



**DANISH
RESEARCH
INSTITUTE OF
TRANSLATIONAL
NEUROSCIENCE**

**ANNUAL REPORT
2013**

TABLE OF CONTENTS

WORDS FROM THE DIRECTOR.....	3
FIRST YEAR OF DANDRITE.....	4
GUESTS & SEMINARS.....	4
CONFERENCE ACTIVITIES.....	4
EMBL & EMBL PARTNERSHIP ACTIVITIES.....	5
DANDRITE GROUP LEADERS.....	6
Nissen Group - Structural and Functional Studies of Membrane Transporters in Brain.....	6
Jensen Group - Neurodegenerative disease.....	7
Nykjær Group - Receptor Biology.....	9
Philipsborn Group- Behavioral genetics and circuit neuroscience.....	10
Denham Group - Stem Cells.....	12
DANDRITE ORGANIZATION STRUCTURE.....	13
EXECUTIVE BOARD.....	13
DIRECTOR.....	13
STEERING COMMITTEE.....	14
OTHER ORGANIZATIONAL BODIES IN PIPELINE.....	14
ADMINISTRATIVE ORGANIZATION.....	14
SCIENTIFIC ADVISORY BOARD.....	14
PERSONNEL.....	15
DANDRITE RESEARCH INFRASTRUCTURE.....	17
NEW PURCHASES.....	18

WORDS FROM THE DIRECTOR



It is with great pride that we present the first annual report from DANDRITE - the Danish Research Institute of Translational Neuroscience and the Danish node of the Nordic-EMBL Partnership for Molecular Medicine.

2013 has been a very busy and rewarding first year, dominated by the establishment and organization of DANDRITE operations and our first recruitments. In the first 9 months we went from three professors with local support to an independent organization with more than 10 new recruitments in the administrative and scientific staff.

EMBL Partnership and inauguration

A renewal of the Nordic-EMBL Partnership agreement was signed at Aarhus University on March 5th, 2013. At the same time DANDRITE was inaugurated on a first 5-year contract between the Lundbeck Foundation, Aarhus University and EMBL. The joint event took place in the main ceremonial hall of the university and gathered the rectors, directors and key representatives of the participating universities, EMBL and the other nodes of the Nordic-EMBL partnership.



DANDRITE organization and recruitments

Important insight was gained from the experience of the other

nodes and EMBL in

setting up procedures for our first group leader call in the summer of 2013. Two group leaders started December 2013/January 2014 and before then technicians were recruited that helped setting up the laboratories for their arrival. A DANDRITE postdoc call and a PhD call in conjunction with the other nodes were opened.



DANDRITE also served as a new model for an interdisciplinary research center in a joint venture with the private Lundbeck Foundation and associating activities from other centres and research grants. The scope is

interdisciplinary with open research programs in neuroscience and a governance structure between two faculties and two departments.

FIRST YEAR OF DANDRITE

March 5, 2013: Inauguration Ceremony of DANDRITE, The Main Hall, Aarhus University, host Aarhus University.

GUESTS & SEMINARS

- November 22, senior editor Karin Dumstrei, EMBO Journal
- November 1, Prof. Jonathan Knowles, FIMM (Finnish Institute for Molecular Medicine), The Molecular Personalization of Medicine: Good Science and Better Medicine, host Poul Nissen.
- October 20, Prof. Ernst Bamberg, Max Planck Institute of Biophysics, Frankfurt am Main, Germany, Optogenetics today and tomorrow, host Anders Nykjær.
- October 20, Prof. Ed Boyden, MIT, Cambridge, Massachusetts, USA: Optogenetics today and tomorrow, host Anders Nykjær.
- May 8, Dr. Christine Ziegler, Max Planck Institute of Biophysics, Frankfurt am Main, Germany – DANDRITE seminar.
- April 24, Prof. Jack Johnson, Scripps Research Institute, La Jolla, USA - joint iNANO-DANDRITE seminar.

CONFERENCE ACTIVITIES

- October 20: THE BRAIN PRIZE 2013 – Optogenetics, organized by Anders Nykjær and NEUROCAMBUS, Aarhus University, Denmark.
- September 17 to 19: Nordic Molecular Medicine Network Meeting, Oslo, Norway, organized by NCMM (Centre for Molecular Medicine Norway).
- September 1 to 5, 75th Harden Conference - Receptor Tyrosine Kinase Structure and Function in Mammalian Health and Disease, University of Sheffield, UK, Anders Nykjær Invited Keynote Speaker with talk entitled: Sortilin receptors: novel regulators of receptor tyrosine kinase activity.
- August 14, 2013: DANDRITE Symposium - New frontiers in molecular and translational neuroscience, Aarhus University, Denmark, organized by DANDRITE.



Photo: AU Communication

EMBL & EMBL PARTNERSHIP ACTIVITIES

November 1, 2013	Visit and lecture at Aarhus by Professor Jonathan Knowles from FIMM.
September 17 to September 19, 2013	<p>Nordic Molecular Medicine Network Meeting. 24 PhD students, postdocs, professors and technical and administrative staff from DANDRITE participated.</p> <p>In addition to the lecture program the network meeting program consisted of student and postdoc gathering, poster sessions, administrative meeting (attended by administrative staff from the four NMMN nodes and EMBL), and The Steering Committee Meeting (attended by heads of administrations, node directors, and EMBL representatives).</p>
August 14, 2013	DANDRITE open symposium (part of the interview process of selecting young group leader candidates). The symposium was attended by most members of assessment and interview committees listed below.
April through August 2013	<p>Hiring process of two young group leaders at DANDRITE. The following professors from NMMN/EMBL participated in the assessments and interview process:</p> <p>Director of the NCMM, Kjetil Tasken; Director of MIMS, Bernt Eric Uhlin; Director of FIMM, Olli Kallioniemi; EMBL Director General, Iain Mattaj; Deputy Head of EMBL Outstation Monterotondo, Cornelius Gross, and Group leader at Monterotondo, Paul Heppenstall.</p>
Marts 27, 2013	Poul Nissen was a collaborator with Dr. Kim L. Hein and Group Leader J. Preben Morth from NCMM in Oslo (http://www.ncbi.nlm.nih.gov/pubmed/22505411).
Marts 5, 2013	<p>DANDRITE inauguration with the participation of Directors, administrators, and rectors from all Nordic NMMN nodes. From EMBL participated Professor Iain Mattaj, Director General of the EMBL, Silke Schumacher, Director International Relations, and Plamena Markova, International Relations Officer.</p> <p>Program:</p> <ol style="list-style-type: none">1) Official Opening ceremony with audience.2) Extended business meeting between DANDRITE Core Group Leaders, NMMN node directors and rectors from node host institutions.
January 23 to January 25, 2013	DANDRITE Director Poul Nissen attended the search committee for two group leader positions at MIMS in Umeå.



DANDRITE GROUP LEADERS

In 2013 DANDRITE research activities were dominated by the founding Core Teams (groups). The new group leaders outline research plans.

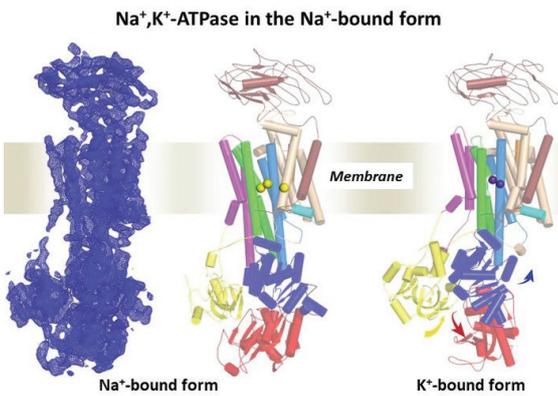
Nissen Group - Structural and Functional Studies of Membrane Transporters in Brain

The Nissen lab investigates molecular mechanisms of membrane transport processes and biomembrane structure. Activities are mainly focused on protein crystallography, biochemistry, electrophysiology, and include also small-angle X-ray scattering and electron microscopy. Main subjects of research concern P-type ATPase (ion pumps and lipid flippases) and Na⁺ dependent transporters, but include also structure based drug discovery and protein engineering.

The first year of DANDRITE research brought new insight into the structure and



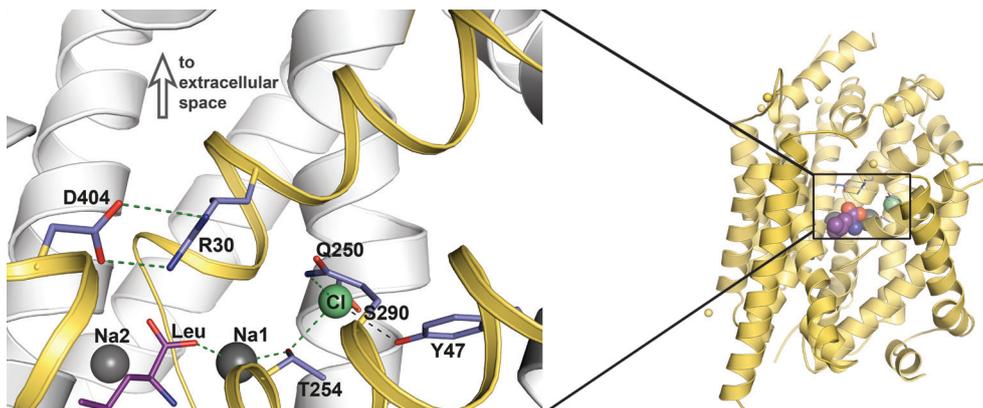
Photo: AU Communication



Graphic: Maria Nyblom, Pontus Gourdon and Poul Nissen

function of Na⁺,K⁺-ATPase, the sodium-potassium pump. This key enzyme consumes some 40-70% of ATP turnover in the brain to maintain vital Na⁺ and K⁺ gradients that power secondary transporters and ion channels receptors. It is also intimately involved in cell volume control, interacts with the extracellular matrix, and controls potassium in the narrow, interstitial space of brain tissue. A crystal structure of the Na⁺ bound form and electrophysiological studies revealed how Na⁺ binding is achieved and hinted at the mechanism of

mutations associated with neurological disease and hypertension. Likewise, a structure of the ouabain inhibited form was determined and revealed the determinants of cardiotonic steroids for tight and specific binding to Na⁺,K⁺-ATPase. A chloride site of neurotransmitter: sodium symporters was revealed from crystallographic studies of a bacterial homologue, and the role of the anion site in transport was analyzed further by enzyme kinetics and molecular dynamics simulations. Future studies will further inquire the role of Na⁺,K⁺-ATPase in neurological and psychiatric disorders, the transport mechanism of neurotransmitter transporters and investigate the higher order structure of membrane protein complexes.



Structural studies pinpointing the chloride site of neurotransmitter:sodium symporters.
Graphic: Kantcheva AK et al., Proc Natl Acad Sci USA, 2013.

Selected publications

- Nyblom M, Poulsen H, Gourdon P et al. (2013). Crystal Structure of Na⁺, K⁺-ATPase in the Na⁺-Bound State. *Science* 342, 123-7
- Azizan EAB, Poulsen H, Tuluc P, Zhou J et al. (2013). Somatic mutations in ATP1A1 and CACNA1D underlie a common subtype of adrenal hypertension. *Nature Genetics* 45, 1055-60
- Laursen M, Yatime L, Nissen P, Fedosova NU (2013). Crystal structure of the high-affinity Na⁺, K⁺-ATPase-ouabain complex with Mg²⁺ bound in the cation binding site. *Proc Natl Acad Sci USA* 110, 10958-63
- Kantcheva AK et al. (2013). Chloride binding site of neurotransmitter sodium symporters. *Proc Natl Acad Sci USA* 110, 8489-94

Jensen Group - Neurodegenerative disease

Our 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 development of new aggregate selective tools.

Based on unbiased screens for misfolded alpha-synuclein effect on proteins interactions and gene expression, kinases regulating cellular alpha-synuclein toxicity and antibodies recognizing misfolded alpha-synuclein we collaborative widely with experts on in vivo modeling, human brain tissue, biophysics and proteomics. The aim is to decipher how cells respond to misfolded alpha-synuclein with respect to cytotoxic and protective mechanisms that can be targeted by therapy. This involves proteostatic mechanisms like autophagy, unconventional secretion, prion-like intercellular propagation and susceptible homeostatic cellular mechanisms being offset by alpha-synuclein aggregates.

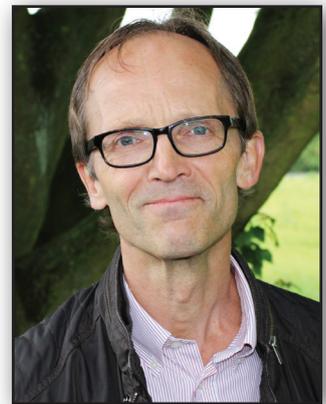
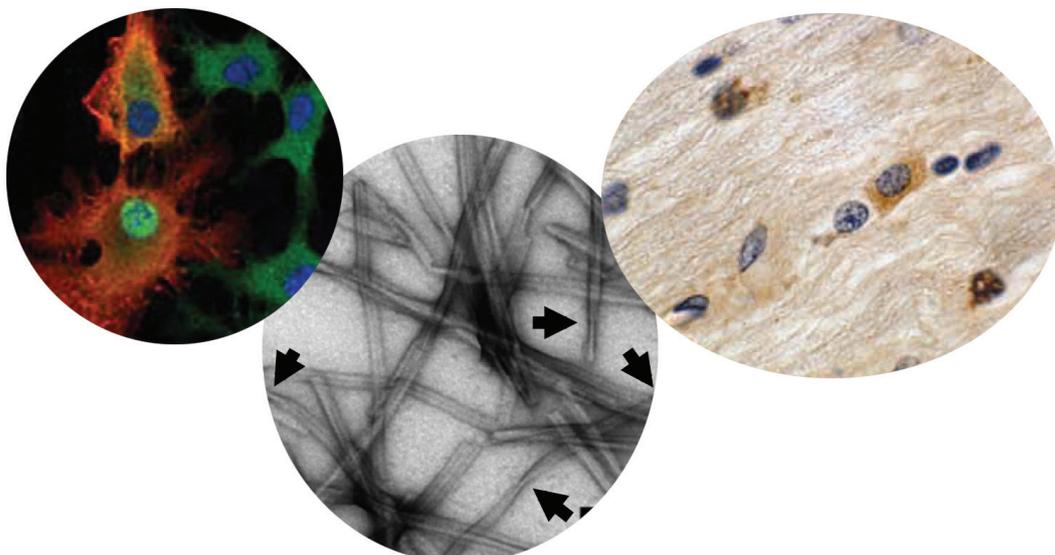
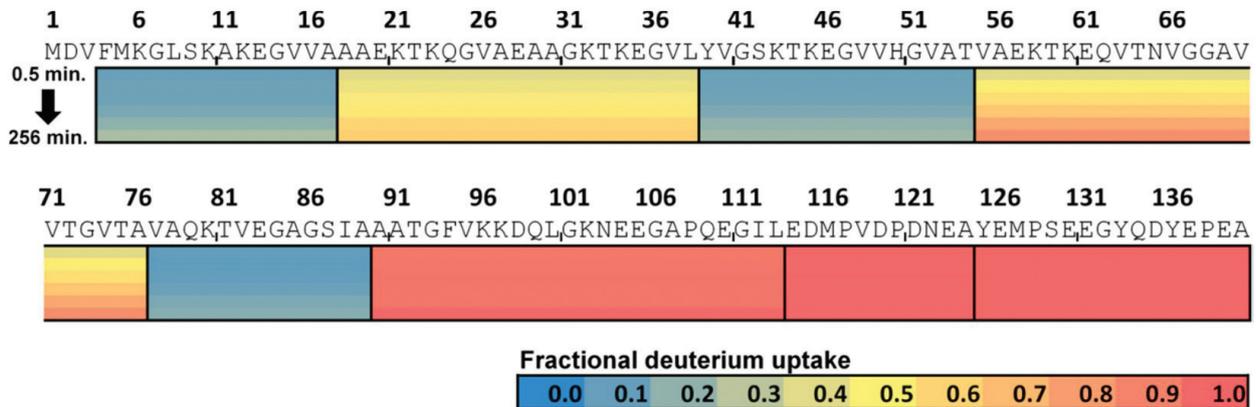


Photo: Else Magård



Photos from left to right: Kragh CL et al., *Neurobiol Dis.* 2014; Bousset L et al., *Nat. Commun* 2013; Kragh CL et al., *PLoS* 2013

Given the confusion on what misfolded and post translationally modified alpha-synuclein species exist in vivo we also work on developing new conformational specific antibodies that can improve cross-validation between labs.



Graphic: Mysling S et al., Biochemistry 2013

Major achievements:

- Demonstrated how intracellular alpha-synuclein aggregates dysregulate cytoprotective NF-kB, prodegenerative FAS, and autophagic signalling in collaboration with Masliah, Halliday, Kahle and Vilhardt labs.
- Demonstrated how different conformational specific epitopes are present on select aggregated alpha-synuclein species and how such epitopes develop in vivo in collaboration with Masliah, Melki and Jørgensen labs.
- Awarded grant from the Michael J Fox foundation to continue developing antibody based tools to identify aggregated alpha-synuclein species.

Selected publications

- Kragh et al. (2013) Fas-dependent cell death in -synuclein transgenic oligodendrocyte models of multiple system atrophy, PlosOne, 8:e55243.
- Mysling S, Betzer C, Jensen PH, Jorgensen TJD (2013) Characterizing the dynamics of alpha-synuclein oligomers using hydrogen/deuterium exchange monitored by mass spectrometry. Biochemistry, 52:9097-103
- Bousset et al. (2013) Structural and functional characterization of two alpha-synuclein strains. Nat Comm, 4:2575.
- Ejlerskov et al. (2013) Tubulin Polymerization Promoting Protein (TPPP/p25a) promotes unconventional secretion of a-synuclein through exophagy by impairing autophagosome-lysosome fusion J Biol Chem, 288:17313-35
- Nuber et al. (2013) Severe Dopaminergic Phenotype Associated with Neurotoxic Conversion of alpha-Synuclein in BAC Transgenic Rats. Brain, 136:412-32.
- Febbraro et al. (2013) Ser129D mutant alpha-Synuclein induces earlier Motor Dysfunction while S129A results in distinctive pathology in a rat model of Parkinson's Disease. Neurobiol Disease, 56:47-58
- V. Sanchez-Guajardo et al. (2013) Alpha-synuclein vaccination prevents the accumulation of Parkinson disease-like pathological inclusions in striatum in association with regulatory T cell recruitment in a rat model. J Neuropath Exp Neurol, 72:624-45

Nykjær Group - Receptor Biology

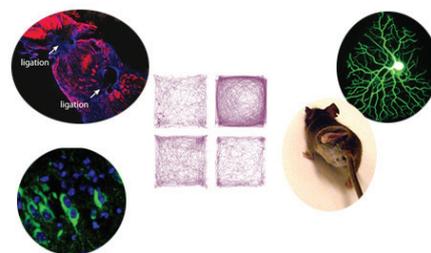
Research activities are focused towards the functional characterization of a family of neuronal type-1 receptors denoted sortilins. They engage in cellular trafficking as well as in signaling from the plasma membrane (Nat. Rev. Neurosci. 2008, 9:899-909; Trends Neurosci. 2012, 5:261-70). Dysfunction of the receptors is associated with neurological, psychiatric and metabolic disorders including Alzheimer's diseases and other neurodegenerative conditions, ADHD, hypercholesterolemia and diabetes. Using transgenic mouse models and a broad repertoire of molecular, cellular and genetic tools it is our goal to understand the function of the receptors in health and disease.



Photo: Private

The sortilin family comprises sortilin, SorLA, and SorCS-1, -2, and -3. Although expression predominates in neurons receptors are also present in specialized cell types outside the nervous system. They bind a vast number of ligands spanning from neurotrophic factors, APP, and progranulin to lipoproteins implying critical roles in the regulation of neuronal survival, differentiation, cell death, pain, and cholesterol metabolism. A major aim of the lab is to understand the mechanisms that govern this multitude of functions. We have found that sortilins can team up with other receptors and their ligands to form ternary complexes; e.g. with the p75NTR and proneurotrophins to induce apoptosis (Nature 2004, Nat. Neurosci. 2007) and with TrkA, -B, and -C to stimulate trophic signalling in neurons (Nat. Neurosci., 2011). In 2013 we extended these observations by showing that SorLA controls neurotrophic activity by lysosomal sorting of GDNF and its receptors GFR α 1 and RET to (Cell Rep.)

Using transgenic mouse models we intend to unravel additional functions of the receptors in as well as outside the nervous system. In particular, a role for SorCS2 in regulating neuron morphology in the dopaminergic system and the consequences for behaviour and disease will be studied.



Graphics: Anders Nykjær

Selected publications

- Gustafsen C, Glerup S, Pallesen LT, Olsen D, Andersen OM, Nykjær A, Madsen P, Petersen CM. Sortilin and SorLA display distinct roles in processing and trafficking of amyloid precursor protein. *J Neurosci.* 33(1): 358-70, 2013
- Coulson EJ, Nykjaer A. Up-regulation of sortilin mediated by amyloid- α and p75(NTR): safety lies in the middle course. *J. Neurochem.* 127(2):149-51, 2013, Editorial Highlight
- Olsen D, Kaas M, Schwartz O, Nykjaer A, Glerup S. Loss of BDNF or its receptors in three mouse models has unpredictable consequences for anxiety and fear acquisition. *Learn. Mem.* 20(9):499-504, 2013
- Glerup S, Lume M, Olsen D, Nyengaard JR, Vaegter CB, Gustafsen C, Christensen EI, Kjolby M, Hay-Schmidt A, Bender D, Madsen P, Saarma M, Nykjaer A, and Petersen CM. SorLA controls neurotrophic activity by sorting of GDNF and its receptors GFR α 1 and RET. *Cell Rep.* 3(1):186-99. 2013

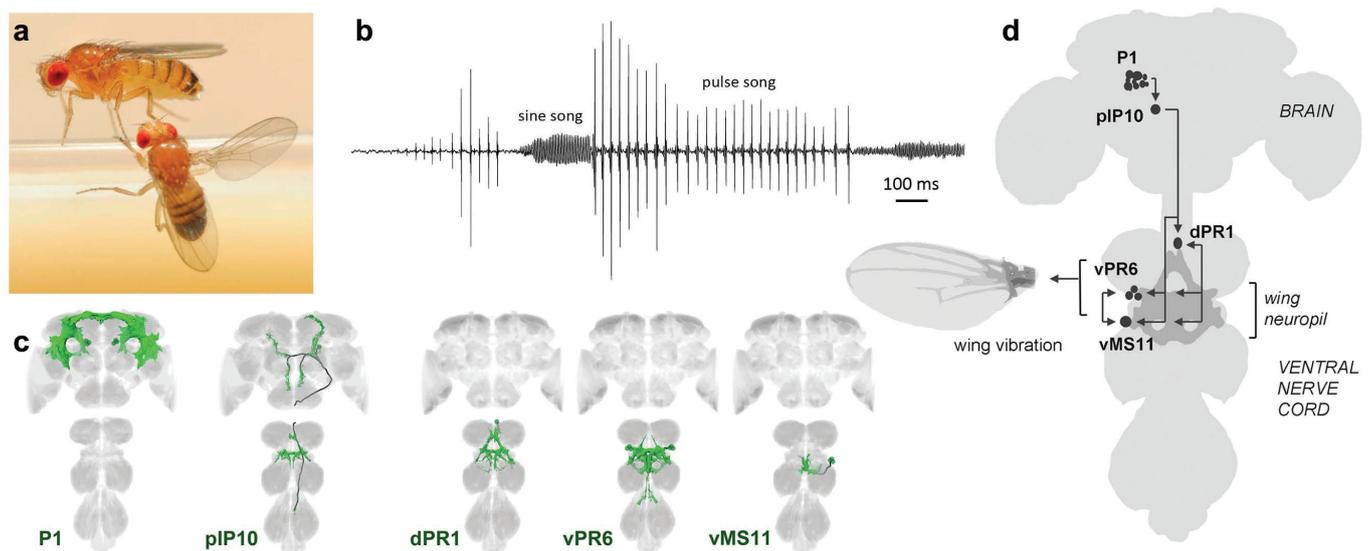
Philipsborn Group- Behavioral genetics and circuit neuroscience

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

We study *Drosophila* courtship behavior with a focus on male specific acoustic signaling. When courting the female, the male fly emits a courtship song by vibrating one wing. We identified and characterized 5 classes of neurons involved in the generation of song. When acutely activated by thermogenetics, these “song neurons” are sufficient to elicit male in the absence of a female. Silencing their activity leads to severely reduced or structurally altered song. The identified neurons are male specific are thought to form an interconnected network.



Photo: Else Magård



a A male fly sings to a female by extending and vibrating one wing. Photo: Solvin Zankl. **b** Oscillogram of courtship song with sine and pulse bouts. **c** Five neuronal classes implicated in courtship song behaviour. **d** Hypothetical neuronal circuit for courtship song generation comprising male-specific or sexually dimorphic fru positive components. Figures c and d modified from von Philipsborn et al. 2011.

Male courtship depends on expression of a sex-specific splice variant of the putative transcription factor fruitless, FruM, which is present in about 2% of the neurons in the *Drosophila* central nervous system, including the above mentioned song neurons. Fruitless is subject to alternative splicing, generating three isoforms FruA, FruB and FruC. FruC is unique in such that it controls the development of male specific neurons involved in pheromone processing and song behavior.

Neuronal circuits for song behavior and motor control

Currently, we investigate how already described and newly identified song neurons interconnect, signal to each

other and control the song pattern. We use song recording as a highly sensitive, high throughput measurement for motor behaviour at millisecond timescale. Genetic tools enable the mapping of circuit connectivity and functionality by combinations of neuronal activity imaging, thermo-/optogenetics and electrophysiology. Simultaneously, we will scrutinize the genetic and molecular basis of circuit dynamics. We are interested in genes pivotal for computational performance and configuration of ensembles of interconnected neurons, namely, genes encoding ion channels, membrane transporters and molecules implicated in neuromodulation. By establishing a comprehensive model circuit for song, we want to uncover neuronal mechanisms for motor pattern generation, bi-functional motor control and behavioural switching, as well as higher-level coordination of motor output. Computational rules and basic principles of action selection and pattern generation which orchestrate *Drosophila* song are expected to be of general relevance for circuit neuroscience.

Molecular and Cellular Models for Neurological Disease in *Drosophila*

Fundamental mechanisms of nervous system function on the molecular, cellular and circuit level are conserved and shared across vertebrates and invertebrates. *Drosophila* can serve as a convenient and genetically accessible *in vivo* model for analyzing the effect of pathological mutations and protein modifications on neuronal physiology. In the future, we will collaborate with other groups at DANDRITE and study for example aspects of Parkinson pathology in a *Drosophila* model system.

Selected publications

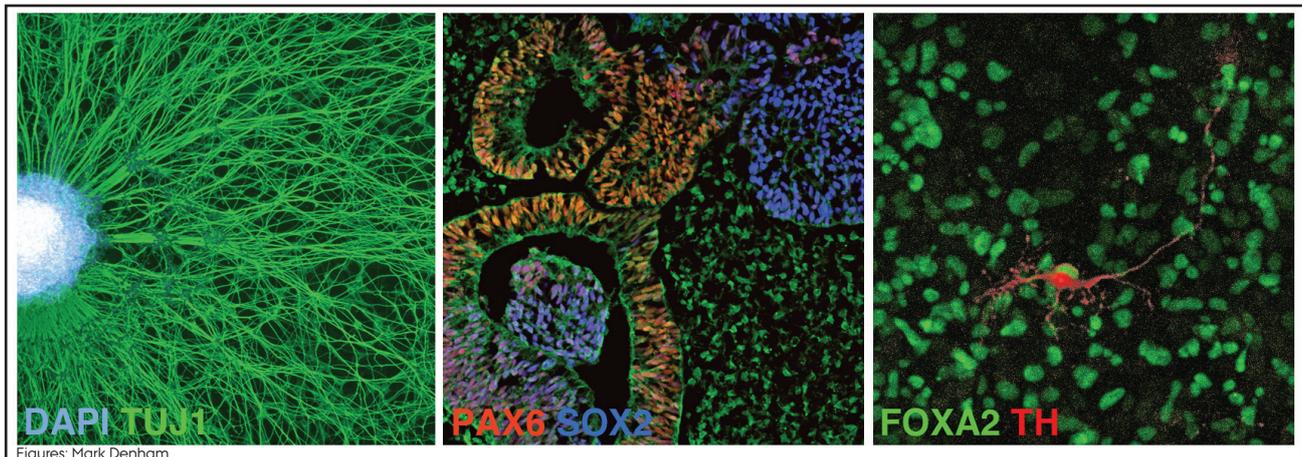
- von Philipsborn, A.C., Jörchel, S., Tirian, L., Demir, E., Morita, T., Stern, David L., and Dickson, Barry J. (2014). Cellular and Behavioral Functions of fruitless Isoforms in *Drosophila* Courtship. *Curr Biol* 24, 242-251.
- von Philipsborn, A.C., Liu, T., Yu, J.Y., Masser, C., Bidaye, S.S., and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

Denham Group - Stem Cells

Our laboratory is interested in understanding how the nervous system develops and the processes involved in neurodegeneration. We use human embryonic stem (ES) cells and induced pluripotent stem (iPS) cells to study the signalling pathways required for their differentiation into precise neural progenitor cell types. In particular, our group is interested in the specification of mesencephalic dopaminergic neurons, the major cell type affected in Parkinson's disease. The objective is to develop in vitro models for studying neural development and disease processes and to identify early cellular changes that underlie the onset of neurodegenerative diseases such as Parkinson's disease. Furthermore, we are also interested in how different neural progenitor subtypes survive and function after transplantation in an adult rodent brain. Our overall goals are to develop potential new treatment strategies for neurodegenerative disorders.



Photo: Melbourne University



Figures: Mark Denham

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

Selected publications

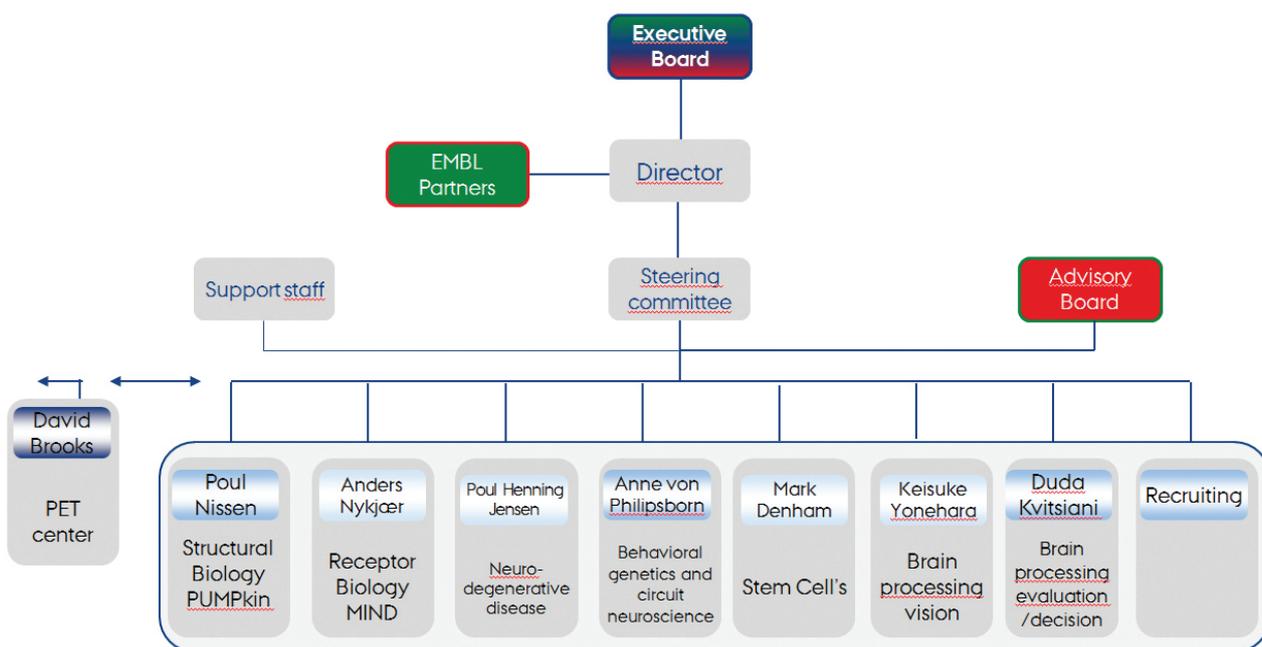
- Denham M, Bye C, Leung J, Conley BJ, Thompson LH, Dottori M. (2012) Glycogen synthase kinase 3 and activin/nodal inhibition in human embryonic stem cells induces a pre-neuroepithelial state that is required for specification to a floor plate cell lineage. *Stem Cells*. 30(11):2400-11
- Denham M, Parish CL, Leaw B, Wright J, Reid CA, Petrou S, Dottori M, Thompson LH. (2012) Neurons derived from human embryonic stem cells extend long-distance axonal projections through growth along host white matter tracts after intra-cerebral transplantation. *Front Cell Neurosci*. 2012 Mar 22;6:11.

DANDRITE ORGANIZATION STRUCTURE

On March 5, 2013 DANDRITE was established as the Danish Node of the Nordic EMBL Partnership in Molecular Medicine. This was made possible thanks to a generous grant from the Lundbeck Foundation and Aarhus University.

DANDRITE is hosted by Aarhus University (AU). At the university organization DANDRITE is placed at two departments which are each part of one of the university's four main academic areas: Department of Biomedicine (part of the main academic area Health) and Department of Molecular Biology and Genetics (part of the main academic area Science and Technology).

DANDRITE is organized with a 3 three-tier management structure consisting of an Executive Board, a Director, and a Steering Committee.



Graphic: Else Magård

EXECUTIVE BOARD

- Professor David Brooks, Department of Clinical Medicine – DNC/PET, chair
- Dean Niels Christian Nielsen, Faculty of Science and Technology
- Dean Allan Flyvbjerg, Faculty of Health Sciences
- Professor Poul Henning Jensen, DANDRITE
- Professor Anders Nykjær, DANDRITE
- Professor Poul Nissen, DANDRITE, Director
- Director of Research Anne-Marie Engel, Lundbeck Foundation (non-voting)
- Secretary support: Else Magård, DANDRITE, Chief Administrative Officer

DIRECTOR

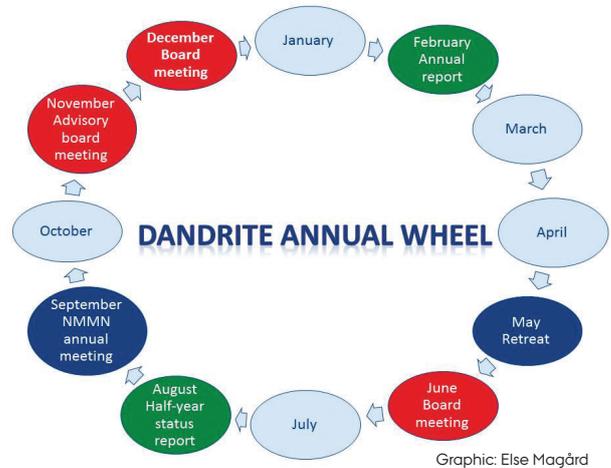
On March 5, 2014 after having served as founding Director Professor Poul Nissen was appointed director of DANDRITE for a term of four years by recommendation from the Executive board.

STEERING COMMITTEE

The steering committee consists of the director, the core group leaders and a representative of the recruited group leaders. The steering committee is responsible for the development of the research strategy, the planning and coordination of activities and distribution of the budget. The steering committee will also be responsible for ensuring the exploitation of the results of DANDRITE research.

In 2013 the following staff members has attended the steering committee meetings which takes place weekly on Monday from 10AM- 11AM.

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



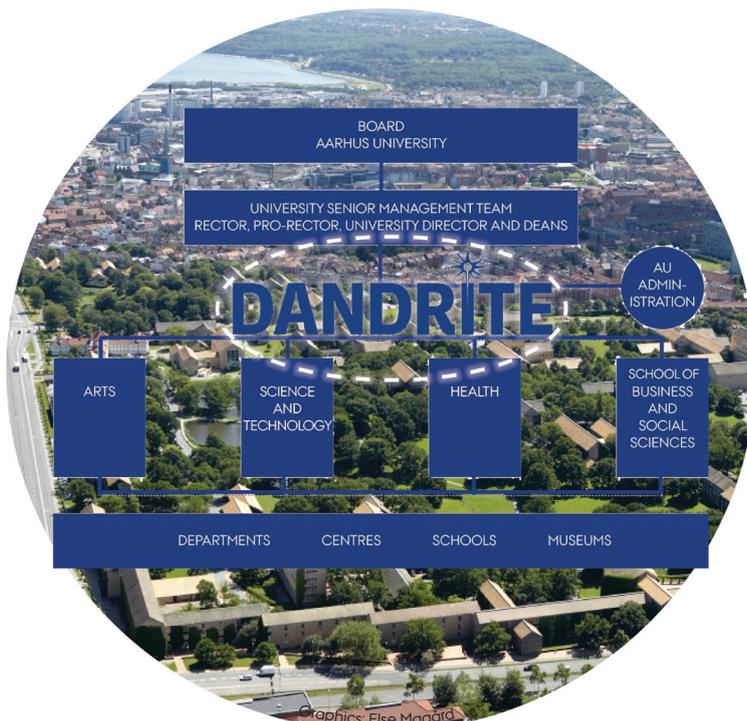
OTHER ORGANIZATIONAL BODIES IN PIPELINE

- Postdoc group, student group, technician group
- Seminar committee
- Social event committee

ADMINISTRATIVE ORGANIZATION

DANDRITE's core research is interdisciplinary and translational so the research activities and administrative organization is crossing traditional collaborative and organizational borders. The goal of the DANDRITE administration is to cater of all needs connected to DANDRITE core activities and facilitate administrative

procedures. AU central administration assist from the following offices: Research and Talent, Finance and Planning, Human Resources, Studies Administration, Communication, IT, and Knowledge Exchange. Furthermore, AU front office administration centers serve the four main academic areas, and DANDRITE is assisted by Health and Science & Technology.



SCIENTIFIC ADVISORY BOARD

The scientific advisory board (SAB) will convene annually and provide independent strategic advice on scientific goals and evaluation of achievements and allocations. The members of the SAB will be international researchers primarily from academia, but also from biotech

and the pharmaceutical industry. The objective of the SAB is to provide independent and strategic advice on future scientific goals and peer review and evaluate on the progress of research conducted by DANDRITE and the scientific aspects of the research. Individual evaluations will also be collected. First advisory board meeting will take place November 6, 2014. DANDRITE SAB members are:

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

PERSONNEL

A main goal of DANDRITE is to recruit five outstanding young group leaders in 2 or 3 campaigns following the EMBL model and finishing spring 2015.

First group leaders were recruited after interviews and contract negotiations concluding in September 2013.

Group Leader Mark Denham started his contract on December 1, 2013 and Group leader Anne von Philipsborn on January 1, 2014.

DANDRITE personnel 2013	Male	Female	Total	%
Professor	3	0	3	7
Senior Researchers	5	1	6	15
Postdoc	6	7	13	32
PhD	5	5	10	24
Other staff (technicians and administration)		9	9	22
Grand Total	18	22	41	100

Graphic: Else Magård

A comprehensive list of all employees and affiliated personnel at DANDRITE during 2013, organized by research group. The list also includes employees that left or joined DANDRITE in 2013.

Structural and Functional Studies of Membrane Transporters in Brain	Oleg Sitsel, PhD Student	Receptor Biology
Poul Nissen, Group leader, Professor	Peter Aasted Paulsen, PhD Student	Anders Nykjær, Group leader, Professor
Thomas Boesen, Associate Professor	Sigrid Thirup Larsen, PhD Student	Olav Andersen, Associate Professor
Anne-Marie Lund Winther, Postdoc	Cristine Juul Fællid Nielsen, Research Assistant	Simon Glerup, Associate Professor
Florian Hilbers, Postdoc	Anna Marie Nielsen, Laboratory Technician	Christian Vægter, Associate Professor
Jacob Lauwring Andersen, Postdoc	Lotte Thue Pedersen, Laboratory Technician	Karen Marie Pedersen, Postdoc
Joseph Lyons, Postdoc	Neurodegenerative disease	Mads Fuglsang Kjølby, Postdoc
Kaituo Wang, Postdoc	Poul Henning Jensen, Group leader, Professor	Niels Wellner, Postdoc
Mette Laursen, Postdoc	Christine Betzer, Postdoc	Ulrik Bølcho, Postdoc
Miriam-Rose Ash, Postdoc	Louise Berkhoudt Lassen, Postdoc	Mette Richner, PhD student
Dorota Focht, PhD Student	Jin Zheng, PhD Student	Ditte Olsen, PhD Student
Franciszek Fijalkowski, PhD Student	Michael Aagaard Andersen, PhD Student	Anja Aagaard Danneskjold Pedersen, Laboratory Technician
Jonas Lindholt Gregersen, PhD Student	Jette Bank Lauridsen, Laboratory Technician	Anne Kerstine Thomassen, Laboratory Technician
Lina Malinauskaite, PhD Student		Benedicte Vestergard, Laboratory Technician

Graphic: Else Magård

DANDRITE RESEARCH INFRASTRUCTURE

DANDRITE focuses on research addressing “structural, mechanistic, translational and medical aspects of transmembrane communication in health and disease of the nervous system”. The research will integrate molecular, cellular and physiological studies drawing on current expertise, including in vivo disease modeling, animal behavioral studies and imaging in animal models and patients, with novel technologies focusing on brain circuitry-penetrating and restorative methodologies. The insight gained from DANDRITE research addresses fundamental questions on the molecular mechanisms underlying brain responses to stimuli, how it defines behavior, and how these mechanisms go wrong in disease and may be modified by drugs. DANDRITE is associated with a range of local, national and international research infrastructures.

Aarhus University infrastructure

NeuroCampus Aarhus - NCA

NCA (neurocampus.au.dk) gathers leading expertise and technology in neuroscience. Currently NCA incorporates more than 30 independent research centres and laboratories comprising more than 250 scientists that collectively master a range of complementary disciplines relevant to molecular and translational neuroscience ranging from PET, laser Doppler techniques, and two-photon microscopy to X-ray crystallography. Among prime activities, NCA fosters interdisciplinary collaborations and knowledge exchange, stimulates internationalization, and strengthens infrastructure and technology platforms.

MEMBRANES

MEMBRANES (membranes.au.dk) is an interdisciplinary AU center in membrane protein research with focus on the action and interactions of membrane proteins, their role in the cell and their importance for understanding, diagnosing and treating human disease affecting all types of organs including CNS. The center encompasses 42 senior scientists with distinguished expertise within a broad subset of membrane receptors, pumps, exchangers/co-transporters, channels, enzymes and adhesion molecules. The laboratories harbor all relevant membrane protein research facilities.

Interdisciplinary Nanoscience Center - iNANO

The interdisciplinary Nanoscience Center (iNANO, inano.au.dk) is a collaboration between research groups at the Institute of Physics and Astronomy, Department of Chemistry, Department of Molecular Biology and Genetics, Department of Bioscience, Department of Biomedicine, and Department of Clinical Medicine as well as groups from the Faculty of Science, Aalborg University. iNANO provides state-of-the-art facilities and expertise in biophysical studies and characterization of biomolecules, including X-ray crystallography and small-angle scattering, X-ray microscopy, liquid and solid-state NMR, single-particle cryo-Electron Microscopy and tomography, Atomic Force Microscopy, High-field Magnetic Resonance Imaging, Mass Spectrometry and fluorescence microscopy in vivo.

National Infrastructures in Denmark

Danish Genetically Modified Animal Resource - DAGMAR

DAGMAR (dagmar.au.dk) was founded in 2000 and offers state-of-the art techniques for obligate and/or conditional genetic manipulation of four species of increasing complexity and clinical relevance: *C. elegans*,

zebrafish, mice, and minipigs. The center is primarily located at Aarhus University and provides advice and practical help from the design and cloning of vectors to the production of the animals and their subsequent phenotyping. DAGMAR is the only national source of transgenic zebrafish and minipigs, and the only facility providing transgenic mice nationwide. For instance, a minipig prone to develop Alzheimer type neural degeneration was recently developed using a new "handmade cloning" technology.

Initiative for Integrative Psychiatric Research - iPSYCH

iPSYCH is an interdisciplinary genetics research center with competences spanning from molecular and basic research to clinical science. Activities are dedicated to the identification of aetiologies and disease mechanisms that underlie severe mental disorders, providing a basis for specific biological disease classification, better diagnosis and improved patient treatment. Technologies employed include genomics/genetics, epigenetics, molecular biology, functional genomics using transgenic animal models, bioinformatics, epidemiology, clinical and preclinical research, and advanced imaging techniques such as MRI and two-photon microscopy. iPSYCH will capitalize on the newly established AU-based Sino-Danish "Platform for Large Scale Sequencing and Bioinformatics" and the close collaboration between AU and Beijing Genomics Institute. iPSYCH further collaborates with e.g. Statens Serum Institut (SSI) under the Danish Ministry of Health, deCode Genetics in Iceland, the Genetic Biobank of the Faroe Islands and the Broad Institute in US.

Danish Centre for the use of Synchrotron X-ray and Neutron facilities - DANSCATT

DANSCATT (danscatt.ku.dk) supports the access to international facilities for Danish laboratories performing research with X-ray and neutron scattering.

International infrastructures

ESFRI Projects (European Strategy Forum on Research Infrastructures)

The DANDRITE director Poul Nissen along with Prof. Niels Chr. Nielsen (now dean at AU Science and Technology) has prepared the affiliation of Denmark to INSTRUCT (Integrating Structural Biology, <http://www.structuralbiology.eu>). DANDRITE will also draw from infrastructures offered by EU-OPENSOURCE (<http://www.eu-openscreen.de/>), ELIXIR (<http://www.elixir-europe.org>) and EATRIS (<http://www.eatris.eu>). Key activities of DANDRITE will relate to the ESFRI single-site facilities XFEL (X-ray Free-Electron Laser, Hamburg), ESS (European Spallation Source, Lund), ESRF (European Synchrotron Radiation Facility, Grenoble) as well as to the EU-supported synchrotron facilities PETRA3 (Hamburg), Max-Lab and Max-IV (Lund), SLS (Villigen), and BESSY (Berlin).

NEW PURCHASES

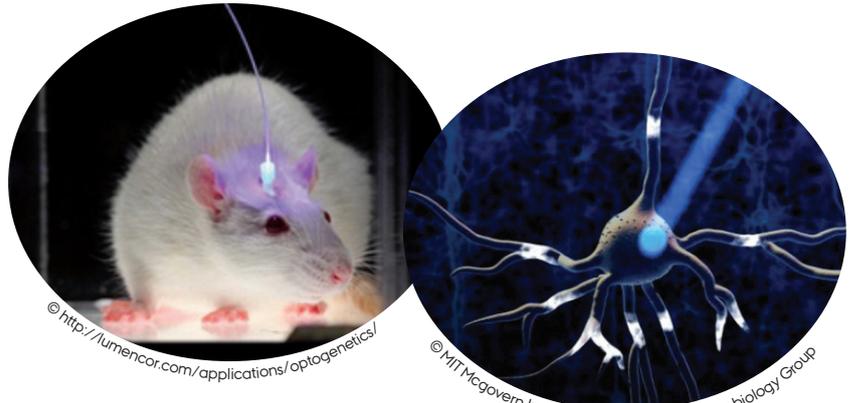
The center is very focused on developing and building up infrastructural capacities and expertise's in order to constantly be in front with newest frontier research areas and technique. Several techniques have our focus in 2013 and will have in the coming years too:

One of the very promising areas is the studies of interactions between pathological protein aggregates and membrane proteins in nanodiscs as well as small scale purifications. For further developing our expertise in this area we have made substantial investment in the form of a Microchromatography apparatus.

The semi-confocal analyses of cells and tissues is one of the methodologies that gets very much attention and from which promising research result emerges. Therefore we are building up capacities by e.g. the purchase of Apotome fluorescent microscope.

Optogenetics is the combination of genetic and optical methods to study synaptic activity in cells in the millisecond timescale. By introducing light-sensitive ion-channels into neurons of mice by genetic engineering it is possible to control and monitor neuronal connectivity and function in the living and freely moving animal. When light is switched on, the ion-channels may either be stimulated or inactivated and the physiological consequences monitored by electrophysiological recordings and by subjecting the animals to behavioral paradigms. This technique will be a major asset to DANDRITE as it will enable the characterization of receptors and transporters in the healthy brain and their role for development of psychiatric and neurological disorders.

Foremost, optogenetics will provide DANDRITE a unique method for validation of new drug targets substantiating the translational objective of DANDRITE.



CLARITY is a method to make the brain transparent allowing visualization of neurons and their circuitries in tissues

sections or the intact brain. Picturing of specific neuronal networks is enabled by labeling the neurons with fluorescence using genetically modified mice or antibodies followed by microscopical techniques. For this purpose an ApoTome.2 AX microscope equipped with an Axiocam 105 camera has been purchased. The technique allows us to rule out the function of specific genes, e.g. encoding disease related transmembrane proteins, in neuronal development, senescence, degenerative processes and neuropsychiatric disorders.

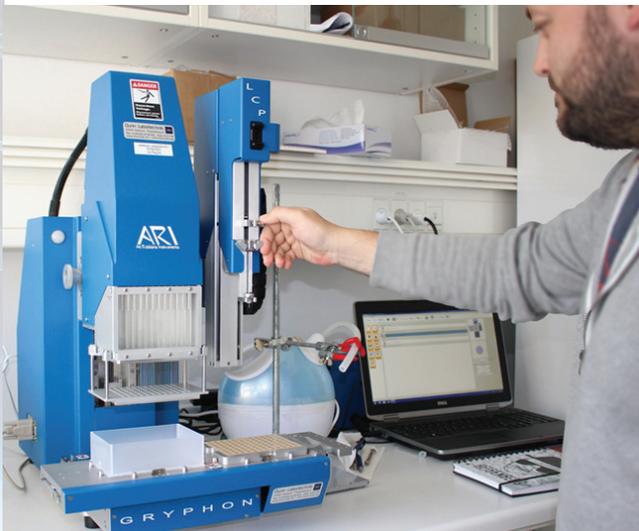


Photo: Karen Bech

Quantification of neurotransmitters is a prerequisite in neuroscience and we have co-invested in an HPLC

equipment connected to a highly sensitive and selective electrochemical detector.

Membrane proteins are of key importance in investigation of signaling and transport across membranes. Their crystal structures are preferably studied in membrane-like environments such as by lipidic cubic phase crystallization. DANDRITE has purchased state-of-the-art lipidic cubic phase robotics (Gryphon), which readily facilitated our analysis of novel crystal structures of neurotransmitter-sodium symporter proteins.

