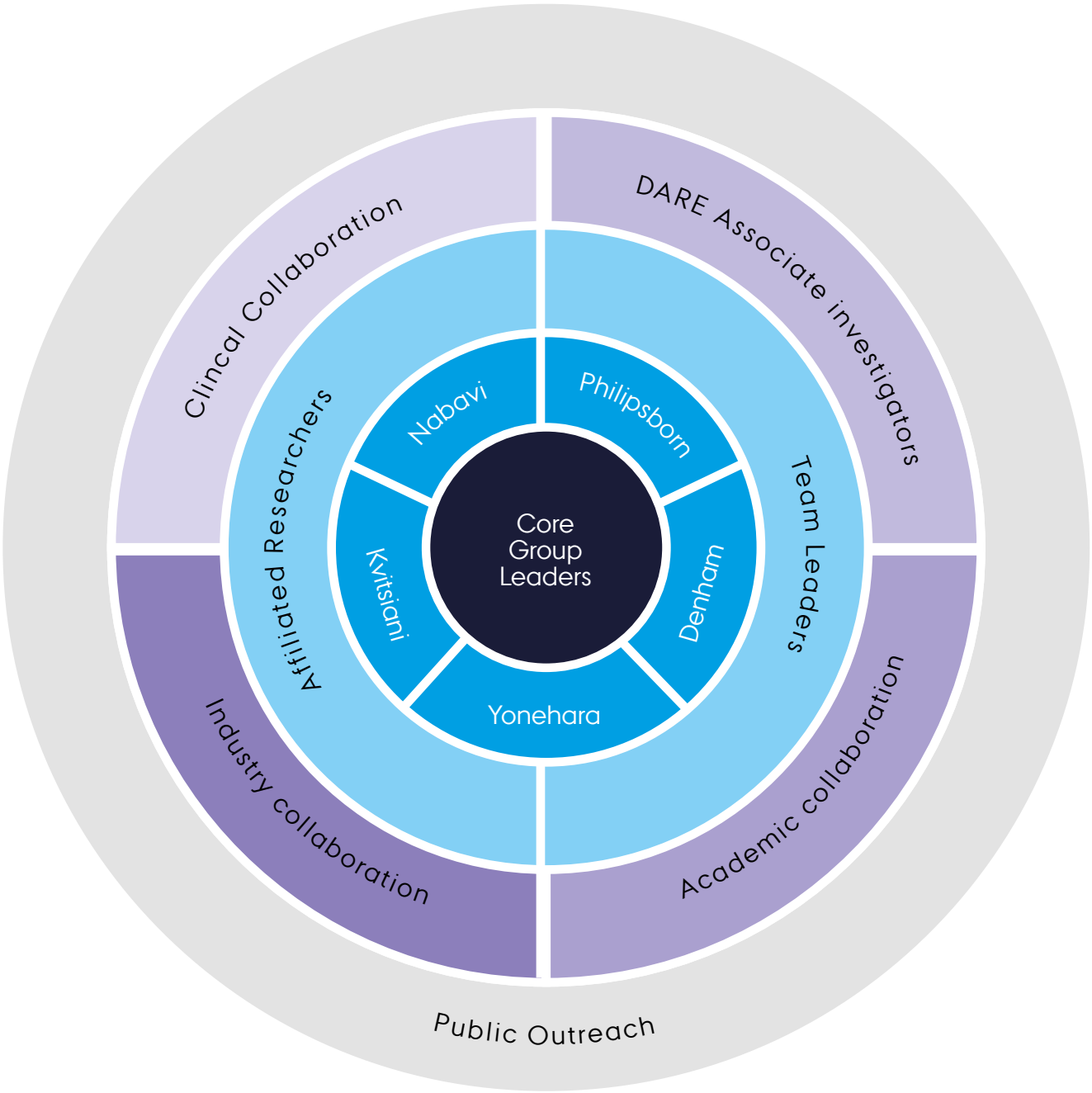
ASSOCIATED DANDRITE RESEARCHERS

DANDRITE Team leaders (TL):
Researchers with a pre-tenure/tenure track position at Aarhus University. A maximum of four TL can be associated to DANDRITE and they complement infrastructural and research-oriented strategies in DANDRITE. A DANDRITE TL appointment is for 3 years with possible extension for a total of maximum 6 years.

DANDRITE affiliated researchers (AFR):
Researchers with permanent positions at Aarhus University that are tightly associated to DANDRITE group leader(s) through e.g. joint grants/research centers, shared laboratories and/or long-standing collaborations. The affiliation can also provide strategic support with AU departments and infrastructures.

DANDRITE researchers & collaborators

Nevertheless research endeavors and collaborations are everything but hierarchical which is illustrated with the circular graphic presentation of DANDRITE's research collaborations and collaborative landscape.



Executive Board

The Executive Board meets twice a year and consists of a chair, the deans of the Faculty of Science & Technology and the Faculty of Health, the director of research from Lundbeck-fonden and the core group leaders. The board members in 2016:

Chairman: Clinical Professor Jens Chr. Hedemann Sørensen (Department of Clinical Medicine, Aarhus University, Aarhus University Hospital-Danish Neuroscience Center, from December 2016)

Professor David Brooks, Department of Clinical Medicine, Aarhus University and Aarhus University Hospital-Danish Neuroscience Center (from 2013 to December 2016)

Aarhus University, Faculty of Science and Technology: Dean Niels Christian Nielsen

Aarhus University, Faculty of Health Sciences: Dean Allan Flyvbjerg (2013 to October 2016)

Aarhus University, Faculty of Health Sciences: Interim dean Ole Steen Nielsen (from October 2016)

DANDRITE: Director, Professor Poul Nissen

DANDRITE: Professor, core group leader Anders Nykjær

DANDRITE: Professor, core group leader Poul Henning Jensen

Lundbeckfonden (non-voting): Director of Research Anne-Marie Engel

Administrative support: Chief Administrative officer Else Magård, DANDRITE

Steering Committee

The steering committee meets weekly and consists of the director, the core group leaders and two representatives of the group leaders (internally elected on two-year terms). DANDRITE's administrative personnel also attends the meetings. The steering committee is responsible for implementation of research, the planning and coordination of activities, strategic developments and the distribution of the running budget. The steering committee is also overseeing public dissemination and outreach of DANDRITE research and activities. The committee in 2016 consisted of the following members:

- Professor Poul Nissen, Director
- Professor Anders Nykjær, core group leader
- Professor Poul Henning Jensen, core group leader
- Group Leader Sadegh Nabavi (from August 2015)
- Group Leader Keisuke Yonehara (from August 2016
- Chief Administrative Officer, Else Magård

Furthermore, the steering committee meetings are attended by: Communications Officer & PA to the Director, Maria Thykær Jensen (maternity cover for Karen Bech since Nov 2016) and Scientific Coordinator & professor PA, Susanne Schousboe Sjøgaard

Monthly Extended Steering Committee Meeting

Every second Monday of each month the steering committee meets for an extended steering committee meeting taking place from 10:30 AM to 11:30 AM. The extended committee consists of all Group Leaders and Team leaders, spokespersons for each personnel category at DANDRITE. In 2016 the participants were:

- All DANDRITE Group Leaders
- All DANDRITE Team Leaders
- Affiliated Researcher spokesperson: Olav Michael Andersen (first half year)
- Affiliated Researcher spokesperson: Simon Glerup (second half year)
- Postdoc spokesperson: Niels Wellner
- PhD student spokesperson: Sara Buskbjerg Jager
- Technician spokesperson: Lotte Thue Pedersen (until November)
- Technician spokesperson: Benedicte Vestergaard (from November)

Monthly Coordination Meeting

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

Young DANDRITE – The PhD & Postdoc Association at DANDRITE

The PhD & Postdoc Association at DANDRITE, "Young DANDRITE", facilitates interaction and unity among the PhD students and postdocs affiliated with DANDRITE. The association meets several times a year for meetings and events, and activities are also planned ad hoc. The PhD and postdoc spokespersons for the extended steering committee (see above) are also selected by Young DANDRITE.

Technician Network

The laboratory technicians from all research groups affiliated with DANDRITE meet 2-3 times per year, to facilitate exchange and alignment of know-how, administrative and regulatory procedures, practical information, and for informal networking. The speaker for the extended steering committee is elected by the network and communicates matters raised or discussed in the technician network or at the extended steering committee.

Administrative Support Unit

The mission of the DANDRITE administration is to cater for the needs connected to DANDRITE activities and to support and align administrative procedures with the general administration at Aarhus University. DANDRITE research encompasses interdisciplinary and translational activities, and therefore an important component of the daily routines is to coordinate among various entities and governance structures. The DANDRITE administrative unit interacts closely with AU administrative divisions: AU Research Support and External Relations, AU Finance and Estates Project Development, AU Human Resources, AU Student Administration and Services, AU IT, and Communications (Rector's Office). Furthermore, a tight collaboration and support is provided by our colleagues at administration centers at the Faculty of Health and the Faculty of Science & Technology.

Scientific Advisory Board

The scientific advisory board (SAB) convenes biannually and provides independent advice on scientific and strategic matters, and evaluations of achievements, ideas and strategies. SAB members are internationally highly reputed researchers. Since the first SAB meeting in Aarhus in 2014, a second meeting was combined with the DANDRITE retreat in September 2016 at the conference center Sandbjerg. The members of the DANDRITE SAB are:

- Professor Rüdiger Klein, Max-Planck-Institute of Neurobiology (chair of the 2016 meeting)
- Professor Mart Saarma, University of Helsinki (chair of the 2014 meeting)
- Professor Kathleen Sweadner, Harvard Medical School
- Professor Moses Chao, New York University (NYU)
- Professor Glenda Halliday, Neuroscience Research Australia (NeuRA)
- Director Matthias Wilmanns, EMBL Hamburg
- Division Director Jan Egebjerg, Lundbeck
- Professor Carl Petersen, École Polytechnique Fedérale de Lausanne EPFL

SAB meeting 2016: DANDRITE participants together with SAB members. Foto DANDRITE.

02 Research Activities

Nissen Group

Structural and Functional Studies of Membrane Transporters in Brain

Professor
Poul Nissen

The Nissen lab investigates molecular mechanisms of membrane transport processes and biomembrane structure in the brain. Activities are mainly focused on protein crystallography, electron microscopy, and biochemistry and include also collaborative studies through e.g. small-angle X-ray scattering, molecular dynamics simulations, super resolution microscopy, and electrophysiology.

The main subjects of research focus on P-type ATPases (ion pumps and lipid flippases) as well as Na+ dependent amino acid/neurotransmitter and chloride transporters. Derived activities include also structure based drug discovery. A major, long-term goal is to investigate and model higher-order networks in cell membranes of the brain, in particular of the Axon Initial Segment that integrates circuit inputs and generates the action potentials in firing neurons.

The P-type ATPase ion pumps and lipid flippases consume some 40-80% of ATP in the brain and maintain constantly the vital lipid distributions and ion gradients that potentiate e.g. lipid bilayer dynamics, secondary transporters, cell volume regulation, ion homeostasis, pH control, and the activity of ion channel receptors. Structural studies of Na,K-ATPase and Ca2+-ATPase revealed mechanisms of inhibition. Functional and structural studies of Na,K-ATPase revealed important roles of isoform combinations on e.g. K+ clearance. The Ca2+-ATPase LMCA1 was engineered for site specific photo-labelling that allows tracking of conformational changes by single-molecule FRET. A general mechanism of inward-to-outward switching of neurotransmitter and amino acid transporters of the SLC6 family was revealed from crystal structures of the LeuT transporter.

TRANSLATIONAL STUDIES

Effects of neurological disease-related mutations of Na,K-ATPase were analyzed in mouse models. Development of allosteric, covalent inhibitors of RSK/MSK kinases was continued. Studies of dysfunctional ATP7B in Wilson's disease was continued with the Danish Wilson's Disease Center at Aarhus University Hospital. The mechanism of the malaria drug artemisinin on the P. falciparum pfATP6 was investigated and refuted.

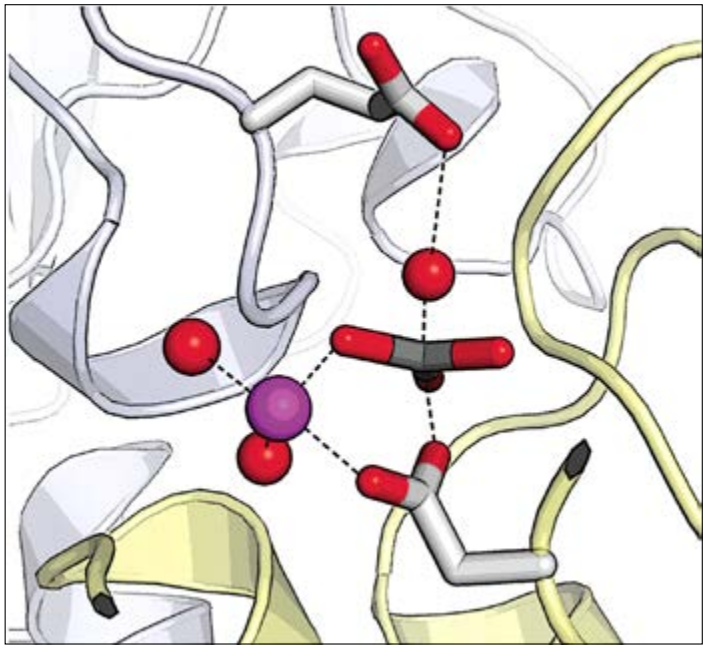
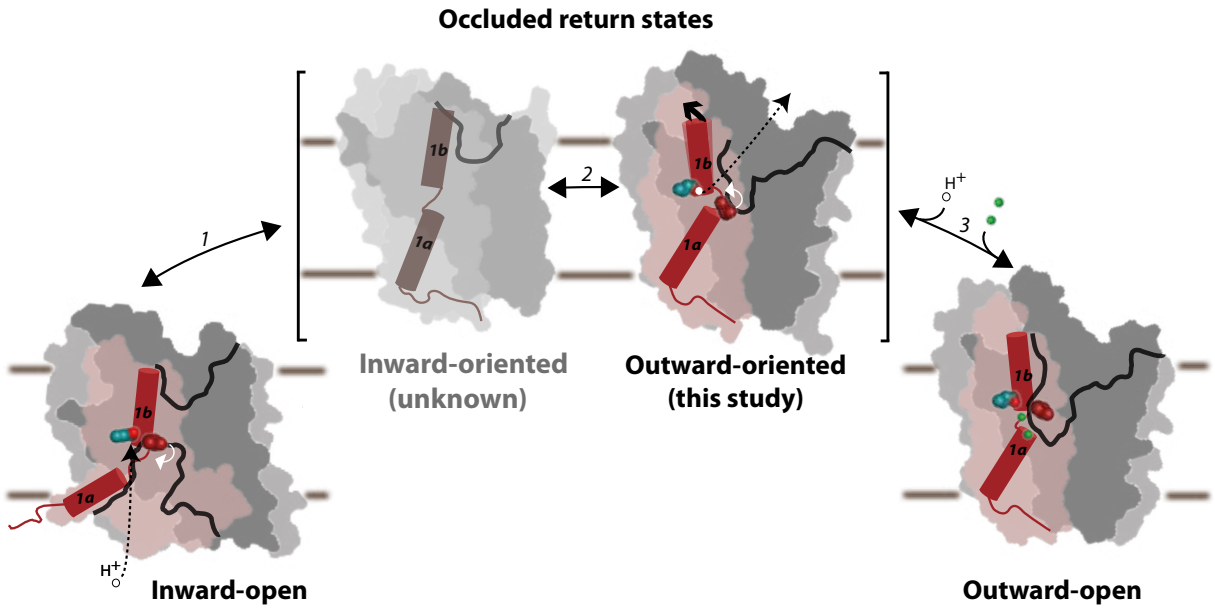


Fig. 1: P-type ATPases consume a staggering 50-80% of ATP-derived energy turned over in neurons. The Nissen group presented a key transition state of ATP hydrolysis trapped by vanadate. Figure by Dr. Johannes Clausen.

Fig. 2: SLC6 represents a large family of Na+ dependent amino acid and neurotransmitter transporters such as the Glycine, GABA, dopamine and serotonin transporters. They are responsible for the reuptake of such neurotransmitters after synaptic release. The Nissen group revealed a critical, generally conserved gating mechanism in SLC6 transporters that allows them to perform transport with tight coupling to the Na+ gradient.



Selected publications 2016

Clausen JD, Bublitz M, Arnou B, Olesen C, Andersen JP, Møller JV, **Nissen P** (2016). Crystal Structure of the Vanadate-Inhibited Ca(2+)-ATPase. *Structure* 24:617-23

Malinauskaite L, Said S, Sahin C, Grouleff J, Shahsavar A, Bjerregaard H, Noer P, Severinsen K, Boesen T, Schiøtt B, Sinning S, **Nissen P** (2016). A conserved leucine occupies the empty substrate site of LeuT in the Na(+)-free return state. *Nat Commun* 7:11673

David-Bosne S, Clausen MV, Poulsen H, Møller JV, **Nissen P**, le Maire M (2016). Reappraising the effects of artemisinin on the ATPase activity of PfATP6 and SERCA1a E255L expressed in Xenopus laevis oocytes. *Nat Struct Mol* Biol 23:1-2

Personnel List Nissen Group

Assistant Professor **Joseph Lyons**
Postdoc **Antoni Kowalski**
Postdoc **Azadeh Shahsavar**
Postdoc **Ingrid Dach**
Postdoc **Jacob Lauwring Andersen**
Postdoc **Michael Voldsgaard Clausen**
Postdoc **Prasad Kasaragod**
Industrial PhD Student **Lars Sørensen**
PhD Student **Aljona Kotsubei**
PhD Student **Caroline Marie Teresa Neumann**
PhD Student **Jakob Ulstrup**
PhD Student **Josephine Nissen**
PhD Student **Marlene Uglebjerg Sørensen**
PhD Student **Milena Laban**
PhD Student **Paula Szalai**
PhD Student **Sigrid Thirup Larsen**
Academic employee **Andreas Bøggild**
Academic employee **Christine Juul Fælled Nielsen**
Laboratory Technician **Anna Marie Nielsen**
Laboratory Technician **Lotte Thue Pedersen**
Research Assistant **Dorota Focht**
Student Assistant **Sofie Stokkebro Schmøkel**
Student Assistant **Line Lindgreen Eriksen**
Professor **Poul Nissen**

Jensen Group

Neurodegenerative Disease

Professor
Poul Henning Jensen

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 and involves the development of new aggregate selective tools.

The aim is with a therapeutic focus to decipher structures of misfolded alpha-synuclein aggregates and how they impact on cells with respect to cytotoxic and protective mechanisms and how cells decide on exporting certain misfolded species that may contribute to the prion-like spreading in tissue. This involves susceptible homeostatic cellular mechanisms being offset by alpha-synuclein aggregates like dysregulated calcium homeostasis and proteostatic mechanisms like autophagy and unconventional secretion.

The main focus in 2016 was to characterize mechanisms whereby kinases regulate alpha-synuclein levels and function, establish disease modifying studies in the in-vivo M83 mouse model of prion-like alpha-synuclein spreading and neurodegeneration and conduct in vivo studies on new alpha-synuclein mice lines and in vivo studies using kinase inhibitors. We obtained a large 5-year project grant from the Lundbeck Foundation to establish the 5-year research project DACAPO focusing on Decisive and early alpha-synuclein aggregate dependent calcium changes in Parkinson's disease. This project will be established in 2017 and expand our research in calcium regulated processes beside current structural and mechanistic studies and in vivo disease modifying investigations.

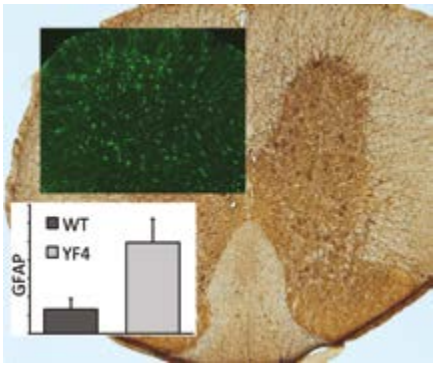


Fig. 1. Spinal cord of new alpha-synuclein transgenic mouse line (YF4) immunostained for alpha-synuclein demonstrates accumulation of alpha-synuclein in neuronal cell bodies (Brown staining). Upper insert depicts GFAP immunofluorescence staining of astrocytes in YF4 line (green). Lower insert depicts increased astrogliosis in YF4 line compared to control wild type mice. Images made by postdoc Louise B. Lassen, postdoc Mette Richter, and Professor Torben Moos, Aalborg University.

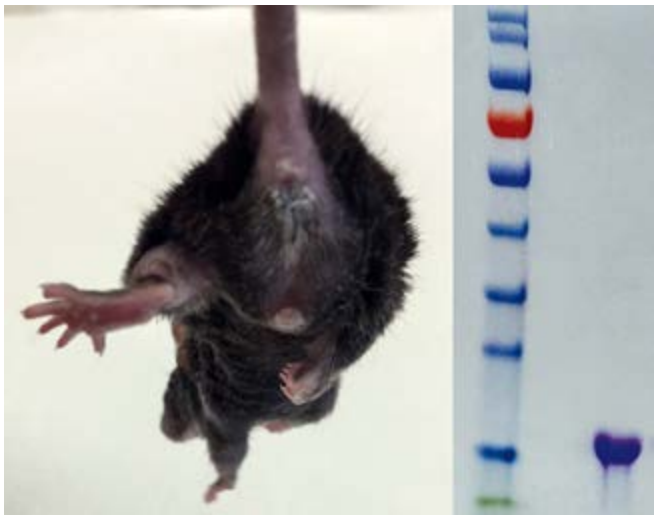


Fig. 2. Preformed fibrils made of pure alpha-synuclein (right panel) is injected into alpha-synuclein transgenic mice to initiate alpha-synuclein aggregate dependent neurodegeneration. Mice display incomplete clasping behavior in left hindleg (Left panel). Images made by postdoc Nelson Ferreira.

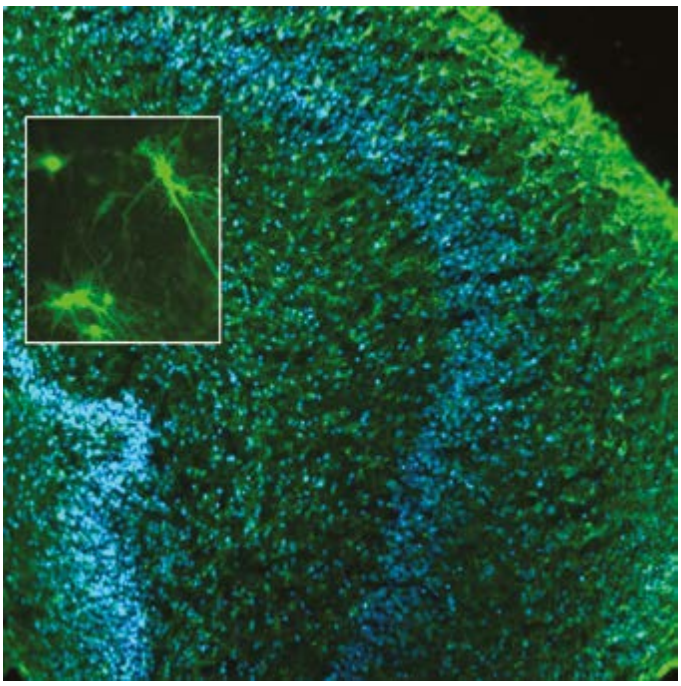


Fig 3. Organotypic hippocampal brain slice culture from mice. Green cells express GFP driven by viral vector. Images made by PhD student Sara Elfarash.

Selected publications 2016

Matrone C, Dzamko N, Madsen P, Nyegaard M, Pohlmann R, Søndergaard RV, Lassen LB, Andresen TL, Halliday GM, **Jensen PH**, Nielsen MS (2016). Mannose 6-Phosphate Receptor Is Reduced in alpha-Synuclein Overexpressing Models of Parkinsons Disease. *PLoS One* 11(8):e0160501.

Lassen LB, Reimer L, Ferreira N, Betzer C, **Jensen PH** (2016). Protein Partners of -Synuclein in Health and Disease. *Brain Pathol* 26(3):389-97. doi: 10.1111/bpa.12374.

Yatime L, Betzer C, Jensen RK, Mortensen S, **Jensen PH**, Andersen GR (2016). The Structure of the RAGE:S100A6 Complex Reveals a Unique Mode of Homodimerization for S100 Proteins. *Structure* 24(12):2043-2052. doi: 10.1016/j.str.2016.09.011.

Personnel List Jensen Group

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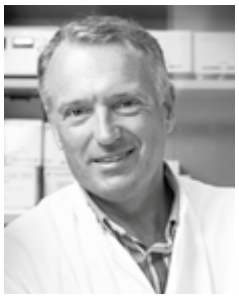
Postdoc **Nelson Ferreira**
PhD Student **Emil Gregersen**
PhD Student **Lasse Reimer**
Industrial PhD Student **Michael Aagaard Andersen**
PhD Student **Rikke Hahn Kofoed**
PhD Student **Sara Elfarrash**
Bioanalyst **Jette Bank Lauridsen**
Professor **Poul Henning Jensenssist**

Nykjær Group

Receptor Biology



Professor
Anders Nykjær

Research activities of the Nykjær Group are focused towards the functional characterization of a family of neuronal type-1 receptors denoted Vps10p-domain receptors or sortilins. Members of this gene family, which comprises sortilin, SorCS1, SorCS2, SorCS3 and SorLA, predominate in neurons but are also present in specialized cell types outside the nervous system.

The receptors are multifunctional as they can bind a vast number of ligands including neurotrophins and their receptors, amyloid precursor protein, progranulin, cytokines, and VLDL, and engage in cellular trafficking and signaling dependent on the cellular context (reviewed in *Trends in Neuroscience* 2012, 35(4):261-70; and *Nature Reviews Neuroscience* 2008, 9: 899-909). Accordingly, sortilin receptors have surfaced as risk genes for psychiatric, neurological, and metabolic diseases.

Patients with variants of the gene encoding SorCS2 are at risk of developing schizophrenia and bipolar disorder. Recently, we reported that SorCS2 stimulates neurotransmission and synaptic consolidation in the hippocampus. It does so by targeting the receptor TrkB, a protein required to induce synaptic strength and growth, to specific microdomains of the synapses. Consequently, neurons in which SorCS2 is dysfunctional fail to send out their projections and properly innervate neighboring neurons, and in mice this translates into behavioral deficits that mimic those observed in patients with schizophrenia and bipolar disorder. Our findings provide a molecular explanation for the genetic association between SorCS2 and the risk of developing psychiatric diseases (Mol. Psych., 2016).

Using a broad repertoire of molecular, cellular and genetic tools combined with transgenic mouse models, we aim to unravel the function of the receptor family in health and disease and to evaluate the potential of the receptors as drug targets. Among other projects, we will characterize the roles of the Vps10p-domain receptor in neurotrophin signaling, synaptic plasticity, and mental disorders, and how the receptors may be implicated in multiple sclerosis, vascular disease of the brain, and other neurodegenerative disorders.

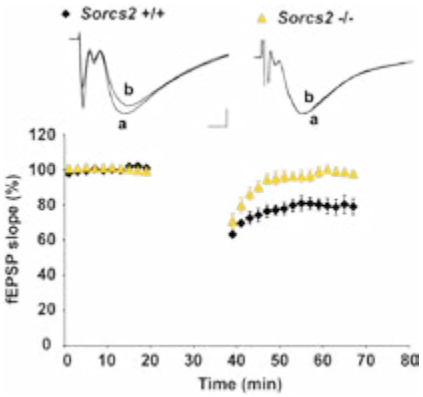


Fig. 1: Impaired long-term depression of synaptic transmission in acute hippocampal slices derived from SorCS2 -/- mice.
Illustration by Ulrik Bølcho

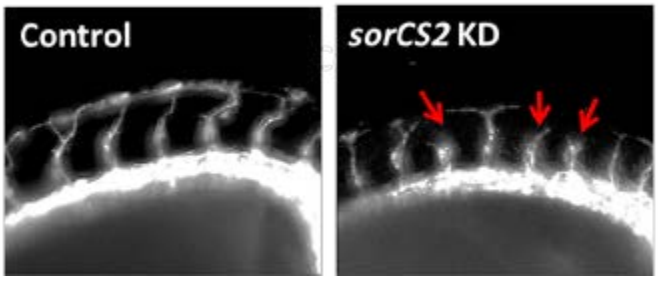


Fig. 2: Impaired growth of intersegmental vessels in SorCS2 knockdown zebrafish. Illustration by Hande Login

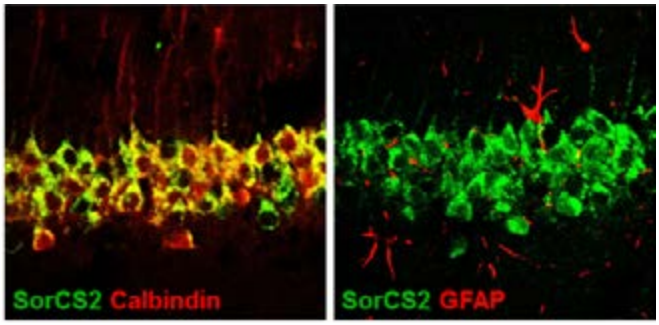


Fig. 3: SorCS2 expression in neurons of the dentate gyrus. Illustration from Mol Psych 2016.

Selected publications 2016

Christiansen GB, Andersen K, Riis S, **Nykjaer A**, Bølcho U, Jensen MS, Holm MM (2017) The sorting receptor SorCS3 is a stronger regulator of glutamate receptor functions compared to GABAergic mechanisms in the hippocampus. *Hippocampus* 27(3):235-248

Molgaard S, Demontis D, Nicholson AM, Finch NA, Petersen RC, Petersen CM, Rademakers R, **Nykjaer A**, Glerup S (2016) Soluble sortilin is present in excess and positively correlates with progranulin in CSF of aging individuals. *Exp Gerontol* 84:96-100

Glerup S, Bolcho U, Molgaard S, Bøggild S, Vaegter CB, Smith AH, Nieto-Gonzalez JL, Ovesen PL, Fjorback AN, Kjolby M, Login H, Holm MM, Andersen OM, Nyengaard JR, Willnow TE, Jensen K, **Nykjaer A** (2016) SorCS2 is required for BDNF dependent plasticity in the hippocampus. *Mol Psych* 21(12):1740-1751

Vázquez CL, Rodgers A, Herbst S, Coade S, Gronow A, Guzman CA, Wilson MS, Kanzaki M, **Nykjaer A**, Gutierrez MG (2016) The proneurotrophin receptor sortilin is required for Mycobacterium tuberculosis control by macrophages. *Sci Rep* 6:29332.

Goettsch C, Hutcheson JD, Aikawa M, **Nykjaer A**, Kjolby M, Rogers M, Michel T, Shibasaki M, Rader DJ, Libby P, Singh SA, Aikawa E (2016) Sortilin mediates vascular calcification via its recruitment into extracellular vesicles. *J Clin Invest* 126(4):1323-36

Personnel List Nykjær Group

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PhD Student **Pernille Bogetofte Thomasen**
PhD Student **Peter Lund Ovesen**
PA, Scientific Coordinator
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Academic employee **Ulrik Bølcho**
Laboratory Staff Member
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Laboratory Technician
Anne Kerstine Thomassen
Laboratory Staff Member
Benedicte Vestergaard Jensen
Student Assistant **Niels Kjærgaard Madsen**
Professor **Anders Nykjær**

Denham Group

Stem Cells

Group Leader
Mark Denham

The Denham lab studies how the human nervous system develops and the processes involved in neural degeneration. They use human embryonic stem cells and human induced pluripotent stem cells (iPSC) to study the signaling pathways required for their differentiation into various neuronal cell types. In particular, the group is interested in the specification of mesencephalic dopaminergic neurons, the major cell type affected in Parkinson's disease. Furthermore, the group is using patient-derived iPSCs to develop in vitro models for studying the disease processes involved in Parkinson's disease, which can subsequently be used to identify early neurodegenerative changes. The overall goals are to develop potential new treatment strategies for Parkinson's disease and other neurodegenerative disorders.

MOLECULAR MECHANISMS CONTROLLING PARKINSON'S DISEASE SUSCEPTIBILITY

The current work of the lab has involved generating a bank of Parkinson's patient iPSC lines, reprogrammed from a diverse range of familial Parkinsonian patient skin samples (Fig1). These cell lines encompass the major familial PD mutations that are currently known. Using a state-of-the-art genetic engineering technique CRISPR, the group is now correcting the mutations in the iPSCs. These iPSC lines along with their CRISPR corrected lines will be used to examine the molecular mechanisms that are linked to the various familial mutations. The unique aspects of pluripotent stem cells are their ability to give rise to all cell types of the body. Exploiting this feature, the group has recently developed a highly efficient and rapid protocol for generating mesencephalic dopaminergic neurons, which now allows for the directly analysis of the cell type most affected in Parkinson's disease, and the ability to derive these from patient specific cells (Fig2). The group is using next generation sequencing of iPSC-derived neurons to identify gene-expression changes between the various patient cell lines. This work is aimed at uncovering the major molecular pathways related to Parkinson's disease.

PATHWAYS REGULATING PROGENITOR CELL FATES

Additionally, the group is investigating the processes involved in stem cell fate choices and the factors involved in neural stem cell self-renewal versus differentiation. In particular, the group has recently identified a new progenitor cell type, NMP "neuromesodermal progenitor", which is a unique cell type found in the developing spinal cord that is capable of giving rise to neural and mesodermal lineages. Specifically, the lab is interested in understanding which cell types the NMPs are able to differentiate into within the central and peripheral nervous system. Understanding these progenitor states will lead to improved in vitro differentiation protocols that can subsequently be used to generate more effective human cellular models for studying neurodegenerative diseases or for developing neuronal repair methods for neuronal damage, such as spinal cord injuries.

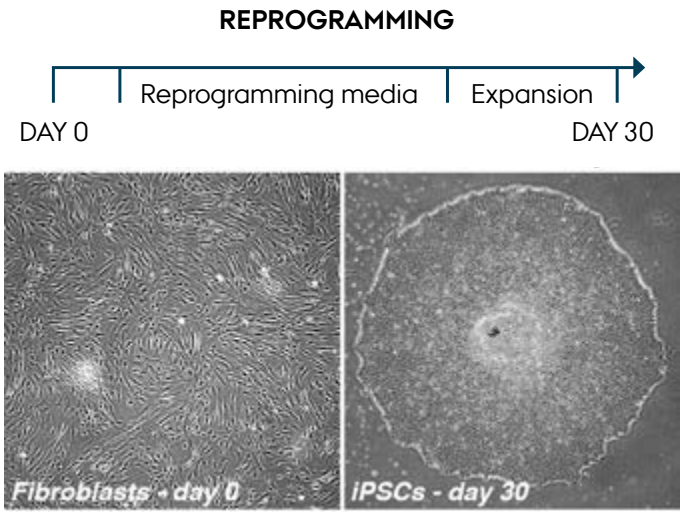

Fig. 1: 30 day sendai virus reprogramming protocol used to convert human patient fibroblast cells into induced pluripotent stem cells in defined media. Left image shows human fibroblast cells prior to reprogramming and right image shows a successfully reprogrammed cell colony.
Image by: Susanne Buchholdt.

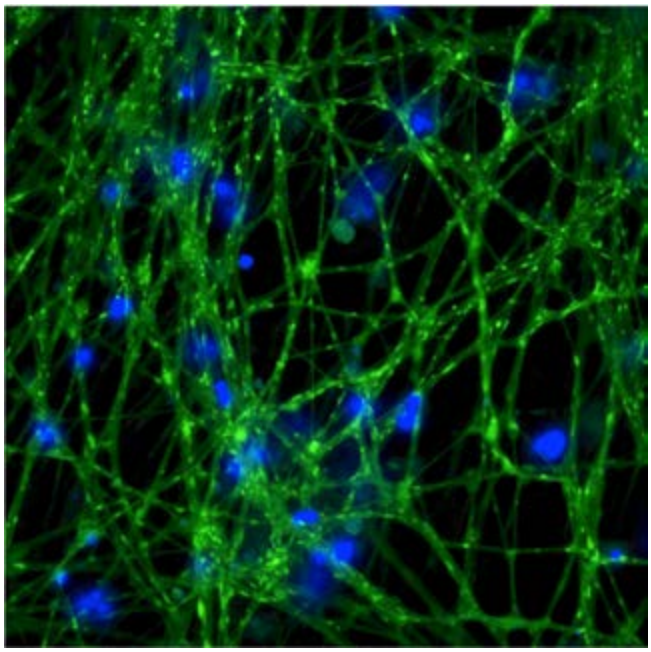

Fig 2: Neurons derived from patient iPSCs
Image by: Muwan Chen

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Postdoc **Muwan Chen**
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Laboratory Technician **Susanne Hvolbøl Buchholdt**
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Group Leader **Mark Denham**

Kvitsiani Group

Neuronal Circuits and Molecular Basis of Effort Based Decision-making

Group Leader
Duda Kvitsiani

We investigate genetic and neural circuit mechanisms underlying decision-making in flies, and rodents. The aim of our research is to build predictive and quantitative models of behavior that will help us uncover mechanistic insights into decision-making. The methods we use include molecular genetics, psychophysics, behavioral electrophysiology and optogenetics.

Our research is centered on a simple basic question: How do animals and humans choose better options? Our aim is to understand the biology of decisions on multiple levels: from molecules to neural circuits. In fruit flies we are undertaking genetic screens to discover single molecules controlling foraging decisions, using extracellular electrophysiology and cell-type specific recordings in rodents we plan to identify circuit level computations in the mouse brain that represent value. Overall, our long-term goal is to use ecology inspired quantitative behavioral models to guide and sharpen scientific questions.

MAJOR ACHIEVEMENTS AND FUTURE GOALS

In previous years, we established a fruit fly probabilistic reward foraging assay (Fig.1A). Our first simple computational model provided a "macroscopic" view on how fly's choices rely on reward history (Fig.1B). In order to explain "microscopic" aspects of the behavior, we are now looking into alternative models to explain not only fly's choices but also the travel trajectory an animal makes while foraging. Furthermore, we decided that a more natural reward delivery system, (droplets of sugar solution rather than the current optogenetic activation of sugar receptors), would be a desirable advancement to the experimental setup. Thus, this new foraging assay will reduce possible sources of uncertainty and errors introduced by the complex genetic background needed to carry out genetic screens.

Using the similar framework as in flies, we established a trial-based probabilistic reward foraging task in mice allowing us to study neural correlates underlying choices. The task allows systematic variation of the reward probability of chosen options and waiting time prior to the decision. Under "basic" conditions (short waiting times prior to the decision), we show that animals follow experienced reward proportions (Fig. 2A, green curves). In contrast, an increase of waiting times evokes increased ignorance of previous rewards resulting in a bias towards a preferred side (Fig. 2B). Currently, we fit mathematical models identifying variables important for the decision process with the ultimate goal to find neural correlates for these variables. To this end, neural inactivation experiments, as well as single-unit recordings are currently in progress.

KEY PUBLICATIONS

Stockinger P*, **Kvitsiani D***, Rotkopf S, Tirian L, Dickson BJ (2005) Neural circuitry that governs *Drosophila* male courtship behaviour" *Cell* Jun 3;121(5):664-6. * *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 (2011) A resource of Cre driver lines for genetic targeting of GABAergic neurons in cerebral cortex. *Neuron* Sep 22; 71(6):995-1013.

Kvitsiani D, Ranade S, Hangya B, Taniguchi H, Huan Kepecs A (2012) Distinct behavioural correlates and network interactions of two interneuron classes in mouse prefrontal cortex. *Nature* June 20; 498(7454):363-6.

Personnel List Kvitsiani Group

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PhD Student Junior **Samuel López Yépez**
PhD Student **Sophie Seidenbecher**
Academic employee **Anna-Liisa Ikart**
Group Leader **Duda Kvitsiani**

Foraging decisions require value computations of available options. It has been known that Neuromodulatory systems play a critical role in those computations. To study how option values are computed we are developing the optical neural activity read out tools that can be used in freely behaving mice. Namely, we are building a photon counter to measure the activity of Dopaminergic neurons by using calcium sensors. Foraging decisions rely also on learning statistical regularities in the environment. In order to understand how the brain achieves learning, we trained animals on simple auditory and visual discrimination tasks. With this simple task, our plan is to track neural activity of the same neurons in an animal, as it progresses through learning stages. The information derived from these recording will be used to build realistic spiking neuron models that achieve biologically plausible learning.

My lab in collaboration with Søren Keiding's lab at Aarhus University is developing a patterned light stimulation tool via multimode optical fibers to activate individual neurons with natural patterns of ensemble activity in behaving animals. Last year we have extended this collaboration to groups at Hungarian Academy of Science (Zoltan Somogyvari and Balazs Hangya's labs) in Budapest to use electrophysiological recordings to guide the spot of light in arbitrary 3D locations within neural tissue.

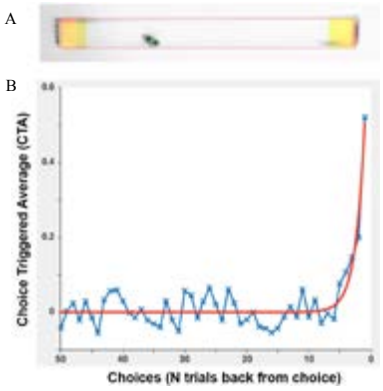

Fig. 1: Probabilistic reward foraging assay for a fruit fly.
A: Video tracking of a single fly in a linear arena. Yellow squares (reward zone) indicate potential reward delivery sites.
B: Choice triggered reward average shows contribution of past rewards to current choices that fly makes when entering the reward zone. Figure by Kvitsiani lab.

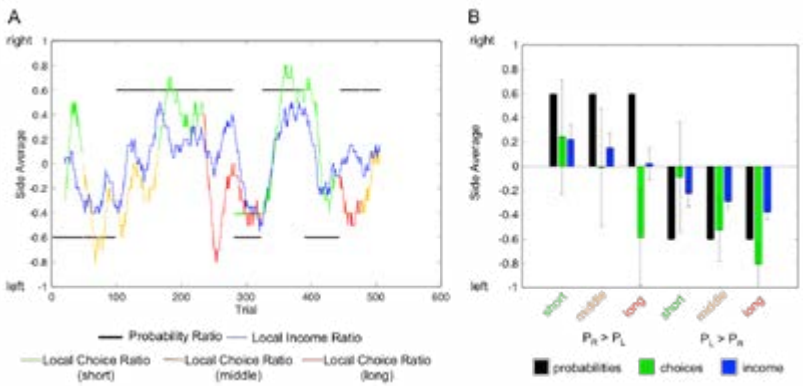

Fig. 2: Choice Behavior of a Single Animal in a Two-Alternative Choice Task with Varying Reward Probabilities and Wait Delays Prior to the Decision.
A: Local choice and income average during a single session.
B: Choice and income average of several sessions categorized according to the set reward probabilities and wait delays. Figure by Kvitsiani lab.

Nabavi Group

Memory Formation and Consolidation at the Synaptic and Circuit Levels

Group Leader
Sadegh Nabavi

Every field has its own million dollar questions. For neuroscience, one is how memories are formed. We went to tackle this question and showed that by changing the strength of connections between neurons, we can engineer an artificial memory. But here is the problem: the brain is a computing device, but unlike any computer that we know, it runs without an operator. So, how can such an unsupervised system decide which information is worthy of storage? This is the question that fascinates our lab members.

We are tackling this question at three levels: circuit, synapse, and molecules (Figure 1).

At the circuit level, the question is: what are the circuits that signal the value of information (Figure 1A). Using light-sensitive proteins, we will identify, monitor and manipulate these circuits. Eventually, we would like to know how each circuit contributes to the process of memory storage, and how weak memories become permanent if formed during an emotional event.

At the synaptic level, our focus is on two types of crucial receptors: receptors for glutamate and neuromodulators (Figure 1B, C). As separate units, these receptors have been widely studied. But it is only when they work together that a new signal emerges and instructs the neuron to store the information. In pursuing this signaling, we are relying on our collaboration with Dr. Poul Nissen and Dr. Magnus Kjærgaard.

And at the molecular level: A hallmark of persistent memories is that they depend on protein synthesis (Figure 1B). Identifying these proteins has been a long quest but with little success. We developed a system for implanting a memory in a defined location (Figure 1D) and we are developing another system that uses an unnatural amino acid to detect only the proteins that are made during memory formation. So, our lab is in a unique position to identify these proteins. On this subject, we are collaborating with Dr. Anders Nykjær.

In addition to memory-based behaviors, we are interested in innate behaviors with the emphasis on innate fear. What intrigues us is that learned fear, and innate fear engages overlapping circuits in the amygdala, the brain's fear center. This raises a dilemma: how two qualitatively different information, one signaling a neutral object and the other an inherently fearful object such as a predator, activate the same part of the amygdala, and yet the animal responds appropriately? We work with Dr. Keisuke Yonehara to resolve this question.

The beauty of memory research is that we can connect the dots from molecules to behavior, with little gap in between. Only by doing this, we fully understand how our unsupervised brain is so good at choosing the right information.

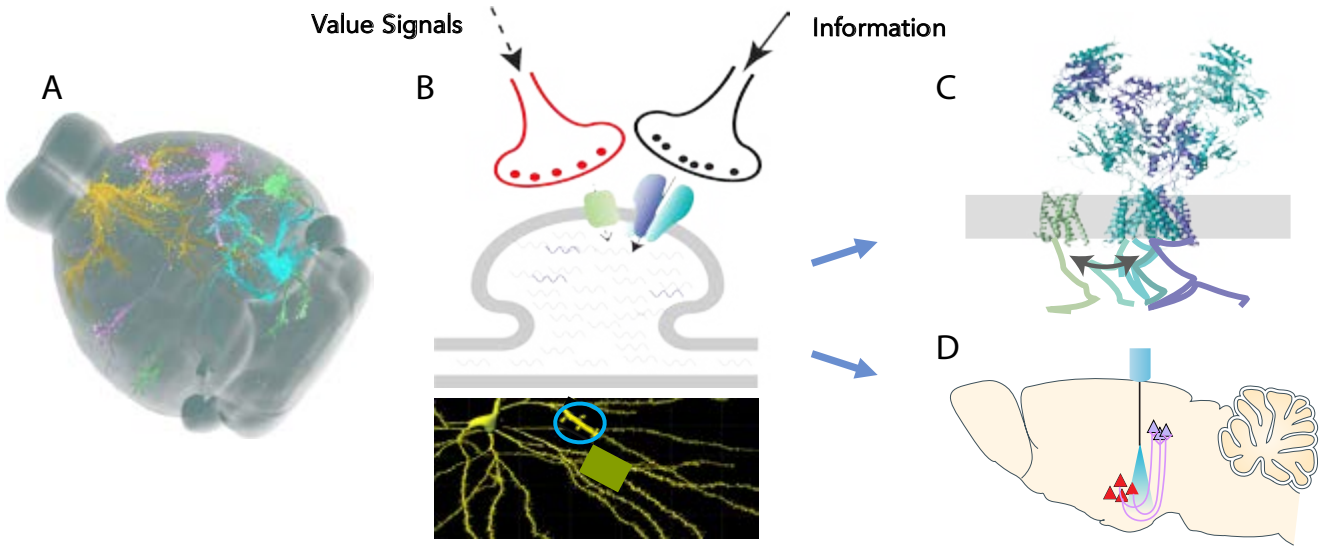

Fig. 1: Investigating the mechanisms underlying memory formation and storage at the circuit, synaptic and molecular levels. Credit: Hanne Poulsen, Majid Erfani, Nathalie Krauth.

Key publications

Nabavi S, Fox R, Proulx CD, Lin JY, Tsien RY, and Malinow R (2014) Engineering a memory with LTD and LTP. *Nature* 511, 348-352

Nabavi S, Kessels HW, Alfonso S, Aow J, Fox R, and Malinow R (2013). Metabotropic NMDA receptor function is required for NMDA receptor-dependent long-term depression. *Proc Natl Acad Sci U S A.* 110, 4027-4032.

Kessels HW, **Nabavi S**, and Malinow R (2013). Metabotropic NMDA receptor function is required for -amyloid-induced synaptic depression. *Proc Natl Acad Sci U S A.* 110, 4033-4038

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Group Leader **Sadegh Nabavi**

Philipsborn Group

Behavioral Genetics and Circuit Neuroscience

Group Leader
Anne von Philipsborn

We are interested in 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.

By studying the neuronal circuits underlying *Drosophila* behavior, we aim at understanding general principles of motor control. We focus on circuits for motor pattern generation and the architecture of neuro-muscular networks, as well as the mechanisms of higher order coordination of complex motor behaviors and behavioral sequences.

As a model behavior, we use *Drosophila* male courtship. Identified neurons are dedicated to the generation of male courtship song, an elaborately patterned acoustic signal. We investigate how the sex-specific song pattern is generated, and how the song circuit is modulated during other motor behaviors. We use audio recording as a highly sensitive, high throughput measurement of motor behavior at millisecond timescale as well as genetic tools for neuronal activity imaging and optogenetic activation and silencing in intact animals.

Simultaneously, we 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.

MECHANISMS OF MULTIFUNCTIONAL MOTOR CONTROL

Flies use their wings for flight as well as for acoustic communication, e.g. the male courtship song. Both behaviors rely on wing muscle motor neurons. We aim at investigating cellular and genetic mechanisms of this multifunctionality.

In collaboration with Michael Dickinson at the Caltech, US, we are investigating neuromuscular activity during different wing behaviors in intact behaving animals. These studies revealed strikingly different patterns of motor neuron ensemble activity during song and flight. With intersectional genetic techniques, we gained genetic access to single classes of wing control muscle motor neurons and are assembling an anatomical and functional atlas of the wing motor neuropil.

Key publications

Verzijden MN, Abbott JK, **Philipsborn A,** Loeschcke V (2015) Male Drosophila melanogaster learn to prefer an arbitrary trait associated with female mating status. *Current Zoology*, Vol. 61, No. 6, p. 1036-1042

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Research Assistant **Hoger Amin**
Laboratory Technician **Anna Prudnikova**
Research Student **Peter James Kerwin**
Research Student **Dylan Jiasheng Yuan**
Student Assistant **Andreas Stokbro**
Student Assistant **Tatiana Adamiec**
Group Leader **Anne von Philipsborn**

BEHAVIORAL HIERARCHY AND COORDINATION- STATE DEPENDENT ACTION SELECTION

How do different behaviors interact and influence each other on a circuit level? During courtship, some behavioral elements are combined and others exclude each other. We discovered that dependent on the state of the animal and the behavior it is engaged in, activation of neuronal classes has drastically different motor outcomes. By using optogenetic circuit interrogation, we explore the neuronal and genetic basis of state dependent action selection, aiming at identifying circuits and neuromodulators for behavioral hierarchy and coordination.

INHIBITORY SIGNALING IN MOTOR CONTROL

Almost all behavior is shaped by both excitatory and inhibitory neuronal control. We find that GABAergic inhibitory signaling impacts on song motor behavior on multiple levels, tuning fine motor structure, intensity and overall coordination of the behavior. With cell specific RNAi mediated knock- down of genes involved in GABAergic signaling, we are elucidating the mechanisms of inhibitory control and its role in pattern generation.

SEX SPECIFIC MOTOR CIRCUITS FOR COMMUNICATION

We discovered that during reproduction, not only male, but also female flies use rhythmic acoustic signals for communication. Females lack most of the male's song neurons and show differential gene expression, which might explain striking differences in the motor output shaped to produce sex-specific sound patterns.

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* is a convenient and genetically accessible in vivo model for analyzing the effect of pathological mutations on neuronal physiology. For example, we are currently collaborating with Hanne Poulsen at DANDRITE to study disease causing mutations of ATP1A3 in a Drosophila model system and with Poul Henning Jensen to explore calcium dynamics during alpha-synuclein mediated neurodegeneration.

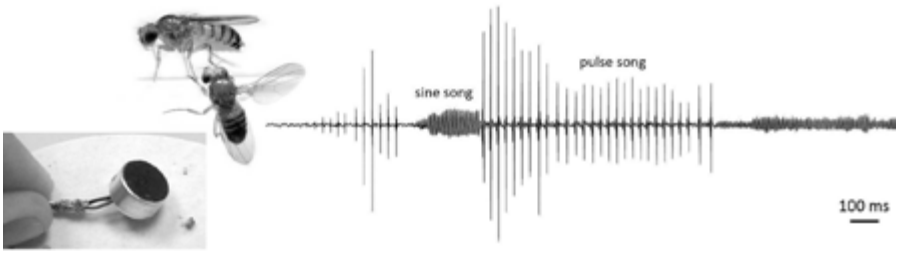


Fig.1. courtship song. A male fly sings to a female by extending and vibrating one wing. Song is recorded by small microphones: the oscillogram shows sine and pulse bouts. Photo by Anne von Philipsborn.

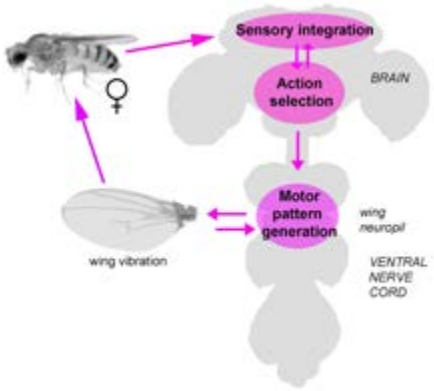


Fig.2. Schematic of the neuronal circuits for courtship song. Illustration by Anne von Philipsborn.

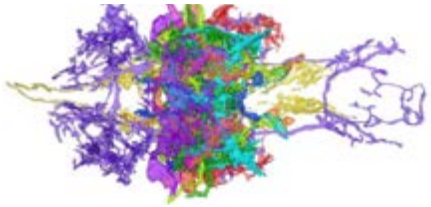
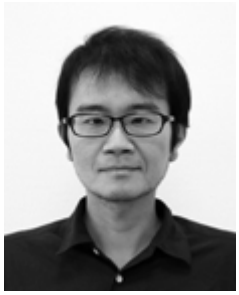


Fig.3. Reconstruction of 3D arborization patterns of wing motor and premotor interneurons contributing to the patterning of wing movements. Illustration by Anne von Philipsborn.

Yonehara Group

Structure, Function, and Development of Neural Circuits in Visual System



Group Leader
Keisuke Yonehara

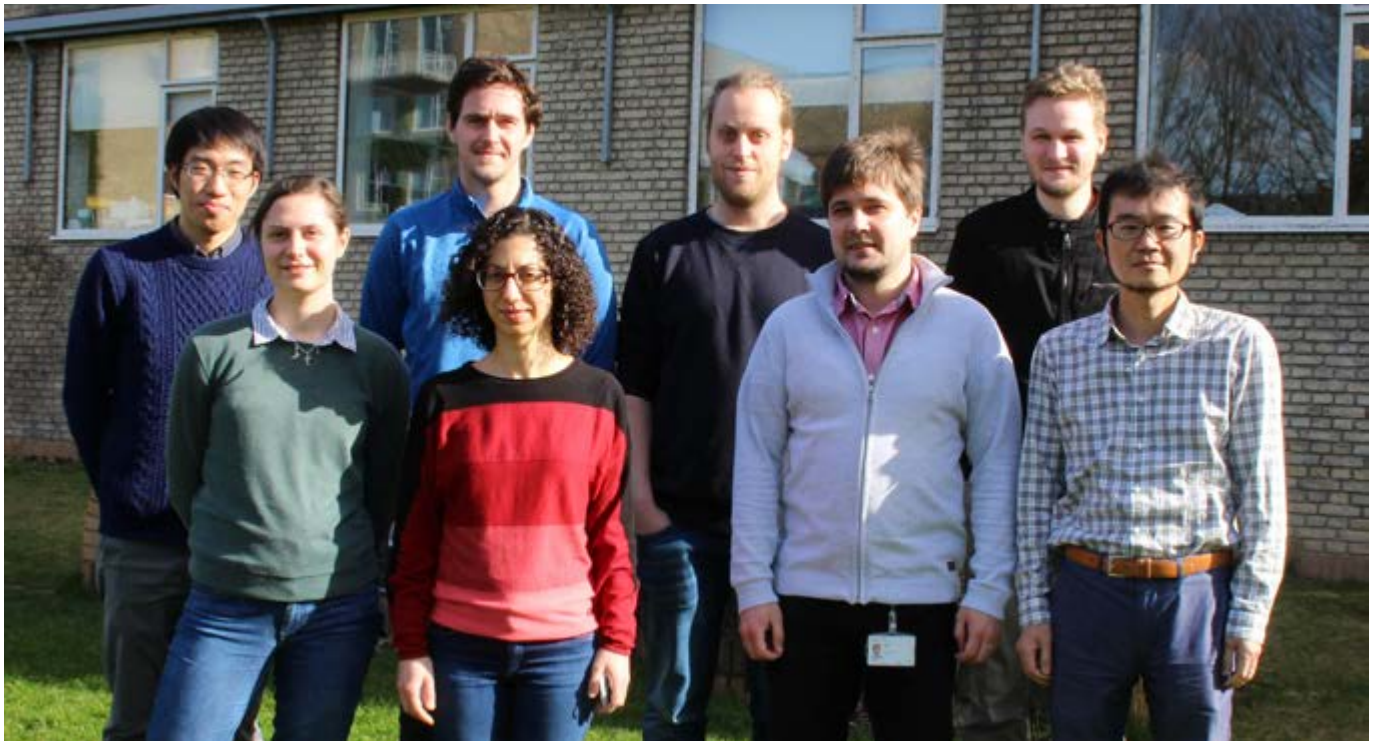
The Yonehara group investigates the structure, function and development of neural circuits using mouse visual system as a model. We are seeking to address the following questions:

1. How are sensory signals processed by neuronal circuits?
2. What is the function of individual cell types in computation and behavior?
3. What are the genetic and activity-dependent mechanisms of circuit development?

We address these questions mainly by focusing on visual circuits across the retina, superior colliculus, thalamus and visual cortex. The logic of our research plan is to first identify a computation performed by a given neuronal circuit that comprises of distinct cell types in the adult brain. Second, 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. Third, to examine the role of individual cell types in transforming the sensory input into output behavior. Finally, to study the genetic mechanisms by which the elementary circuit motifs are assembled, and how its dysfunction can lead to disease.

We perform cell-type-specific experiments that require a wide spectrum of experimental approaches from molecular biology, genomics, genetics, electrophysiology, optogenetics, multi-photon functional imaging, trans-synaptic viral tracing, and behavioral analysis. We are developing new genetic and viral technologies that facilitate probing circuit function in healthy and diseased systems.

Yonehara group members outside lab building. Photo DANDRITE.



DISSECTING THE FUNCTIONAL ORGANIZATION OF MOUSE VISUAL CIRCUITS

In the visual system, sensory processing begins in the retina where the visual scene is divided into 20 information channels before reaching the brain. The superior colliculus is one of the main recipients of retinal output and mediates visually-guided behaviors. However, it remains unknown how visual signals from individual retinal ganglion cell types are processed by collicular neurons to achieve specific computations relevant to behaviors. Recently we have identified several transgenic mouse lines in which specific collicular cell types are labeled. Using these mouse lines, we are characterizing the response properties and neuronal connectivity of individual types of collicular neurons. In the near future, we will dissect the role of collicular neurons in visually-guided behavior and investigate the developmental mechanism of circuit connectivity. We also started to investigate circuit mechanisms of motion computation in mouse visual cortex.

PATHWAY-SPECIFIC FUNCTION OF INDIVIDUAL RETINAL GANGLION CELL TYPES

Output neurons of the retina are retinal ganglion cells, which are composed of more than 30 distinct types encoding distinct visual features. A striking feature of the central projection of retinal ganglion cells is the massive degree of conversion and diversion. Recently we have characterized some transgenic mouse lines in which distinct ganglion cell type is genetically labeled. By manipulating the activity of individual visual pathways using these mouse lines we aim to understand the fundamental logic of visual processing.

AN INVESTIGATION OF THE ROLES OF GENES ASSOCIATED WITH CONGENITAL NYSTAGMUS IN RETINAL CIRCUIT ASSEMBLY

Idiopathic congenital nystagmus, a disease that severely impacts eye movement, leaves approximately 1 in 1500 people with seriously impaired vision. Today, there is no cure or reliable treatment for this disease. In 70% of cases studied, mutations have been found in the FRMD7 gene. Very recently, we published results linking mutations in FRMD7 to defects in retinal circuits underlying motion detection and the control of eye movement (Yonehara et al., Neuron, 2016). Our aim is to understand key mechanisms underlying the establishment of synaptic specificity by investigating the role of FRMD7 signaling cascades on the development of the retinal circuit implicated in congenital nystagmus.

Key publications

Yonehara K, Fiscella M, Drinnenberg A, Esposti F, Trenholm S, Krol J, Franke F, Scherf BG, Kusnyerik A, Müller J, Szabo A, Jüttner J, Cordoba F, Reddy AP, Németh J, Nagy ZZ, Munier F, Hierlemann A, Roska B (2016) Congenital nystagmus gene FRMD7 is necessary for establishing a neuronal circuit asymmetry for direction selectivity**.** *Neuron.* Vol. 89, No. 1, 06.01.2016, p. 177-93

Wertz A, Trenholm S, **Yonehara K**, Hillier D, Raics Z, Leinweber M, Szalay G, Ghanem A, Keller G, Rózsa B, Conzelmann KK, Roska B (2015) PRESYNAPTIC NETWORKS. Single-cell-initiated monosynaptic tracing reveals layer-specific cortical network modules. *Science.* 349: 70-74

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

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. Commentary in *Nature Reviews Neuroscience.*

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Laboratory Technician **Gurmeet Kaur Singh**
Laboratory Assistant **Misugi Yonehara**
Research Assistant **Kranti Karande**
Research Assistant **Rune Rasmussen**
Group Leader **Keisuke Yoneharah**

Kjærgaard Team

Synaptic Plasticity and Intra-cellular Signaling Complexes in Memory Formation

Team Leader
Magnus Kjærgaard

We are interested in understanding how proteins in the post-synaptic density modulate synaptic sensitivity and signaling. These proteins are crucial for memory formation but are difficult to study due to their flexibility. We use a range of biophysical techniques including NMR spectroscopy and single molecule FRET spectroscopy to answer mechanistic questions about brain proteins.

A key mechanism of memory formation is the modulation of ionotropic glutamate receptors by their intra-cellular ligand occupancy and phosphorylation state. The intra-cellular domains of these receptors coordinate many binding partners and affect the conductivity of the channels, but are difficult to study by traditional structural techniques as they are examples of so-called intrinsically disordered proteins. These proteins are highly flexible and devoid of fixed structures. We use a range of state-of-the-art spectroscopic techniques to study the interactions of the intra-cellular domains of the NMDA receptor with post-synaptic proteins, focusing particularly on the kinase CaMKII that functions as a molecular switch, and thus provide a mechanism for long-term memory storage.

Receptor activation can lead to many different downstream events depending on the cellular context, e.g. which other signaling pathways are active. The coordination between signaling pathways is carried out by large flexible molecular assemblies called signaling complexes. These complexes connect receptors to enzymes and substrates. The signaling complexes act as molecular match-makers by determining which molecules encounters each other. We would like to understand quantitatively how signaling complexes work at the molecular level. To this end, we have developed a quantitative assay for measuring effective concentrations in signalling complexes, which is likely to be crucial to understand kinase activity in signalling complexes.

Key Publications

Shammas SL, Kumar S, Garcia GA, **Kjaergaard M**, Horrocks MH, Shivji N, Mandelkow E, Knowles TPJ, Mandelkow EM, Klenerman D (2015) A mechanistic model of tau amyloid aggregation based on direct observation of oligomers *Nature Communications. 6*:7025

Lešmantavičius V, Dogan J, Jemth P, Teilum K, **Kjaergaard M** (2014) Helical Propensity in an Intrinsically Disordered Protein Accelerates Ligand Binding. *Angew. Chem. Int. Ed. Engl* 53(6):1548 51

Lešmantavičius V, Jensen MR, Ozenne V, Blackledge M, Poulsen FM, **Kjaergaard M** (2013) Modulation of the intrinsic helix propensity of an intrinsically disordered protein reveals long-range helix-helix interactions. *J. Am. Chem. Soc* 135(27):10155-63

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Postdoc **Mateusz Dyla**
Postdoc **Xavier Warnet**
Team Leader **Magnus Kjærgaard**

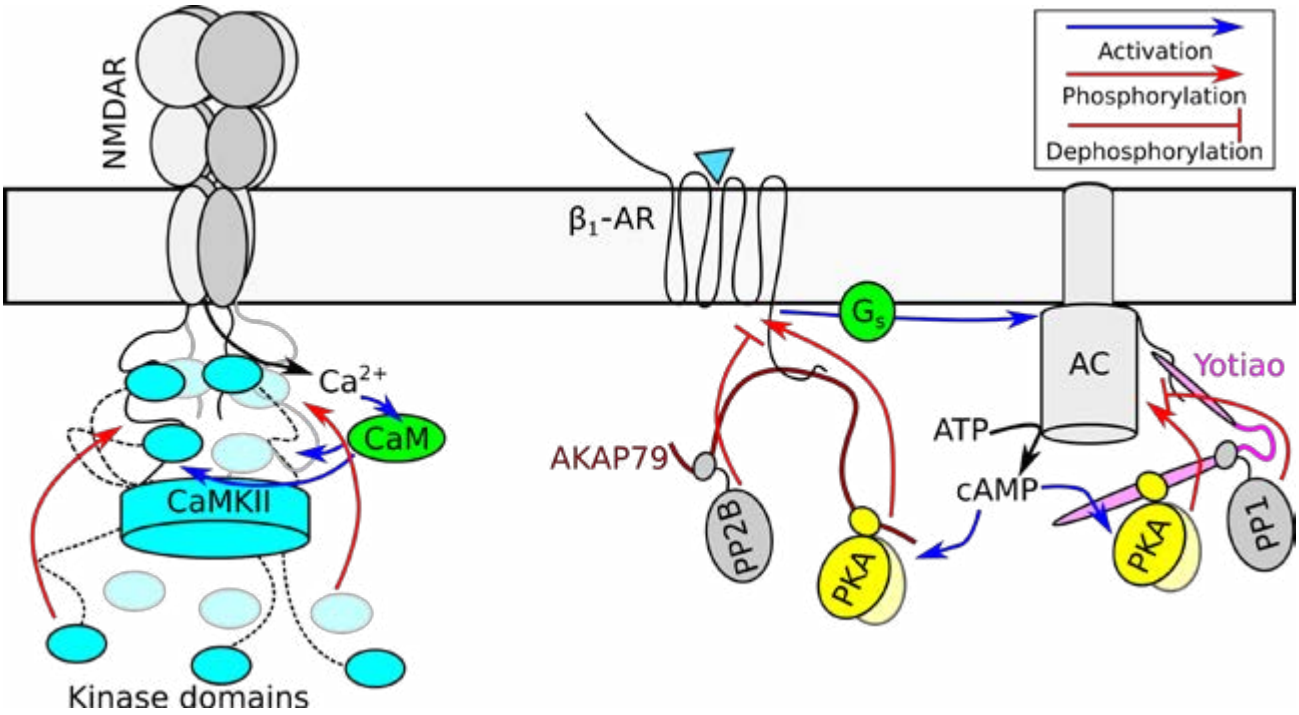


Fig. 1. Signalling complexes coordinate subsequent molecules inside a signalling pathway. Illustration by Magnus Kjærgaard.

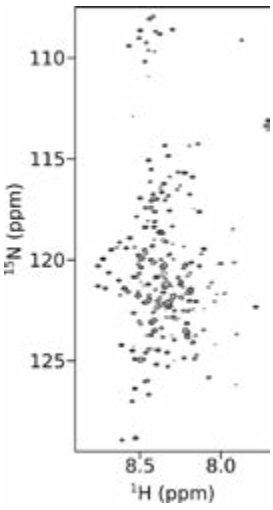


Fig. 2. NMR spectrum of the intracellular domain of the NMDA Receptor subunit 2B. Illustration by Magnus Kjærgaard.

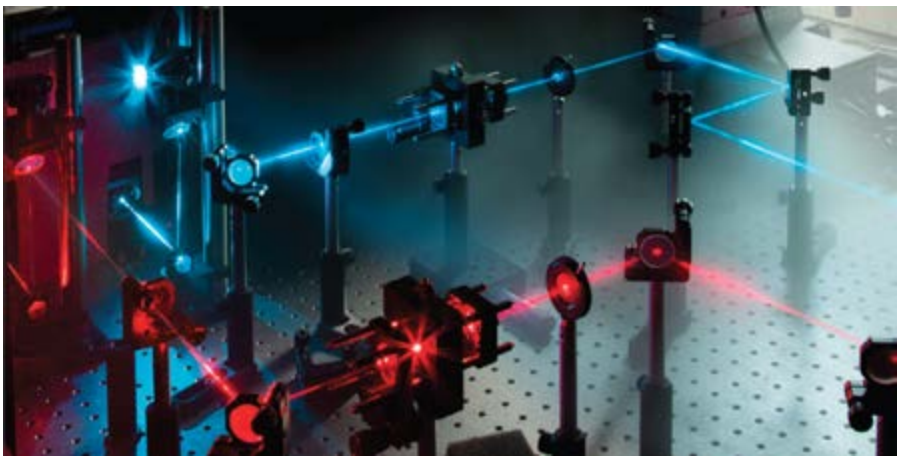


Fig. 2. Single molecule FRET microscope allows structural interrogation of individual molecules. Courtesy of Mathew H. Horrocks, Cambridge University.

Poulsen Team

Electrophysiology of Electrogenic Transporters and Ion Channels

Team Leader
Hanne Poulsen

MAJOR ACHIEVEMENTS

In 2016, we have published two studies that describe molecular mechanisms of the Na,K-ATPase. In (1), we show that the beta2 subunit, which is essential for cerebellar function, has an unexpected marked impact on the catalytic properties of any of the alpha subunits, and we find that the tilt angle of the transmembrane helix is the determining factor.
In (2), we show that the testes-specific alpha4 (which is essential for male fertility) is uniquely adapted to the changes in environments that a sperm cell experiences, being much less sensitive to temperature, extracellular ionic concentrations and membrane potential than the ubiquitously expressed alpha1 subunit. Furthermore, we contributed to a study (3) on the Plasmodium falsiparum calcium ATPase, PfATP6, showing that it is not the molecular target of the currently most valued anti-malarial drug, artemisinin.

FUTURE PLANS

In 2017, the main focus will be on establishing voltage-clamp fluorometry using the unnatural amino acid Anap to study the Na,K-ATPase, the GABA transporter and TRP channels. The electrophysiology gives time-resolved functional insight into electrogenic membrane proteins, and atomic structures reveal snapshots in the catalytic cycle. We hope that the use of Anap for voltage-clamp fluorometry will bridge the two methods, shedding light on protein movements and function simultaneously.

PhD student Mette Ozol has successfully incorporated the fluorescent, unnatural amino acid Anap into almost 20 positions in the Na,K-ATPase and measured whether it is tolerated functionally, and PhD student Saida Said has been making and testing constructs for expressing the GABA transporter GAT-1 with Anap. Postdoc Helle Bakke Krog joins the group after Easter and she will incorporate Anap to track physical movement in the TRP channel and correlate that with channel activity in order to build a model for the molecular mechanism of a major, yet unanswered question of what the molecular mechanism of temperature sensation is.

Additionally, we are examining disease-causing mutations in the Na,K-ATPase genes. In collaboration with MD professor Lisbeth Tranebjærg (KU), we are examining the effect of one single dominant mutation in the alpha3 gene, which – in contrast to all other disease-causing mutations in the gene – causes deafness and blindness. It is highly intriguing that a single residue has this profound and unique effect. Lisbeth has currently 17 patients identified (most in Denmark, but also in other countries) with the mutation.
In collaboration with MD Emma Matthews (UCL), we are examining a mutation in the alpha2 gene that seems to cause periodic paralysis. Previously, mutations in the gene have been found to cause hemiplegic migraines with aura – but none of the migraine-associated mutations affect the ion binding residues.

In collaboration with deCODE in Iceland, we are examining a mutation in the alpha1 gene that seems to cause hyperaldosterionism. Mutations in this gene have never been described before, and it is one of the most well-conserved of all genes.

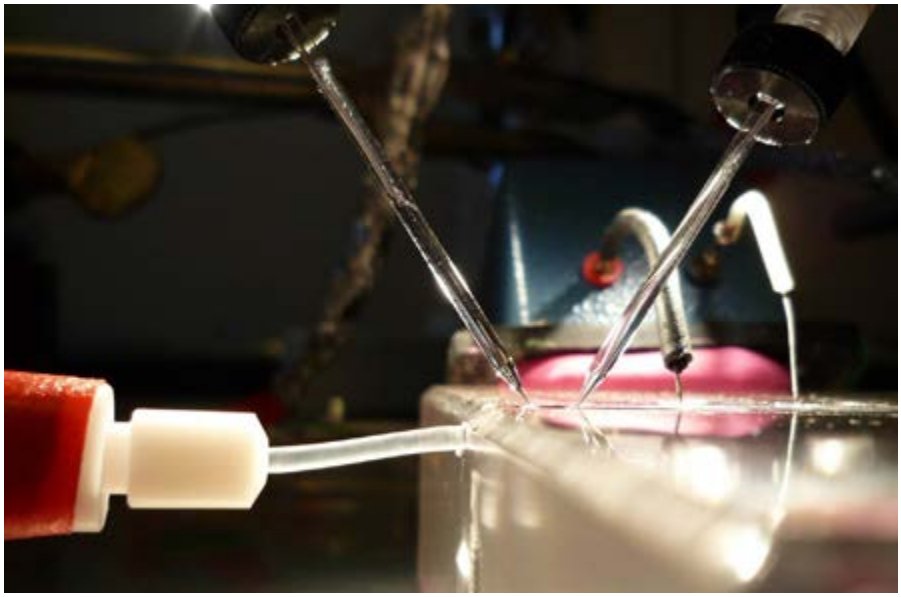


Fig. 1. Two-electrode voltage clamping. The two glass electrodes are in a Xenopus laevis oocyte, and the external buffer is controlled at the inlet to the left. Photo by Hanne Poulsen

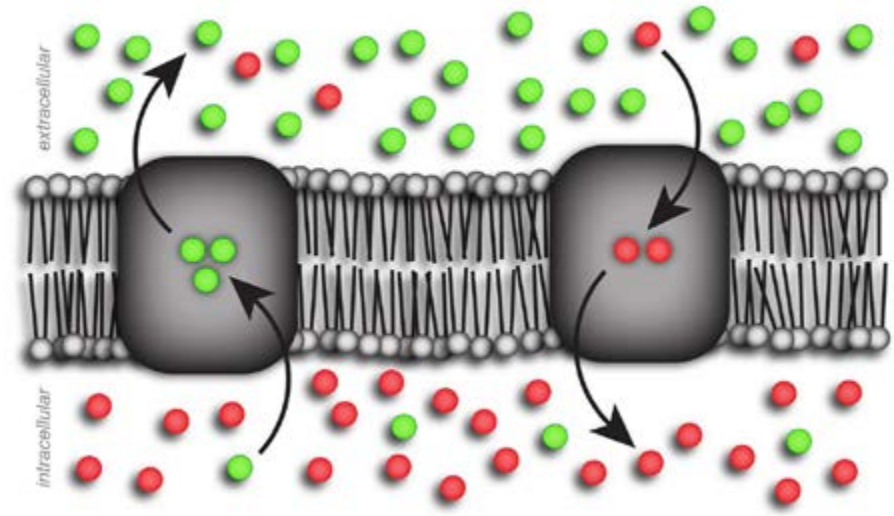


Fig. 2. Schematic illustration of the Na,K-ATPase actiity. Outside a cell, the concentration of sodium (green spheres) is high, inside a cell, the concentration of potassium (red spheres) is high due to the pumping of the Na,K-ATPase. In each round, the pump transports three sodium ion out of and two potassium ions into the cell at the expense of one ATP molecule. Illustration by Hanne Poulsen.

Publications 2016

Hilbers F, Kopec W, Isaksen TJ, Holm TH, Lykke-Hartmann K, Nissen P, Khandelia H, Poulsen H (2016) Tuning of the Na,K-ATPase by the beta subunit. Scientific Reports, Vol. 6, No. 20442, 2016. Hamma

Voldsgaard CM, Nissen P, Poulsen H (2016) The 4 isoform of the Na+ ,K+ -ATPase is tuned for changing extracellular environments. The F E B S Journal (Online), Vol. 283, No. 2, 2016, p. 282-293.

David-Bosne S, Clausen MV, Poulsen H, Møller JV, Nissen P, le Maire M (2016). Reappraising the effects of artemisinin on the ATPase activity of PfATP6 and SERCA1a E255L expressed in Xenopus laevis oocytes. Nat Struct Mol Biol 23:1-2

Personnel List Poulsen Team

Postdoc **Florian Hilbers**
Postdoc Trine **Kvist Carlino**
PhD Student **Mette Ozol**
PhD Student **Saida Said**
Team Leader **Hanne Poulsen**

03
Events, Visitors, Guests & Seminars

EVENTS, VISITORS, GUESTS & SEMINARS

DECEMBER

EVENT: Joint iNANO and DANDRITE **Inauguration**: *The first Danish cryo-EM facility placed at Aarhus University.*

EVENT: Joint iNANO and DANDRITE **PhD course: Cryo-EM Days**: *Cryo-electron microscopy methodology (two-day PhD course).*

INVITED LECTURER: Group Leader **Carsten Sachse**, EMBL-Heidelberg, Germany, *Advances in segmented helical reconstruction*

INVITED LECTURER: MRC – **Research Scientist Rafael** Fernández Leiro, MRC Laboratory of Molecular Biology (LMB), UK, *Single-particle analysis using RELION*

INVITED LECTURER: Leverhulme Early Career Fellow **Christopher J Russo**, MRC Laboratory of Molecular Biology (LMB), UK, *Specimen preparation for high-resolution cryo-EM*

INVITED LECTURER: Professor **Ariane Briegel**, Institute of Biology Leiden, Leiden University, Netherlands, *New insights into bacterial behavior from electron cryotomography*

INVITED LECTURER: Group Leader **Arne Möller**, Max Planck Institute of Biophysics, Frankfurt, Germany, *Nanomachines in action – EM-based analysis of dynamic macromolecules*

EVENT: **Site Visit** to DANDRITE by external Review Panel and representatives from Lundbeckfonden and EMBL, Germany (one day event – see details below).

SEMINAR: Professor **Baruch Kanner**, IMRIC, Hebrew University of Jerusalem, Israel, *The Extended Transmembrane Domain 10 of the GABA Transporter GAT-1 enables Efficient Ion-Coupled Transport*

SEMINAR: **Joint DANDRITE & Kjeldgaard Lecture**, Principal Investigator **Patrick Laurent**, University of Brussels, Belgium, Neurogenetic aging studies in C. elegans

NOVEMBER

GUEST: PhD student **Stella Nolte**, Christian-Albrects-Universität zu Kiel, Germany

SEMINAR: **DANDRITE Lecture**, Professor **Kevin Eggan**, Harvard Department of Stem Cell and Regenerative Biology, Harvard University, *New insights into motor neuron disease from novel, animal and cellular models*

SEMINAR: PhD student **Volker Berendes**, Department for Animal Physiology, University of Cologne, Germany, *Speed-dependent interaction of sensory signals and local, pattern-generating activity during walking in Drosophila*

SEMINAR: Postdoc **Ollie Humle**, Danish Research Center for Magnetic Resonance from Hvidovre Hospital, University of Copenhagen, *The Utility of Utility: A Theory of Homeostatic Choice*

SEMINAR: Postdoctorial Associate **Tomonori Takeuchi**, Richard Morris lab, University of Edingburgh, UK, *Dopamine-dependent memory consolidation and locus coeruleus*

OCTOBER

SEMINAR: Assistant Professor **Joshua Plotkin**, Department of Neurobiology and Behavior, Stony Brook University School of Medicine, Stony Brook, NY, USA, *Dendritic synaptic integration in striatal spiny projection neurons and Huntington's disease*

SEMINAR: Graduate student **Linda Westin**, Swedish Academy member, Department of Women's and Children's Health, Karolinska Institutet, Solna, Sweden, *Super-resolution studies on Na,K-ATPase a1 and 3 distribution and their relationship to NMDA receptors in hippocampus neutrons, and results on the functional interaction between Na,K-ATPase and NMDA receptors in hippocampus neurons*

SEMINAR: Professor **Anita Aperia**, Swedish Academy member, Department of Women's and Children's Health, Karolinska Institutet, Solna, Sweden, *Neuronal Na,K-ATPase in health and disease*

SEMINAR: PhD student **Paula Szalai**, Joint PhD Student between NCMM and DANDRITE, Centre for Molecular Medicine Norway, University of Oslo, Norway, *The role of the SERCA Pump in Cell Death and Autophagy*

SEPTEMBER

EVENT: **DANDRITE SAB**, Scientific Advisory Board Meeting – one day event, hosted by DANDRITE at Sandbjerg Manor, Denmark. Attended by all DANDRITE members

EVENT: **DANDRITE Retreat 2016** – Two days event 13th to 14th September, hosted by DANDRITE at Sandbjerg Manor, Denmark. Attended by all DANDRITE members

INVITED LECTURER: Associate Professor **Jacob Friis Sherson**, Dept. Physics and Astronomy, Aarhus University, *Human strategy and intuition formation in online problem solving*

INVITED LECTURER: Professor **Anders Børglum**, Director of the iPSYCH center & the iSEQ center, Aarhus University, *The Lundbeck Initiative for Integrative Psychiatric Research – iPSYCH*

INVITED LECTURER: Professor **Carl Petersen**, Brain Mind Institute, Laboratory of Sensory Processing, EPFL-SV-BMI-LSENS, Switzerland, *Sensorimotor integration*

INVITED LECTURER: Professor **James McGaugh**, Center for the Neurobiology of Learning and Memory, University of California, *Modulation of Memory Consolidation: Roles of stress hormones and amygdala activation*

INVITED LECTURER: Professor **Lars Juhl Jensen**, NNF Center for Protein Research, University of Copenhagen, Network biology: *A crash course on STRING and Cytoscape*

INVITED LECTURER: Professor **Marco Capogna**, Dept. Biomedicine, Aarhus University, *Juxtacellular recording and labelling of neurons*

SEMINAR: **DANDRITE Lecture**, Professor **James McGaugh**, Center for the Neurobiology of Learning and Memory, University of California, Irvine, *Emotional Arousal and Lasting Memories*

SEMINAR: **Joint DANDRITE & MEMBRANES Lecture**, Professor **Kathleen J. Sweadner,** Laboratory of Molecular Neurophysiology, Massachusetts General Hospital & Harvard Medical School, *The molecular landscape of Na,K-ATPase mutations: genotype/phenotype relationships in human disease*

GUEST: Visiting researcher **Ebru Demir**, Columbia University, USA (1 month)

AUGUST

GUEST: Assistant Professor **Mentor Sopjani,** University of Prishtina, Kosovo (1 month)

GUEST: Research Assistant **Christian Skoven**, Danish Research Centre for Magnetic Resonance, Copenhagen University Hospital Hvidovre, Denmark (1 month)

GUEST: Visiting researcher **Kerstin Imrell**, Karolinska Institutet, Sweden

JUNE

SEMINAR: Guest **Tomoe Ishikawa**, Laboratory of Chemical Pharmacology, Graduate School of Pharmaceutical Sciences, University of Tokyo, Japan, *Dendritic Filtration of Presynaptic Cell Assembly*

EVENT: **EMBL Partnership Conference**, hosted by EMBL Heidelberg, Germany, June 6th to 8th, attended by a large DANDRITE delegation

GUEST: Visiting researcher **Friedrich Kretschmer,** Max Planck Institute for Brain Research, Germany

GUEST: Dr. **Laura Parkkinen**, Nuffield Department of Clinical Neurosciences, University of Oxford, UK

GUEST: **Letitia Moscato**, University of Pavia, Italy

GUEST: PhD student **Gemma Gou Alsina**, Biomedical Research Institute Sant Pau, Spain

GUEST: PhD student **Giulia Torromino**, Sapienza University of Rome, Italy

GUEST: PhD student **Megha Mohan**, Griffith University, Australia

GUEST: PhD student **Michala Kolarova**, National Institute of Mental Health, Czech Republic

GUEST: Postdoc **Maria Tsiarli**, Brown University, USA

GUEST: **Senem Merve Ötzka**, Finland

SEMINAR: DANDRITE Lecture, Dr. **Armin Lak**, Institute of Ophthalmology, University College London, (X days), *The roles of dopamine in perceptual and economic decision making*

SEMINAR: Group leader **Ganesh Pitchai,** Oxford Parkinson's Disease Centre and Nuffield Dept. Clinical Neurosciences, University of Oxford, UK, *α-synuclein detection from various biological samples: a potential biomarker in Parkinson's disease*

SEMINAR: **Joint MBG & DANDRITE Topical Seminar**, Medical Researcher **Koh-ichi Nagata**, Institute for Developmental Research, Departments of Molecular Neurobiology, Kasugai, Japan, *Comprehensive approach to understand pathophysiological role of genes causing neurodevelopmental disorders*

SEMINAR: **Joint MBG & DANDRITE Topical Seminar,** Postdoc **Camilla Stampe Jensen**, Dept. Biomedical Sciences, The Panum Institute, University of Copenhagen, Denmark, *Ion Channel Clustering in the Axon Initial Segment Revealed by Super-Resolution Imaging*

MAY

EVENT: **Neuroscience Day 2016** – Brain Matters! Hosted by NeuroCampus Aarhus and supported by DANDRITE, venue: Lakeside Lecture Theatres, Aarhus University

GUEST: ERASMUS student **Zuzanna Matysiak-Burzynska**, Medical University of Lodz, Poland

GUEST: Postdoc **Joshua Sanders**, Cold Spring Harbor Laboratory, USA

SEMINAR: Researcher **Ganesh Pitchai**, Ian Hickson's group at Center for Protein Research, *Molecular Characterization of PICH Interactome in Mitosis*

SEMINAR: **Joint DANDRITE & iNANO Topical Seminar, Dr Rafael Fernández Leiro**, MRC Laboratory of Molecular Biology, Cambridge Biomedical Campus, UK, *Mechanistic insights on DNA replication and repair by cryo-EM*

SEMINAR: **Joint DANDRITE & AIAS Seminar**, Senior Investigator **Dr. Joseph Mindell**, Membrane Transport Biophysics Section, National Institute of Neurological Disorders and Stroke (NINDS), Maryland, USA , *Life's ups and downs: elevator mechanisms in transporter biology*

APRIL

EVENT: **Festival of Research 2016**, hosted by Aarhus University at Navitas, 8000 Aarhus C. Attended by several DANDRITE research groups (one day national event)

GUEST: Dr. **Arne Möller**, Max-Planck-Institute of Biophysics, Germany

GUEST: Professor **May-Britt Moser**, Kavli Institute for Systems Neuroscience, Norwegian University of Science and Technology, Norway

SEMINAR: **Joint AIAS & DANDRITE Topical Seminar,** Junior Research Fellow **Mathew H. Horrocks**, Dept. of Chemistry, University of Cambridge, UK, *Single-molecule techniques for studying the aggregates of proteins associated with Parkinson's and Alzheimer's disease*

MARCH

EVENT: Inauguration of **The JOINT** – The Electrophysiology, Optogenetics & Behavior workshop, Aarhus University, building 1182, room 319

SEMINAR: PhD Candidate **Katherine Gill**, Centre for Eye Research Australia & Department of Ophthalmology, University of Melbourne, Australia, *Modelling glaucoma with pluripotent stem cells*

SEMINAR: **DANDRITE Topical Seminar/MBG Focus Talk**, Instrument Scientist **Esko Oksanen**, Neutron Macromolecular Crystallography, European Spallation Source ERIC, Lund, Sweden, *NMX – A Macromolecular Diffractometer at the European Spallation*

SEMINAR: **Joint DANDRITE & Kjeldgaard Lecture**, Professor **Liz Carpenter**, Structural Genomics Consortium, Nuffield Department of Medicine, University of Oxford, United Kingdom (X days), *Structural Biology of Human Membrane Proteins at the SGC*

FEBRUARY

EVENT: **DANDRITE Encounters 2016**, hosted by DANDRITE, venue: AIAS auditorium, Aarhus University (one-day event)

GUEST: ERASMUS student **Muyesier Maimaitili**, University of Camerino, Italy (6 months)

GUEST: ERASMUS student **Patricia Lorente Labrado**, University of Barcelona, Spain (6 months)

SEMINAR: CEO **Jens Frauenfeld**, Salipro Biotech AB, Södertälje, Sweden, *The Saposin lipoprotein nanoparticle system for membrane proteins*

SEMINAR: postdoctoral candidate **Eleonora Passeri**, Johns Hopkins Hospital, School of Medicine, Baltimore, MD, *Molecular and cellular signature of neuronal cells affected by genetic and environmental factors of major mental illnesses*

JANUARY
GUEST: ERASMUS student **Akhil Pukkattu John**, University of Skövde, Sweden (7 months)

GUEST: ERASMUS student **Jennet Baltayeva**, IMC Fachhochschule Krems, Austria (6 months)

GUEST: ERASMUS student **Roberta Fresia**, Italy (5 months)

GUEST: Guest student **Christina Batlle Carreras**, Institute of Biotechnology and Biomedicine of Barcelona, Spain (4 months)

GUEST: PhD student **Sherif Mahmoud Galal Idriss**, University of Antwerp, Belgium

SEMINAR: Postdoctoral candidate **Bhavin Shah**, Institute of Molecular Cell Biology, University of Münster, Germany, *The role of Rap1 GTPases during neuronal polarization and cortical development*

SAB meeting: Poster session. Foto DANDRITE.

SAB meeting: Research presentation. Foto DANDRITE.

SAB MEETING

DANDRITE's second Scientific Advisory Board (SAB) meeting was held on Monday September 12th, 2016 (DANDRITE's first SAB were held November 2014). The SAB members present were Professor Moses V. Chao, Professor Glenda M. Halliday, Professor Rüdiger Klein (chair), Professor Carl Petersen, Professor Kathleen J. Sweadner, and Professor Matthias Wilmanns. Professor Mart Saarma and Vice President Jan Egebjerg were excused. The focus of this year's SAB meeting was on progress and integration of individual group leaders and their research plans ahead for the prolongation application.

The SAB writes in evaluation report:
"...The SAB congratulates DANDRITE researchers for having succeeded in fulfilling their primary goal to serve as a generator for new initiatives in neuroscience, and an introducer of technologies new to Denmark. During the last 3 years, the scientific program of DANDRITE has undergone an amazing development and now covers a tremendous range of state-of-the-art technologies and experimental approaches of modern neuroscience. Should the institute continue on a similar track in the following years and begin publishing breakthrough discoveries, DANDRITE will establish itself as a world leading research centre in molecular and translational neuroscience. Through collaborations with affiliated researchers, DANDRITE will also spread its expertise to other institutions in Denmark..."

RETREAT

Students and postdocs gave elevator talks, and everybody therefore presented research in one or another way. The presentations gave rise to an exciting retreat challenge of generating ideas of new collaborative projects that were presented at the last session.

The Retreat 2016 program included plenary lectures by SAB member Professor **Carl Petersen** on: *Sensorimotor integration* and Professor **James McGaugh** (University of California) on: *Modulation of Memory Consolidation: Roles of stress hormones and amygdala activation.*

Furthermore, invited speakers gave presentations and crash courses.

Day 1:
Associate professor **Jacob Friis Sherson**
(Department of Physics and Astronomy, Aarhus University): *Human strategy and intuition formation in online problem solving*

Professor **Anders Børglum**
(Department of Biomedicine, Aarhus University) on: *The Lundbeck Initiative for Integrative Psychiatric Research – iPSYCH.*

Day 2:
Professor **Marco Capogna**
(Affiliated Researcher, Department of Biomedicine, AU) *Juxtacellular recording and labelling of neurons*

Professor Lars Juhl Jensen
(University of Copenhagen)
Network biology: A crash course on STRING and Cytoscape

Group Leader **Keisuke Yonehara** (DANDRITE) *Transsynaptic tagging*

The 2016 Retreat also emphasized social interactions such as team challenges, a festive dinner, and the already now traditional late-night bonfire at the shore that was even blessed by a white nights at its best.

Professor **James McGaugh** concluded our retreat by giving an open DANDRITE lecture at Aarhus University, The AIAS auditorium in the afternoon of the following Wednesday 14th entitled: *Emotional Arousal and Lasting Memories.* The lecture was of great interest for a broad audience; a video from the lecture is available at the DANDRITE web site:
http://dandrite.au.dk/currently/events/open-events/dandrite-seminar-series/dandrite-lectures/video-of-dandrite-lecture-by-dr-james-mcgaugh/

Retreat: Elevator talk by PhD student Juliane Martin. Foto DANDRITE.

Retreat: Elevator talk by PhD student Junior Samuel Lopez Yepez. Foto DANDRITE.

Retreat: Late-night bonfire. Foto DANDRITE.

SITE VISIT

Year 2016 concluded with DANDRITE submitting the grant prolongation application and the initiation of evaluation procedures for a second five-year funding cycle, for the period 2018 – 2023. A key element of the evaluation procedure was a site visit review by an external Review Panel that was conducted on December 2, 2016. The review panel members were: Professor Cornelius Gross (EMBL-Monterotondo - chair), Professor Maiken Nedergaard (University of Copenhagen, Denmark), Professor Kjetil Tasken (NCMM, Norway). Associated observers included Associate Director of Research, Sissel Vorstrup (Lundbeckfonden), Vice President Jan Egebjerg (H. Lundbeck A/S, Denmark, DANDRITE SAB representative), and Head of Government and EU Relations Plamena Markova (EMBL, Germany). The goal of the review panel was to provide an evaluation of the accomplishments and potential of the institute to the Lundbeckfonden as a scientific basis for their decision on further funding.

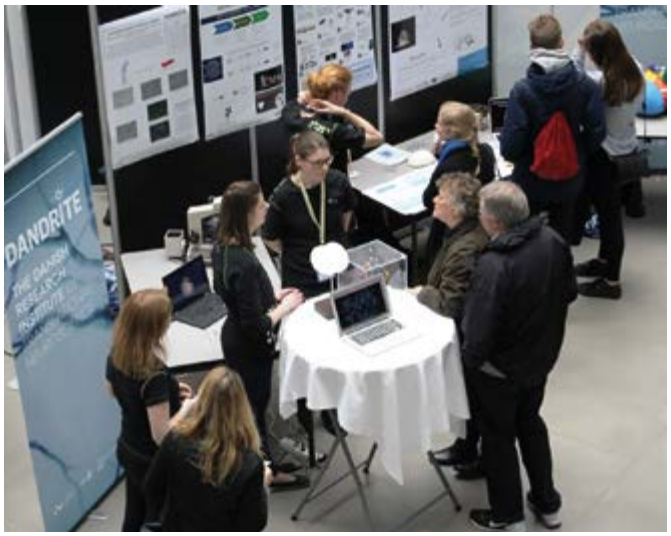
Summary sections from Review Panel Report:

Since its founding in March 2013 DANDRITE has successfully completed the initial ramp-up of its activities, including the hiring of five internationally-recruited young group leaders and two externally funded team leaders and the establishment of significant scientific infrastructure, including top-level electron microscopy and optogenetics/electrophysiology facilities, both unique in the national context. DANDRITE Group and Team Leaders have used this investment to leverage significant additional national and international funding, including two ERC Starting Grants. This rapid ramp-up has created a unique and precedent-setting research center that promises to bring scientific excellence in molecular and circuit neurobiology to Denmark and places DANDRITE in a strong position among its peers in the Nordic EMBL Partnership."...

"Collaborations between the research teams have appeared and the panel noted with particular interest those bridging structural biology with circuit/behavior research as these are otherwise rare and could represent a unique contribution of DANDRITE to the neuroscience field."...

FESTIVAL OF RESEARCH

The theme for Festival of Research 2016 was "Fascinating Research". DANDRITE researchers and students had a great day communicating their indeed fascinating research in the brain and the nervous system to the general public. Among many activities, stem cells were showcased and details on how they are used in disease models, treatments, and the newest understanding of Parkinson were explained. Models for behavioural studies of decision making as well as how the brain's molecular mechanisms form memories were also displayed and engaged with the public.



DANDRITE researchers at Festival of Research. Foto DANDRITE.

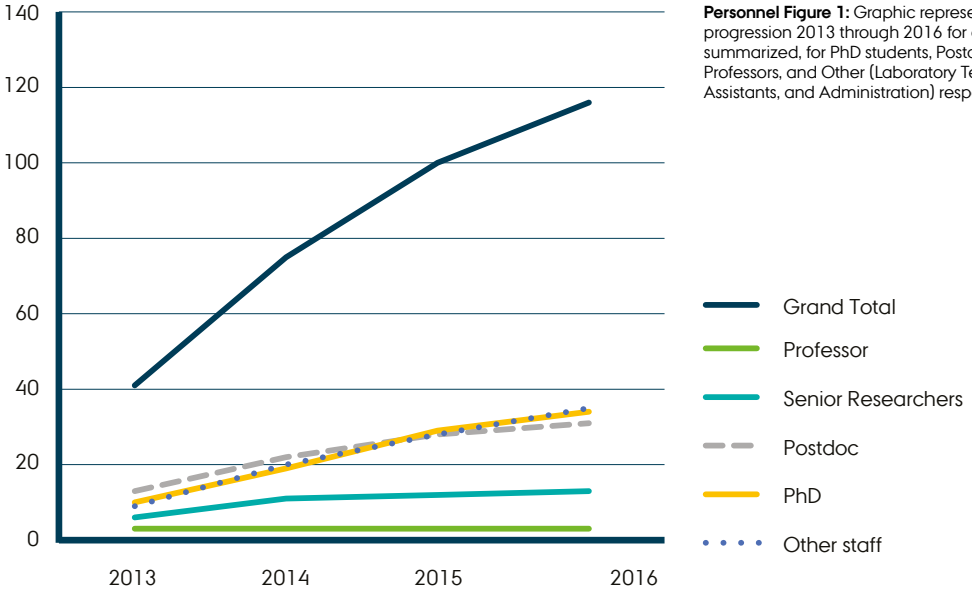
DANDRITE researchers at Festival of Research. Foto DANDRITE.

DANDRITE researchers at Festival of Research. Foto DANDRITE.

04
Personnel

Personnel

Mid-2015 DANDRITE achieved the initial important goal of recruiting five outstanding young group leaders following the EMBL mode, namely Group Leader **Mark Denham** (December 2013), Group leader **Anne von Philipsborn** (January 2014), Group Leader **Duda Kvitsiani** (November 2014), Group Leader **Keisuke Yonehara** (January 2015), and Group Leader **Sadegh Nabavi** (July 2015). Each one of the five young group leaders during 2016 continued the successful establishment and build-up of their groups with students, technical support staff, and promising postdoctoral fellows. Additionally, all groups have attracted several summer students, interns, and research visitors from EU, Denmark, as well as rest of the World.

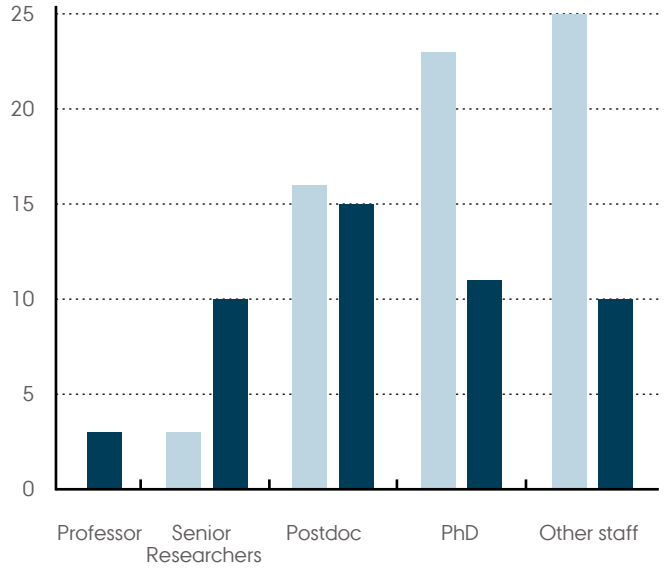


Personnel Figure 1: Graphic representation of personnel progression 2013 through 2016 for all appointment categories summarized, for PhD students, Postdocs, Senior Researchers, Professors, and Other (Laboratory Technicians, Research Assistants, and Administration) respectively.

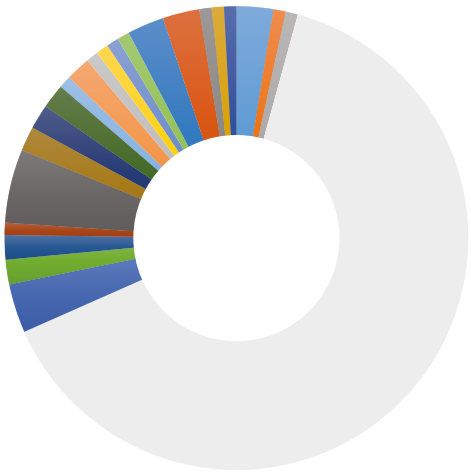
COUNT AND PERCENTAGES OF PERSONNEL EMPLOYED AND AFFILIATED DURING 2016 GROUPED BY APPOINTMENT CATEGORY AND GENDER

DANDRITE Personnel categories	Female	Male	Grand total	% Personnel per category
Professor		3	3	3
Senior Researchers	3	10	13	11
Postdoc	16	15	31	27
PhD	23	11	34	29
Other staff (Laboratory Technician, Research Assistant, and administration)	25	10	35	30
Grand Totalt	67	49	116	100
% Male/Female	58	42	100	

Personnel figure 2: Count and percentages of personnel employed and affiliated during 2016 grouped by appointment category and gender.

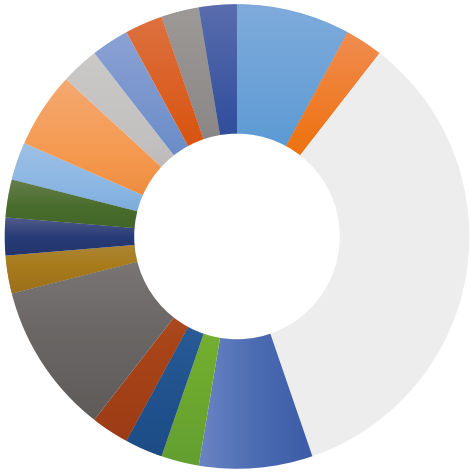


Personnel figure 3: Graphic representation of personnel employed and affiliated during 2016 grouped by appointment category and gender.



Personnel figure 4: Graphic representation of all employees and affiliated members during 2016 grouped by nationality.

Australia
China
Czech Republic
Denmark
Egypt
Estonia
France
Georgia
Germany
India
Iran
Ireland
Italy
Japan
Latvia
Lithuania
Mexico
Norway
Poland
Portugal
Romania
Turkish
US



Personnel figure 5: Graphic representation of employees in the five young Group Leader's groups during 2016 grouped by nationality.

Australia
China
Denmark
Egypt
Estonia
France
Georgia
Germany
Indien
Iran
Ireland
Italy
Japan
Latvia
Mexico
Portugal
Romania
US

Awards

DECEMBER
Article by **Keisuke Yonehara** awarded "**Best of Neuron 2016**": Keisuke Yonehara *et. al. "Congenital Nystagmus Gene FRMD7 Is Necessary for Establishing a Neuronal Circuit Asymmetry for Direction Selectivity"*

NOVEMBER
Poul Nissen awarded the **Director Ib Henriksen Foundation's Researcher Award 2016**

OCTOBER
Keisuke Yonehara (together with Michele Fiscella and Antonia Drinnenberg) received Swiss OphthAward in the category "Best Experimental Work" for the outstanding publication "Congenital Nystagmus Gene FRMD7 Is Necessary for Establishing a Neuronal Circuit Asymmetry for Direction Selectivity"

AUGUST
Poul Nissen awarded the **Order of Dannebrog** by Her Majesty the Queen

MARTS
Poul Nissen awarded **The Gregori Aminoff Prize 2016** by the Royal Swedish Academy of Sciences

Grants for Aarhus University Hosted Research Activities

PhD Student **Ole Søndergaard Schwartz**: Three year PhD fellowship: *Development of neuronal circuit for direction selectivity in the mouse superior colliculus* DKK 1.6 million, Lundbeckfonden

PhD Student **Mette Habekost**: Four year PhD Fellowship: *The regulatory role of A PP Intracellular Domain in Alzheimer's Disease* DKK 1.5 million, Faculty of Health, Aarhus University

Group Leader **Duda Kvitsiani**: *Next generation tools to record fine temporal and spatial activity of neurons in freely behaving animals* DKK 1.2 million, AUFF NOVA, Aarhus University

Affiliated Researcher **Marco Capogna**: *Functional, anatomical and pharmacological mechanisms of GABAergic inhibitory circuits in the human cerebral cortex* DKK 5.2 million, Horizon2020, The European Research Council

Group Leader **Sadegh Nabavi**: *Novel Neuron Types in the Mammalian Brain* DKK 2.0 million, AUFF NOVA, Aarhus University

Group Leader **Poul Henning Jensen**: *DACAPO: Decisive early calcium changes in Parkinson's disease* DKK 10.0 million, Lundbeckfonden

Group Leader **Sadegh Nabavi**: *Mapping the Neural Circuit for an Innate Fear Behaviour* DKK 0.7 million, Novo Nordisk Foundation

Group Leader **Anders Nykjær**: *Functional characterization of the multiple sclerosis risk gene SORCS3* DKK 0.4 million, Scleroseforeningen

Group Leader **Anders Nykjær:** *SorCS1 – boosting energy expenditure in obesity* DKK 0.8 million, Novo Nordisk Foundation

Group **Leader Sadegh Nabavi**: *Mapping the Neural Circuit for an Innate Fear Behaviour* DKK 2.0 million, AUFF NOVA, Aarhus University

Affiliated Researcher **Marco Capogna**: *The role of GABAergic neurons of the mouse amygdala on sleep-wake cycle* DKK 2.0 million, AUFF NOVA, Aarhus University

Group Leader **Poul Henning Jensen**: *Generation of stable -synuclein oligomers – Can chemical stabilization of oligomers by cross linkers be obtained without abolishing their aggregate-specific surface properties* DKK 0.25 million, Michael J Fox Foundation

Group Leader **Mark Denham**: *Combining Stem Cells and Novel Bioactive Scaffolds to develop new Parkinson's Disease Therapies* DKK 60.000, Parkinsonforeningen

Postdoc **Xavier Warnet**: One year Postdoctoral Fellowship: *Interactions between the NMDA receptors and CaMKII kinase in order to better understand the molecular basis of memory* DKK 0.2 million, Fondation pour la Recherche Médicale

Group Leader **Poul Henning Jensen**: *Can caffeine treatment rescue alpha-synecluin aggregation dependent disease spreading and neuron loss?* DKK 0.3 million, Parkinsonforeningen

Group Leader **Poul Nissen**: Five year research project "BRAINSTRUC": *Study of the complex and dynamic interaction between proteins, membranes and other biological molecules in the human brain* DKK 10.4 million, Lundbeckfonden

Group Leader **Poul Nissen**: Equipment grant BRAINSTRUC center DKK 3.5 million, Lundbeckfonden

PhD Student **Emil Gregersen**: Two year PhD project co-financing: *The role of USP19 in the excretion and cytotoxicity of alpha-synuclein and the hypothetical prion-like intercellular spreading of alpha-synuclein pathology* DKK 0.4 million, H. Lundbeck A/S

Nissen was awarded the Gregori Aminoff Prize in crystallography 2016 by The Royal Swedish Academy of Sciences. Photo: Alexander Mahmoud/ The Royal Swedish Academy of Sciences.

Yonehara received: Swiss OphthAWARD in the category "Best Experimental Work" for his outstanding publication "Congenital Nystagmus Gene FRMD7 Is Necessary for Establishing a Neuronal Circuit Asymmetry for Direction Selectivity". Foto Swiss ophthAWARD.

SAB meeting: Presentation. Photo DANDRITE.

PhD Student **Lasse Reimer**: Three year PhD project co-financing: *Kinase-dependent regulation of Alpha Synuclein cellular functions* DKK 0.6 million, H. Lundbeck A/S

Postdoc **Mette Richner**: *Sortilin i neuropatisk smerte* DKK 0.2 million, Dagmar Marshalls Foundation

Affiliated Researcher **Christian Vægter**: *Running costs* DKK 50.000, Augustinus fonden

Affiliated Researcher **Christian Vægter**: *Neurotrophin Signaling following Nerve Injury* DKK 0.1 million, Dagmar Marshalls Foundation

Postdoc **Szilard Sajgo**: Three year postdoc Fellowship: *An investigation of the roles of genes associated with congenital nystagmus in retinal circuit assembly* DKK 2.1 million, VELUX Fonden

PhD Student **Niels Andersen**: One year PhD fellowship: *Synaptic tagging and capture* DKK 0.5 million, Faculty of Science and Technology, Aarhus University

Invited Talks

DECEMBER

Keisuke Yonehara: *Cell-type-specific computations and disease in the visual system*, Nippon Medical School, Japan

Keisuke Yonehara: C*ell-type-specific computations and disease in the visual system*, Osaka University, Japan

Keisuke Yonehara: *Cell-type-specific computations and disease in the visual system*, Ritsumeikan Unviersity, Japan

Keisuke Yonehara: *Cell-type-specific computations and disease in the visual system*, Kanazawa Unviersity, Japan

NOVEMBER

Duda Kvitsiani: *Biologically inspired neural networks, Summit on Human Problem Solving and Artificial Intelligence*, Sandbjerg, Denmark

Poul Nissen: *Structural Dynamics of P-type ATPases studied by single-molecule FRET and time-resolved scattering techniques, Symposium on new paradigms in fluorescence-based approaches to study membrane proteins*, University of Copenhagen, Denmark

Anders Nykjær: *SorCS receptors engage receptor tyrosine kinases to r egulate synaptic plasticity and insulin sensitivity, VIB Center for the Biology of Disease*, Leuven, Belgium

Poul Henning Jensen: *Kan caffeine behandling beskytte imod alfa-synuclein aggregations sygdomsspredning og nervecelletab?*

Poul Henning Jensen: *Kinase dependent regulation of alpha-synuclein levels and phosphorylation, Pathogenic mechanisms in Parkinson's disease and multiple systems atrophy*, Lund University, Sweden

Mark Denham: *Designing 3D Neuronal circuit models of Parkinson's Disease, Danish Parkinson's Foundation, Copenhagen, Denmark*
Sadegh Nabavi: Synapses and Memory, New Talent talk, Brain Prize, Denmark

OCTOBER

Affiliated Researcher Marco Capogna: *Hippocampal theta input to the amygdala shapes feedforward inhibition to gate heterosynaptic plasticity*, Brain Prize Meeting 2016, Denmark

Poul Henning Jensen: *Characterization of MJFF Alpha-synuclein filament specific antibodies*, Michael J Fox Foundation Parkinson's disease Therapeutics conference, New Yourk, USA
Poul Nissen: *Structural and functional studies of SLC6 transporters MhsT and LeuT*, Sanofi, Frankfurt, Germany

Poul Nissen: *Membrane Proteins – where do we go?*
INTERREG – MAX4ESSFUN annual meeting, Lund, Sweden

Anders Nykjær: *SorCS2 Regulates Dopaminergic Wiring and BDNF-dependent Plasticity*, Virginia – Nordic Precision Neuroscience, Roanoke, Virginia, USA

Anders Nykjær: *Sortilins as regulators of tyrosine kinase receptor activity: Implications in mental disorders and diabetes*, University of Wisconsin-Madison

SEPTEMBER

Poul Nissen: *Crystallographic studies of the structure and mechanism of P-type ATPase pumps*, Symposium, Honoris Causa Doctorate for Wayne Hendrickson, Sapienza, Rome, Italy

Affiliated Researcher Marco Capogna: *Juxtacellular recording and labelling of neurons*, DANDRITE retreat 2016, Denmark

Affiliated Researcher Marco Capogna: *Amygdala circuits: key role of GABAergic neurons in health and disease*, 2016 Brain Circuits and Diseases Symposium, Academia Sinica, Taipei, Taiwan

Affiliated Researcher Marco Capogna: *GABAergic neuron diversity in the hippocampus-amygdala circuit in health and disease*, Taipei, Taiwan, Yang-Ming University

Poul Nissen: *Completing the NSS transport cycle structure of an occluded return state of LeuT*, SFB35 Symposium 2016, Vienna, Austria

Mark Denham: *Generation of Peripheral and Central Nervous System Cell types, Molecular Life of Stem Cells*, Ljubljana, Slovenia

Mark Denham: *Modelling Parkinson's Disease with Stem Cells*, SAB Dandrite retreat, Sandbjerg, Denmark.

AUGUST
Affiliated Researcher Simon Glerup: *Sortilins in ADHD and addictio, Rodent Models 2016*, Tartu, Estonia

Affiliated Researcher Simon Glerup: S*ortilins in ADHD and addiction, K.G. Jebsen Centre for Research on Neuropsychiatric Disorders*, Bergen, Norway

Poul Nissen: *Introduction to Membrane Protein Research*, BSR16, Standford, San Francisco, USA

Mark Denham: *Investigating the role of Alpha-Synuclein in GBA1 iPSC-derived neurons*, BrainStem Symposium, Odense, Denmark.

JUNE
Poul Nissen: *Structure and function of membrane transporters in brain*, ENCODS Symposium FENS 2016, Elsinore, Denmark

Poul Nissen: *Pumping, channeling and exchanging….*, Honorary symposium for Käthi Geering and Jean-Daniel Horisberger, University of Lausanne, Switzerland

Poul Nissen: *Structure and function of active transporters – research and excellence*, Zealand pharamceutical visit to Aarhus University, Denmark

Poul Nissen: *Future of structural biology research*, ESS Workshop, Aarhus – Danish Agency for Research and Innovation, Denmark

MAY
Poul Nissen: *Crystal structure analysis of the ion pumping P-type ATPases*, 48th Sandbjerg Meeting on Membrane Transport, Sønderborg, Denmark

Poul Nissen: *Structural and Functional Studies of Membrane Transporters – from crystals and as single molecules*

APRIL
Poul Nissen: *Crystallographic studies of membrane proteins*, ESS/MAX-IV Symposium, University of Copenhagen, Denmark

Poul Nissen: *Structure, mechanism and regulation of ion pumps in health and disease*, University of Minnesota, Minneapolis, USA

Poul Nissen: *A Molecular Perspective of Ion Pumps in Health and Disease*, Peter Curran Lecture, Yale School of Medicine, USA

MARCH
Poul Nissen: *Crystal structure analysis of the ion pumping P-type ATPases*, The Aminoff Lecture, Gothenburg, Sweden

Poul Nissen: *P-type ATPases – CopA, lipid flippases, and Na,K-ATPase*, MRCT venture funds visit to Aarhus University, Denmark

Poul Nissen: *Snapshots of P-type ATPases – from crystal structures to single-molecule studies*, 60th annual meeting of the Biophysical Society, Los Angeles, USA

FEBRUARY
Sadegh Nabavi: *Synaptic plasticity: From molecules to behavior.* COSYNE, Snowbird, Utah, USA

Poul Henning Jensen: *Reduced Cytosolic Calcium Caused by SERCA Activation is an Early and Pathogenic Event in Cellular Stress Caused by a-synuclein Oligomers*, Institute of Neurobiology, Interdisciplinary Center for Neurosciences (IZN), University of Heidelberg, Germany

Anders Nykjær: *Studies of sortilin receptors in neuronal development and signaling*, DANDRITE encounters 2016, Aarhus University, Denmark

Anne von Philipsborn: C*ircuit neuroscience and behavioural genetics in Drosophila*, DANDRITE encounters 2016, Aarhus University, Denmark

Duda Kvitsiani: *Behavioural studies of molecular and circuit basis of effort based decision making*, DANDRITE encounters 2016, Aarhus University, Denmark

Keisuke Yonehara: *Function and dysfunction of motion-sensitive circuits in the visual system*, DANDRITE encounters 2016, Aarhus University, Denmark

Mark Denham: *Modelling human neural development and disease with stem cells*, DANDRITE encounters 2016, Aarhus University, Denmark

Poul Henning Jensen: *Neurodegenerative diseases and the role of alpha-synuclein*, DANDRITE encounters 2016, Aarhus University, Denmark

Poul Nissen: *Structural and functional studies of membrane transporters in brain.* DANDRITE encounters 2016, Aarhus University, Denmark

Sadegh Nabavi: M*emory formation and consolidation at the synaptic and circuit levels*, DANDRITE encounters 2016, Aarhus University, Denmark

JANUARY
Poul Nissen: A *career in membrane protein structural biology, Keynote at Gordon Research Symposium*, Il Ciocco, Italy

Poul Nissen: *How do primary and secondary transporters switch sides?* Keynote at Gordon Research Symposium, Il Ciocco, Italy

05 Publications

Publications

1. **Andersen OM**, Rudolph I-M, Willnow TE (2016) Risk factor SORL1: from genetic association to functional validation in Alzheimer's disease. *Acta Neuropathologica*, 132(5):653-665

2. Bocchio M, Fisher SP, Unal G, Ellender TJ, Vyazovskiy VV, **Capogna M** (2016) Sleep and serotonin modulate paracapsular nitric oxide synthase expressing neurons of the amygdale. *eNeuro* 26 September 2016, ENEURO.0177-16.2016; DOI: https://doi.org/10.1523/ENEURO.0177-16.2016

3. Boggild S, Molgaard S, **Glerup S**, Nyengaard JR (2016) Spatiotemporal patterns of sortilin and SorCS2 localization during organ development. *B M C Cell Biology*, Vol. 17, 2016, p. 8.

4. Bøttger P, **Glerup S**, Gesslein B, Illarionova N, Isaksen TJ, Heuck A, Clausen BH, Füchtbauer, E-M, Gramsbergen JB, Gunnarson E, Aperia, A, Lauritzen M, Lambertsen KL, **Nissen P**, Lykke-Hartmann K (2016) Glutamate-system defects behind psychiatric manifestations in a familial hemiplegic migraine type 2 disease-mutation mouse model. Scientific Reports, Vol. 6, No. 22047, 25.02.2016.

5. Clausen JD, Bublitz M, Arnou B, Olesen C, Andersen JP, Møller JV, **Nissen P** (2016). Crystal Structure of the Vanadate-Inhibited Ca(2+)-ATPase. *Structure* 24:617-23

6. David-Bosne S, Clausen MV, **Poulsen H**, Møller JV, **Nissen P**, le Maire M (2016). Reappraising the effects of artemisinin on the ATPase activity of PfATP6 and SERCA1a E255L expressed in Xenopus laevis oocytes. *Nat Struct Mol Biol* 23:1-2

7. Demontis D, Lescai F, Børglum A, **Glerup S**, Østergaard SD, Mors O, Li Q, Liang J, Jiang H, Li Y, Wang J, Lesch K-P, Reif A, Buitelaar JK, Franke B (2016). Whole-Exome Sequencing Reveals Increased Burden of Rare Functional and Disruptive Variants in Candidate Risk Genes in Individuals With Persistent Attention-Deficit/Hyperactivity Disorder. *American Academy of Child and Adolescent Psychiatry.* Vol. 55, No. 6, 06.2016, p. 521-3.

8. **Dyla M, Andersen J, Kjaergaard M**, Birkedal V, Terry DS, Altman RB, Blanchard S, **Nissen P**, Knudsen CR (2016) Engineering a prototypic P-type ATPase Listeria Monocytogenes Ca(2+)-ATPase 1 for single-molecule FRET studies. Bioconjugate Chemistry, Vol. 27, No. 9, 2016, p. 2176-2187.

9. **Glerup S**, **Bolcho U**, Molgaard S, Bøggild S, **Vaegter CB**, Smith AH, Nieto-Gonzalez JL, Ovesen PL, Fjorback AN, Kjolby M, **Login H**, Holm MM, **Andersen OM**, Nyengaard JR, Willnow TE, Jensen K, **Nykjaer A** (2016) SorCS2 is required for BDNF dependent plasticity in the hippocampus. Mol Psych 21(12):1740-1751

10. Goettsch C, Hutcheson JD, Aikawa M, **Nykjaer A**, Kjolby M, Rogers M, Michel T, Shibasaki M, Rader DJ, Libby P, Singh SA, Aikawa E (2016) Sortilin mediates vascular calcification via its recruitment into extracellular vesicles. J Clin Invest 126(4):1323-36

11. Gregersen JL, Fedosova N, **Nissen P, Boesen T** (2016) Reconstitution of Na,K-ATPase in Nanodiscs. *Methods in Molecular Biology*, Vol. 1377, 2016, p. 403-409.

12. Hilbers F, Kopec W, Isaksen TJ, Holm TH, Lykke-Hartmann K, **Nissen P**, Khandelia H, **Poulsen H** (2016) Tuning of the Na, K-ATPase by the beta subunit. *Scientific Reports*, Vol. 6, No. 20442, 2016.

13. Holm TH, Isaksen TJ, **Simon G**, Heuck A, Bøttger P, Füchtbauer E-M, Nedergaard ST, Nyengaard JR, Andreasen M, **Nissen P**, Lykke-Hartmann K (2016). Cognitive deficits caused by a disease-mutation in the 3 Na(+)/K(+)-ATPase isoform. *Scientific Reports*, Vol. 6, No. 31972

14. Horrocks MH, Lee SF, Gandhi S, Magdalinou NK, Chen SW, Devine MJ, Tosatto L, **Kjaergaard M**, Beckwith JS, Zetterberg H, Iljina M, Cremades N, Dobson CM, Wood NW, Klenerman D (2016) Single-molecule imaging of individual amyloid protein aggregates in human biofluids. A C S *Chemical Neuroscience*, Vol. 7, No. 3, 22.01.2016, p. 399–406

15. **Jager SB, Vaegter** CB (2016) Avoiding experimental bias by systematic antibody validation. *Neural Regeneration Research*, Vol. 11, No. 7, 07.2016, p. 1079-80.

16. Kirscht A, Kaptan SS, Bienert GP, Chaumont F, **Nissen P**, de Groot BL, Kjellbom P, Gourdon P, Johanson U (2016) Crystal Structure of an Ammonia-Permeable Aquaporin. PLoS Biology, Vol. 14, No. 3, 03.2016, p. e1002411.

17. Larsen, JV, Kristensen AM, Pallesen LT, Bauer J, **Vægter CB**, Nielsen MS, Madsen P, Petersen CM (2016) Cytokine-like factor-1 (CLF-1): An essential facilitator of cardiotrophin-like cytokine: CNTF (CLC:CNTFR) signalling and sorLA mediated turnover. *Molecular and Cellular Biology*, 2016. Mol. Cell. Biol. doi:10.1128/MCB.00917-15

18. **Lassen LB, Reimer L, Ferreira N, Betzer C, Jensen PH** (2016). Protein Partners of -Synuclein in Health and Disease. *Brain Pathol* 26(3):389-97. doi: 10.1111/bpa.12374.

19. Lindholt J, Mattle D, Fedosova N, **Nissen P,** Schuldt L (2016) Isolation, crystallization and crystal structure determination of bovine kidney Na+,K+-ATPase. *Acta Crystallographica. Section F: Structural Biology and Crystallization Communications*, Vol. 72, No. Pt. 4, 01.04.2016, p. 282-287.

20. **Lyons JA, Shahsavar A**, Paulsen PA, Pedersen BP, Nissen P (2016) Expression strategies for structural studies of eukaryotic membrane proteins. *Current Opinion in Structural Biology*, Vol. 38, 27.06.2016, p. 137-144.

21. Malinauskaite L, **Said S**, Sahin C, Grouleff J, Shahsavar A, Bjerregaard H, Noer P, Severinsen K, **Boesen T**, Schiøtt B, Sinning S, **Nissen P** (2016). A conserved leucine occupies the empty substrate site of LeuT in the Na(+)-free return state. *Nat Commun* 7:11673

22. Matrone C, Dzamko N, Madsen P, Nyegaard M, Pohlmann R, Søndergaard RV, **Lassen LB**, Andresen TL, Halliday GM, **Jensen PH**, Nielsen MS (2016). Mannose 6-Phosphate Receptor Is Reduced in alpha-Synuclein Overexpressing Models of Parkinsons Disease. PLoS One 11(8):e0160501.

23. Molgaard S, Demontis D, Nicholson AM, Finch NA, Petersen RC, Petersen CM, Rademakers R, **Nykjaer A, Glerup S** (2016) Soluble sortilin is present in excess and positively correlates with progranulin in CSF of aging individuals. *Exp Gerontol* 84:96-100

24. Molgaard S, Ulrichsen M, Olsen D, **Glerup S** (2016). Detection of phosphorylated Akt and MAPK in cell culture assays. *MethodsX*, Vol. 3, 2016, p. 386-98.

25. Montigny C, **Lyons J**, Champeil P, **Nissen P,** Lenoir G (2016) On the molecular mechanism of flippase- and scramblase-mediated phospholipid transport. *B B A – Molecular and Cell Biology of Lipids*, Vol. 1861, No. 8, Part B, 2016.

26. Pedersen BP, Gourdon P, Liu X, Karlsen JL, **Nissen P** (2016) Initiating heavy-atom-based phasing by multi-dimensional molecular replacement. *Acta crystallographica. Section D. Structural biology*, Vol. 72, No. Pt 3, 01.03.2016, p. 440-445.

27. Reinert LS, Lopušná K, Winther H, Sun C, Thomsen MK, Nandakumar R, Mogensen TH, Meyer M, **Vægter C**, Nyengaard JR, Fitzgerald KA, Paludan SR (2016) Sensing of HSV-1 by the cGAS-STING pathway in microglia orchestrates antiviral defence in the CNS. *Nature Communications*, Vol. 7, 10.11.2016, p. 13348.

28. Rollo B, Zhang D, Stamp L, Menheniott T, Stathopoulos L, **Denham M**, Dottori M, King S, Hutson J, Newgreen D (2016). Enteric Neural Cells from Hirschsprung Disease Patients form Ganglia in Autologous Aneuronal Colon Muscle Tissue. *Cellular and Molecular Gastroenterology and Hepatology*, Vol. 2, No. 1, 01.2016.

29. Sengupta A, Bocchio M, Bannerman DM, Sharp T, **Capogna M** (2016) Control of amygdala circuits by 5-HT neurons via 5-HT and glutamate co-transmission. *Journal of Neuroscience* 13 January 2017, 2238-16; DOI: https://doi.org/10.1523/JNEUROSCI.2238-16.2016

30. Vázquez CL, Rodgers A, Herbst S, Coade S, Gronow A, Guzman CA, Wilson MS, Kanzaki M, **Nykjaer A**, Gutierrez MG (2016) The proneurotrophin receptor sortilin is required for Mycobacterium tuberculosis control by macrophages. Sci Rep 6:29332.

31. **Voldsgaard CM, Nissen P, Poulsen H** (2016) The 4 isoform of the Na+ , K+ -ATPase is tuned for changing extracellular environments. *The F E B S Journal* (Online), Vol. 283, No. 2, 2016, p. 282-293.

32. Yatime L, **Betzer C**, Jensen RK, Mortensen S, **Jensen PH**, Andersen GR (2016). The Structure of the RAGE:S100A6 Complex Reveals a Unique Mode of Homodimerization for S100 Proteins. *Structure* 24(12):2043-2052. doi: 10.1016/j.str.2016.09.011.

33. **Yonehara K**, Fiscella M, Drinnenberg A, Esposti F, Trenholm S, Krol J, Franke F, Scherf BG, Kusnyerik A, Müller J, Szabo A, Jüttner J, Cordoba F, Reddy AP, Németh J, Nagy ZZ, Munier F, Hierlemann A, Roska B (2016) Congenital Nystagmus Gene FRMD7 Is Necessary for Establishing a Neuronal Circuit Asymmetry for Direction Selectivity. *Neuron*, Vol. 89, No. 1, 06.01.2016, p. 177-93.

34. **Yonehara K**, Roska B (2016) "MAPseq"-uencing Long-Range Neuronal Projections. *Neuron*, Vol. 91, No. 5, 07.09.2016, p. 945-947.

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