CTNR
Centre for Transdisciplinary Neurosciences Rostock

CTNR Activity Report 2019|2020

From the Model to the Patient to the Community

Contents

Foreword

From the Model to the Patient to the Community

True to the motto “Translational Research: From Cell Model to Patient” another two thriving years of CNTR have passed and the neuroscientists at University Medical Centre Rostock have moved closer together. This can be seen in intensive networking of the members among each other through joint publications and through a common application culture, for example Else-Kröner programs or in the application marathon around the research building "NeuroPart".

After a successful evaluation in 2020 and the additional funding period for another four years we have the possibility to create ideas for new projects. In this sense, it is planned to establish a master’s course in "Translational Neuroscience", to implement a common Neuroscience Campus between Lund and Rostock as well as to apply for a DFG Research Training Group. In addition to this promotion of young talents, beside the Clinician Scientist program, a Medical Scientist program has also been launched to strengthen motivated researcher in the CTNR. We have also succeeded in creating a Lecture of Excellence in order to gather outstanding researchers in the field of neuroscience to Rostock.

These are just a few highlights of the last two years. For a deeper look into the activities of the CNTR we would like to invite you to enjoy this brochure.

CTNR Board

About

Our vision

The research levels of the CTNR range from the identification of neuroprotective and neuroregenerative factors at the molecular and cell biological level to the investigation of cognitive and physical resources at the patient level to socio-medical aspects at the population level. Our vision is to use the understanding of resilience factors to open up new perspectives for the development of diagnostic and prognostic markers and ultimately to develop instruments for disease-modifying therapeutic interventions in primary and secondary neurodegeneration. The focus thus offers an integrative platform for the entire range of clinical-neuroscientific research with strongly interdisciplinary convergent approaches of basic-oriented, disease-oriented and patient-oriented research (see Fig. 1).

Figure 1: Subject and goals of the CTNR.

For our longterm stragegy, specific research goals are the development of biological, technical and psychosocial markers of resilience and therapy response in neurodegeneration as well as the development and evaluation of biological and psychosocial intervention strategies to strengthen resilience in neurodegeneration. Overall, the focus pursues a translative approach, with overarching research designs in basic and clinical research for the development of new therapy/prevention approaches, which in turn are validated and evaluated from animal models to human studies (see Fig. 2).

Our aims

In 2020, 1.6 million people with dementia and 420,000 people with Parkinson's disease lived in Germany. The estimated costs of dementia in 2016 in Germany amounted to 34 billion euros[1]. Neurodegenerative brain diseases are the third most common cause of mortality and morbidity in old age and one of the most important health economic challenges for Germany.

- ✓ The overall scientific aim of the Centre for Transdisciplinary Neurosciences Rostock (CTNR) is to identify and target resilience mechanisms in neurodegeneration to implement innovative therapeutic concepts for primary and secondary neurodegenerative processes.
- ✓ The location-specific peculiarity of the CTNR is the integration of biomedical and engineering-scientific expertise for the translation from the model to the clinic and home research approach.

The detailed knowledge of these resilience factors provides new perspectives for disease-modifying therapeutic interventions in primary and secondary neurodegeneration. The CTNR is organized into three tightly connected topics to lead to a qualitative leap in three dimensions:

- ✓ Strong focus on mechanisms of resilience und their interplay with neurodegenerative processes to overcome the current standstill in the development of causative treatments for major neurodegenerative diseases.
- ✓ Adoption of the concept of precision medicine to neurodegenerative disease care to establish predictors for cerebral resilience in primary and secondary neurodegeneration in humans.
- ✓ Adoption of continuous bi-directional translation pathways where patient centeredness and patient-relevance and sustainability for the care system are the guiding principles for the development of new treatments and preventions for neurodegenerative insults.

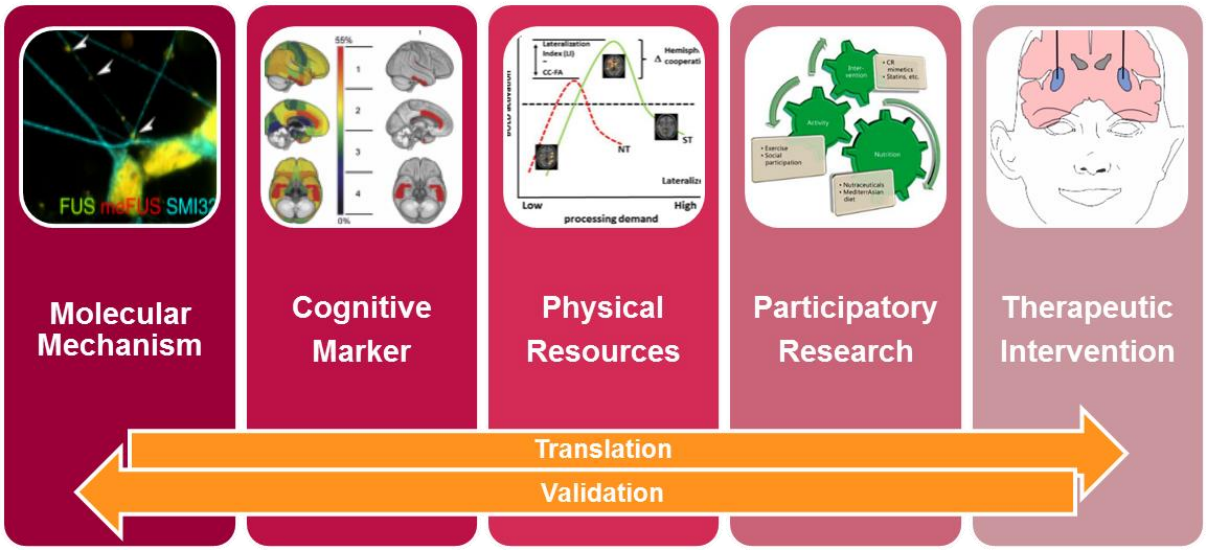

Figure 2: Translational pathway of the neuroscience research at the CTNR.

[1] According to the Federal Health Gazette 2019.

Our organisation

The Centre for Transdisciplinary Neurosciences Rostock (CTNR) was founded to bundle the scientific activities of neurosciences, to improve the visibility and outcomes and to represent one of the three main scientific areas (Forschungsschwerpunkte) of the University Medical Centre Rostock (UMR).

At the end of 2020, 27 institutions of the University of Rostock, University Medical Centre Rostock and associated institutes were part of the CTNR (see Fig. 3).

Figure 3: The CTNR and its affiliated institutes.

Since 2017, the scientific area has been strengthened through investments by the faculty (UMR) through strategic appointments in neurology, Schilling professorship in neurodegeneration, psychosomatics, anatomy, child and adolescent psychiatry, laboratory medicine and forensic psychiatry as well as through the establishment of the core facility "Multimodal Small Animal Imaging". The CTNR received a start-up funding in 2017[2] and additional funding for the 1st (2018-2020) and 2nd (2021 – 2025) funding period.

The CTNR is a scientific unit of the University Medical Centre Rostock and is supervised by the CTNR Board. It has its own bylaws and organisational structure under the head of the regulations of the UMR. The decision body is composed of three entities: the Member Assembly, the CTNR Board and the Speaker/Co-speaker. Members of the CTNR Board are elected every 3 years by the CTNR Member Assembly and include the CTNR Speaker, Co-Speaker and three elected research area leaders.

CTNR Board members 2017 – 2019 were:

- ✓ Alexander Storch (Speaker), Department of Neurology, UMR
- ✓ Rüdiger Köhling (Co-Speaker), Oscar-Langendorff-Institute of Physiology, UMR
- ✓ Stefan Teipel, German Center for Neurodegenerative Diseases (DZNE), Department of Psychosomatic and Psychotherapeutic Medicine, UMR
- ✓ Andreas Wree, Institute of Anatomy, UMR
- ✓ Uwe Zettl, Department of Neurology, Section Neuroimmunology, UMR

According the CTNR bylaws, the term of office of the CTNR board members mentioned above ended on November 22, 2020.

[2] For the results of the implementation phase of the CTNR see also the Activity Report 2017-2018: https://ctnr.med.uni-rostock.de/activity-report-2017-2018

At the 4th members meeting on October 30, 2020, the CTNR members elected the following board members for the next period (2020 – 2023):

- ✓ Alexander Storch (Speaker), Department of Neurology, UMR
- ✓ Rüdiger Köhling (Co-Speaker), Oscar-Langendorff-Institute of Physiology, UMR
- ✓ Markus Kipp, Institute of Anatomy, UMR
- ✓ Angela Kuhla, Rudolf-Zenker-Institute for Experimental Surgery, UMR
- ✓ Stefan Teipel, German Center for Neurodegenerative Diseases (DZNE), Department of Psychosomatic and Psychotherapeutic Medicine, UMR

The term of office of the new Board members began on November 23, 2020 and will end after three years. In 2019/2020, seven meetings of the CTNR Board for strategic discussions and decisions and two general members meetings were held. The CTNR office represented by the scientific coordinator Virginia Bolowski and the scientific assistant Jacqueline Hofrichter is responsible for the administration and organisation of the CTNR.

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Our members

Anyone who belongs to the University Medical Centre Rostock (UMR), the University of Rostock (UR) or to an external research institution in Rostock (e.g. DZNE) can become a member of the CTNR.

In addition, the member must be qualified to do independent scientific work (usually after completion of the doctorate, leading a working group with publication and third party funding activities) in the field. Prerequisite for the membership is the proven expertise in neuroscience research.

Since the foundation of the CTNR in November 2017, the number of members has risen to 47 by the end of 2020 (see Fig. 4).

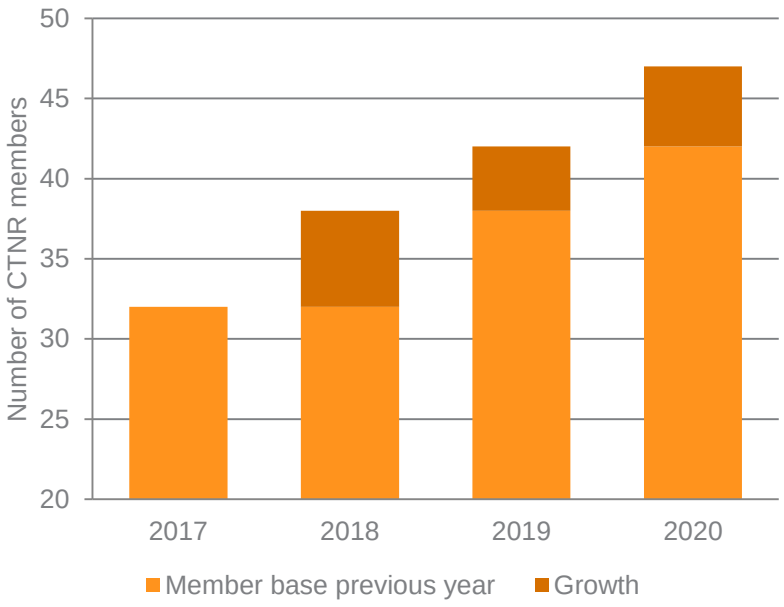

Figure 4: Annual membership growth (admitted minus resigned members).

The sum of citations per member in Figure 5 was calculated from the entire publication record of all CTNR members for the years 2017-2020 in relation to the total number of members in the respective year. The increase in citations per member demonstrates a growing visibility of the CTNR members in their scientific community during the last years.

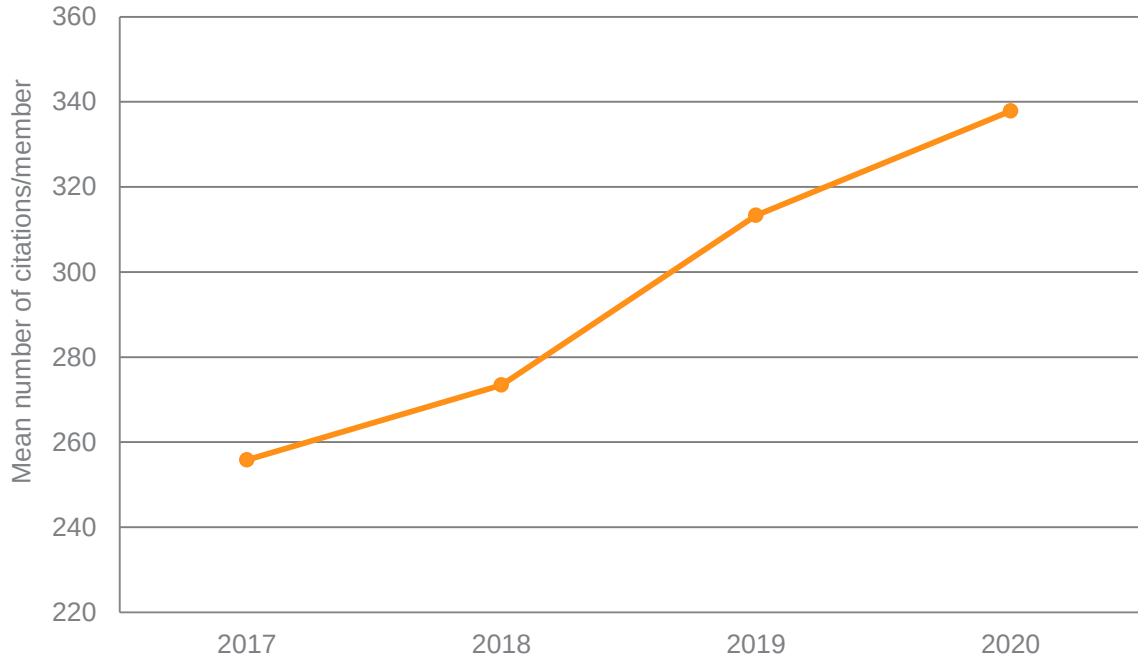

Figure 5: Citations per CTNR member 2017-2020. Source: Scopus, without self-citations.

Table 1 shows the CTNR members and alumni in 2020, their institutions and main research topics.

Table 1: CTNR members and Alumni in 2020.

Member	Institute	Research Topic
Altiner, Attila	Institute of General Practice	Rational pharmacotherapy, respiratory infections and antibiotics
Baltrusch, Simone	Institute of Medical Biochemistry and Molecular Biology	Peripheral diabetic neuropathy
Berger, Christoph	Department of Psychiatry, Neurology, Psychosomatics, and Psychotherapy in Childhood and Adolescence	EEG and fMRI in psychiatry
Bertsche, Astrid	Department of Neuropaediatrics	Drug therapy safety in epileptology
Brandenburg, Lars-Ove	Institute of Anatomy	Innate Immunity in the CNS
Buchmann, Johannes	Department of Psychiatry, Neurology, Psychosomatics, and Psychotherapy in Childhood and Adolescence	Motor development, pain
Büttner, Andreas	Institute of Legal Medicine	(Forensic) Neuropathology
Frech, Moritz	Translational Neurodegeneration Section "Albrecht Kossel"	IPSC based disease models
Freiman, Thomas	Department of Neurosurgery	Pathology of Temproal Lobe Epilepsy
Fuellen, Georg	Institute for Biostatistics and Informatics in Medicine and Ageing Research	Health, disease, ageing and senescence

Geßler, Florian	Department of Neurosurgery	Novel therapeutic approaches for glioma
Hermann, Andreas	Translational Neurodegeneration Section "Albrecht Kossel"	Translational Neurodegeneration
Holzmann, Carsten	Institute of Medical Genetics	Neurodegenerative diseases
Junghanß, Christian	Department of Internal Medicine, Medical Clinic III	Palliative Care Research and Oncology
Jürgens, Tim	Department of Neurology	Pathophysiology & treatment of headaches
Kipp, Markus	Institute of Anatomy	De- and remyelination
Kirschstein, Timo	Oscar-Langendorff-Institute of Physiology	Novel antiepileptogenic treatments
Kirste, Thomas	Institute of Visual & Analytic, Computing Mobile Multimedia Information Systems	Computational Behavior Analysis
Köhling, Rüdiger	Oscar-Langendorff-Institute of Physiology	Models of chronic neurological diseases
Kölch, Michael	Department of Psychiatry, Neurology, Psychosomatics, and Psychotherapy in Childhood and Adolescence	Children at risk for psychiatric disorders
Krause, Bernd Joachim	Department of Nuclear Medicine	Molecular imaging of neurodegenerative diseases
Kropp, Peter	Institute of Medical Psychology and Medical Sociology	Non-medical treatment in migraine
Kuhla, Angela	Rudolf-Zenker-Institute for Experimental Surgery	Hallmarks of neurodegenerations
Kumbier, Ekkehardt	History of Medicine	History of Psychiatry and Neurology
Lange, Falko	Oscar-Langendorff-Institute of Physiology	Glioma-associated epilepsy and ageing
Langner, Sönke	Institute of Diagnostic and Interventional Radiology, Pediatric Radiology and Neuroradiology	New techniques in neuroradiology
Lehmann, Fritz-Olaf	Institute of Biological Sciences Department of Animal Physiology	Locomotor systems in insects
Lukas, Jan	Translational Neurodegeneration Section "Albrecht Kossel"	Novel drugs in rare hereditary diseases
Luo, Jiankai	Translational Neurodegeneration Section "Albrecht Kossel"	Neurodegeneration in NPC1 disease
Lüthje, Corinna	Faculty of Philosophy, Institute for Media Research	Participatory research, science and scholarly communication
Mlynski, Robert	Department of Otorhinolaryngology, Head and Neck Surgery, ”Otto Koerner“	Middle ear implants, stem cell biology, lateral skull base disease
Pützer, Brigitte M.	Institute of Experimental Gene Therapy and Cancer Research	Antineurogenic therapies in cancer
Reis, Olaf	Department of Psychiatry, Neurology, Psychosomatics, and Psychotherapy in Childhood and Adolescence	Developmental psychopathology
Schmitt, Oliver	Institute of Anatomy	Dynamics of neurodegenerative diseases
Spitzer, Carsten	Department of Psychosomatics and Psychotherapeutic Medicine	Traumatic stress and health

Storch, Alexander	Department of Neurology, German Center for Neurodegenerative Diseases	Novel treatments in Parkinson's
Teipel, Stefan	Department of Psychosomatic and Psychotherapeutic Medicine, German Center for Neurodegenerative Diseases	Dementia diagnosis and treatment
Thierfelder, Kolja M.	Institute of Diagnostic and Interventional Radiology, Pediatric Radiology and Neuroradiology	Functional cross sectional imaging
Tiedge, Markus	Institute of Medical Biochemistry and Molecular Biology	Mitochondria in type 2 diabetes
Völlm, Birgit	Forensic Psychiatry	Forensic psychiatry
Vollmar, Brigitte	Rudolf-Zenker-Institute for Experimental Surgery	Hallmarks of neurodegenerations
Walter, Uwe	Department of Neurology	Neurodiagnostics in parkinsonism and stroke
Weber, Marc-André	Institute of Diagnostic and Interventional Radiology, Pediatric Radiology and Neuroradiology	Multimodal dedicated imaging
Witt, Martin	Institute of Anatomy	Olfaction and neurodegeneration
Wolkenhauer, Olaf	Institute of Computer Science, Department of Systems Biology and Bioinformatics	Systems biology & bioinformatics
Wree, Andreas	Institute of Anatomy	Intrastriatal botulinum neurotoxin-A
Zettl, Uwe	Department of Neurology	Molecular research in multiple sclerosis

Alumni	**Former Institute**	**Research Topic**
Grothe, Michel	German Center for Neurodegenerative Diseases	Neuroimaging patterns of dementia
Kronenberg, Golo	Department of Psychiatry and Psychotherapy	Biological psychiatry
Spittau, Björn	Institute of Anatomy	Microglia functions

Interfaces to health care and teaching

The scientific objective of the CTNR is clearly translational. The interlocking collaboration between preclinical and clinical groups is an essential element of the research strategy, which ultimately extends from molecular principles to participatory research with the involvement of society. Patient-oriented research is already finding its special expression through the integration of groups from the German Center for Neurodegenerative Diseases (DZNE). The establishment of a master's course in "Translational Neurosciences" is an important element of the medium-term objective of integrating research and teaching as modules of research-based learning.

Evaluation

At the end of 2019, the report of the CTNR and its members' activities in 2017 and 2018 was published[3]. The report presents the development of the CTNR in the first two years after its founding and provides a snapshot of ongoing activities. It contains the research profiles of the members as well as the description of the education and transfer activities.

Figure 6: CTNR Activity Report 2017-2018.

In February 2020, the CTNR was evaluated by representatives of the head of the UMR and the external consultant Markus Thielbeer (Dr. Thielbeer Consulting). The conversation was about exchanging ideas about past and future developments of the scientific area of neurosciences. The CTNR speaker and co-speaker presented developments and measures of the implementation phase of the CTNR, planned future central goals and procedures and needs for adjustments and support.

In August 2020, the CTNR received the commitment for the continuation of funding for the second funding period (2021 – 2025).

At the end of 2020, the CTNR Board was also involved in the preparation of the strategy report in research and teaching 2030 and the upcoming evaluation of the UMR by an external review board in 2021.

CTNR strategy 2030

Long term structural goals and measures are the expansion of the transfer through the development of a culture of exploitation, the promotion and generation, recruitment, training and internationalisation of young researchers. This is currently done by integrating the CTNR into the UMR's Clinician Scientist program (Rostock Academy for Clinician Scientists), by implementing a master's degree in "Translational Neurosciences" planned for 2021 and by continuously developing the further education and qualification program. The implementation of a United Neuroscience Campus Lund – Rostock is planned for internationalisation. The main goals of the CTNR by 2030 are:

- ✓ Elaboration of the unique selling point "Translational Research: From Cell Model to Patient"
- ✓ Research building "NeuoPart" for the structural bundling of research
- ✓ DFG Research Training Group as the basis for collaborative research
- ✓ Establishment of a master's degree in "Translational Neurosciences" for recruitment
- ✓ Internationalisation through the implementation of a Campus Lund – Rostock

[3] https://ctnr.med.uni-rostock.de/activity-report-2017-2018

Joint activities

Innovative neuroscience projects in Rostock

In the field of research, the CTNR is nationally and internationally competitively positioned. Our goal is the continuation of offering excellent scientists and research groups an attractive framework for cutting-edge research. In addition, we plan to concentrate our resources to expand the link between research and clinical application and to further develop the collaborations at the location Rostock. Below are joint projects (starting in 2019/2020) with CNTR members involved.

Senescence-Associated Systems diagnostics Kit for cancer and stroke

With aging comes cellular senescence, and (multi-)morbidity. Cellular senescence is a key driver of an interconnected disease network including cancer and stroke. We wish to utilize systems modelling and bioinformatics, learning from omics and other lab data, to design and develop a biomarker and software kit with a focus on measuring and interpreting senescence related signatures for precise (and early) diagnosis, prognosis, and, ultimately, therapy, of pancreatic cancer and ischemic stroke/thromboembolism. We build upon publications describing how cellular senescence and the senescence-associated secretory phenotype are directly involved in the comorbidity of pancreatic cancer, ischemic stroke, and more generally, of cancer and coagulation problems. We propose observational human studies for pancreatic cancer and ischemic stroke, measuring senescence markers in particular, preparing the power analyses and the companion diagnostics for larger interventional trials. For pancreas, we propose co-culture studies of cancerous and stellate cells, and a mouse cancer allograft model. For stroke, we study brain slices and stroke recovery in mice. High-throughput gene expression and protein array data are taken from blood and tissue of mice, and from blood of human, to allow the bioinformatics to extrapolate protein expression and pathway activation for the inaccessible tissue of humans, providing optimized input to machine learning of the best sets of biomarkers.

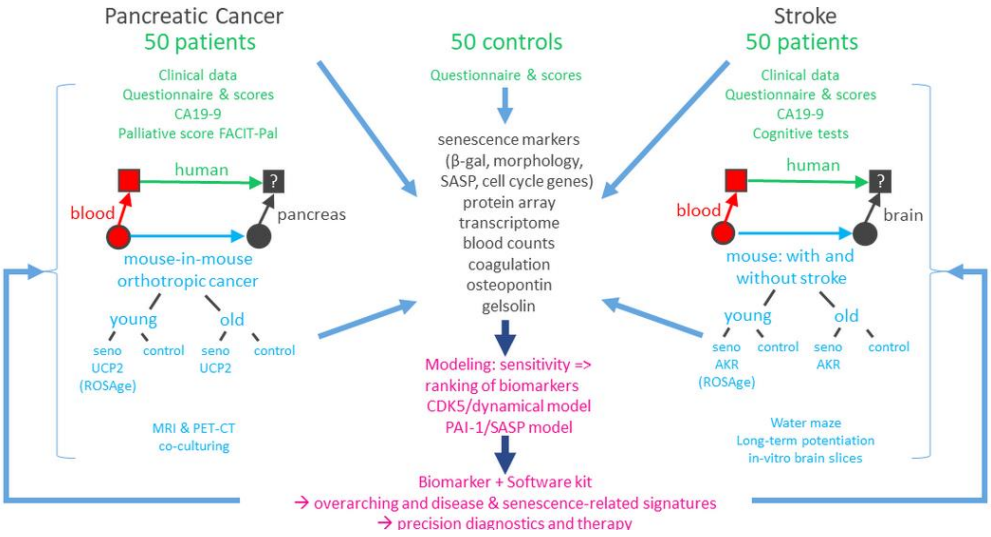

Figure 7: Project overview SASKit.

Funding period: 2019 – 2022

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CTNR members: Georg Fuellen (Principal Investigator), Olaf Wolkenhauer (TP 2), Christian Junghanß (TP 4), Uwe Walter (TP 5), Rüdiger Köhling (TP 6)

www.sys-med.de/en/alliances/saskit/

Provenance Research on the Non-European Anthropological Collection of the University Medical Centre Rostock

Picture 1: Plaster cast of a skull presented by Ekkehardt Kumbier, Markus Kipp and Anna-Maria Begerock (left to right).

The Department of the History of Medicine and the Institute of Anatomy at the Rostock University Medical Centre are investigating the collection of non-European human skulls that are currently housed in the Institute of Anatomy. Around 150 years ago, the physician Friedrich Merkel (1845-1919) brought these to the Institute of Anatomy "Race-skull collection" in order to expand his teaching areas, to include anthropology.

In the preparatory phase of the project, the skulls had been photographically documented and recorded in a catalogue. The first phase of the project was now devoted to research in archives in search of a more precise founding date of the collection as well as to rediscover information on those persons and contacts that once directly brought or arranged for the skulls to be brought to Rostock. This is particularly important in order to be able to later evaluate the circumstances and practices of acquisition with regard to the presumed contexts of injustice. Another project goal is the creation of guidelines for handling human remains in university collections (from colonial contexts).

Deutsches Zentrum Kulturgutverluste

Funding period: 2020 – 2021

CTNR members: Ekkehardt Kumbier, Markus Kipp

https://geschmed.med.uni-rostock.de/forschung/projekte/provenienzforschung-in-der-aussereuropaeischen-anthropologischen-sammlung-der-universitaetsmedizin-rostock

DigiCare: Digital Training of Nursing and Health Management

The goal of the overall project is the digitalisation of teaching in the field of nursing and health management. To achieve that, existing lectures will be recorded and organised in a semantic structure, so that at the end of the project, the lecture materials will interactively support both on-site lectures and distance learning. Furthermore, case-based dialogue system will be provided that will help the students to learn how to practically cope with different nursing cases.

DigiCare

Europäische Fonds EFRE, ESF und ELER in Mecklenburg-Vorpommern 2014-2020

Funding period: 2019 – 2022

CTNR members: Thomas Kirste, Stefan Teipel

https://pidi.informatik.uni-rostock.de/forschung/projekte/digicare/

CARE-FAM-NET - Children affected by rare disease and their families – network

The group CARE-FAM-NET aims at facing the mental sympto ms, comorbidities and their chronification of children and adolescents at the age of 0 to 21 years who are affected by RD, their siblings and parents with the help of diagnostics, early detection and early treatment. The main aims are the implementation and evaluation as well as the transfer of two new evidence-based psychosocial types of care (CARE-FAM and WEP-CARE) for children with RD and their families at 17 clinical centers in 13 federal states. That is why CARE-FAM-NET is connecting children's hospitals with centers for psychosocial care and centers for rare diseases at those 17 clinical locations.

CTNR members: Astrid Bertsche, Peter Kropp

https://www.carefamnet.org/en/

Gemeinsamer Bundesausschuss Innovationsausschuss

e:Med Systems Medicine – MelAutim – Systems medicine of melanoma and autoimmunity in the context of immunotherapy

Immune-checkpoint inhibitors have shown clinical activity in advanced melanoma, with significant survival benefit and response rates for anti-CTLA-4 (19%), anti-PD-1 (36-44%) and combined therapy (58-61%). While responses can be durable, a significant proportion of patients show autoimmune side effects, including autoimmune colitis, hepatitis and musculoskeletal side effects. In about one third of cases patients exhibit side effects in more than one organ system. In a fraction of the patients autoimmunity is present prior the therapy and may exacerbate. To be able to predict the risk of appearance of these severe autoimmune side effects would enable physicians to personalize the anticancer treatment to the patient and understanding mechanisms of these autoimmune reactions could improve therapy.

The aim of the project is to improve our understanding of the molecular and cellular mechanisms underlying the interplay between autoimmunity and cancer, with an interest on the role of predisposing factors in the appearance or exacerbation of autoimmunity under immunotherapy. The project uses melanoma, inflammatory bowel and rheumatoid diseases as models. Under the systems medicine paradigm, we will generate in vivo/patient data-based molecular networks and multi-level models accounting for the mechanisms behind the immune activation involved in the autoimmunity-cancer-immunotherapy axis. Combining data and network analysis, computer simulations and model experimentation, wewill generate molecular and phenotypic signatures accounting for the emergence or enhancement of autoimmunity under checkpoint inhibitor therapy, and will correlate these signatures with published and de novo patient data. We expect the project to pave the way towards the translation into clinical practice of systems medicine-based methods for monitoring autoimmunity in melanoma patients receiving immunotherapy and establish a basis for rationale treatment approaches for autoimmunity in cancer patients.

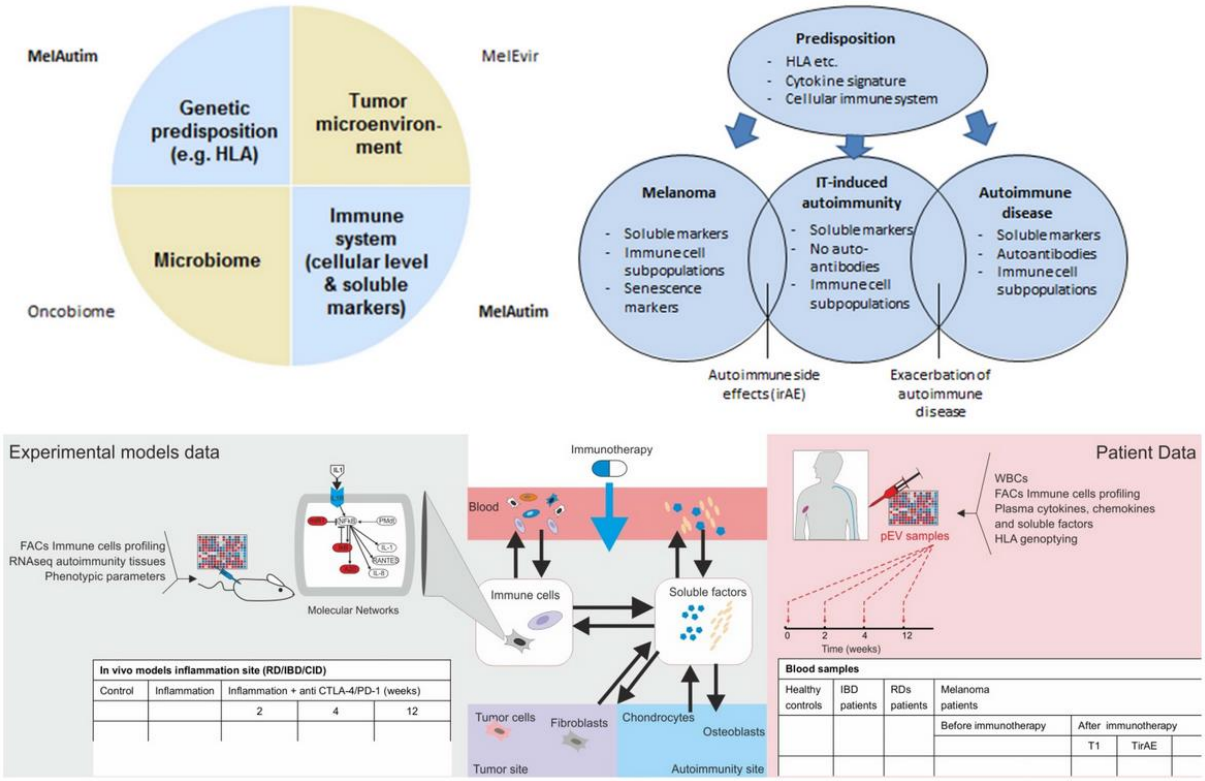

Figure 8: Top: factors influencing response and autoimmunity of cancer patients. Bottom: concept of data integration in the project. Source: e:Med Systems Medicine

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Funding period: 2019 - 2022

CTNR members: Brigitte M. Pützer (SP1), Olaf Wolkenhauer (SP4)

https://www.sys-med.de/en/alliances/melautim/

Networking and interdisciplinarity

In recent years, the scientific area of neurosciences has become an integral part and an important driving force of the neuroscientific community in Rostock. The CTNR bundles strengths and forces in the fields of medical, clinical and experimental neurosciences as well as bioinformatics and bioengineering in order to find innovative strategies and solutions for patients with neurodegenerative diseases. The focus was strengthened through several strategic appointments (neurology, Schilling professorship, psychosomatics, anatomy, child and adolescent psychiatry, laboratory medicine, forensic psychiatry) and investments by the UMR (e.g. the establishment of the core facility “Multimodal Small Animal Imaging”). More than ten joint proposals for project and infrastructure funding have been submitted to various third-party funding bodies since 2017. The network around the CTNR has steadily expanded through many different cooperation activities (see Fig. 9).

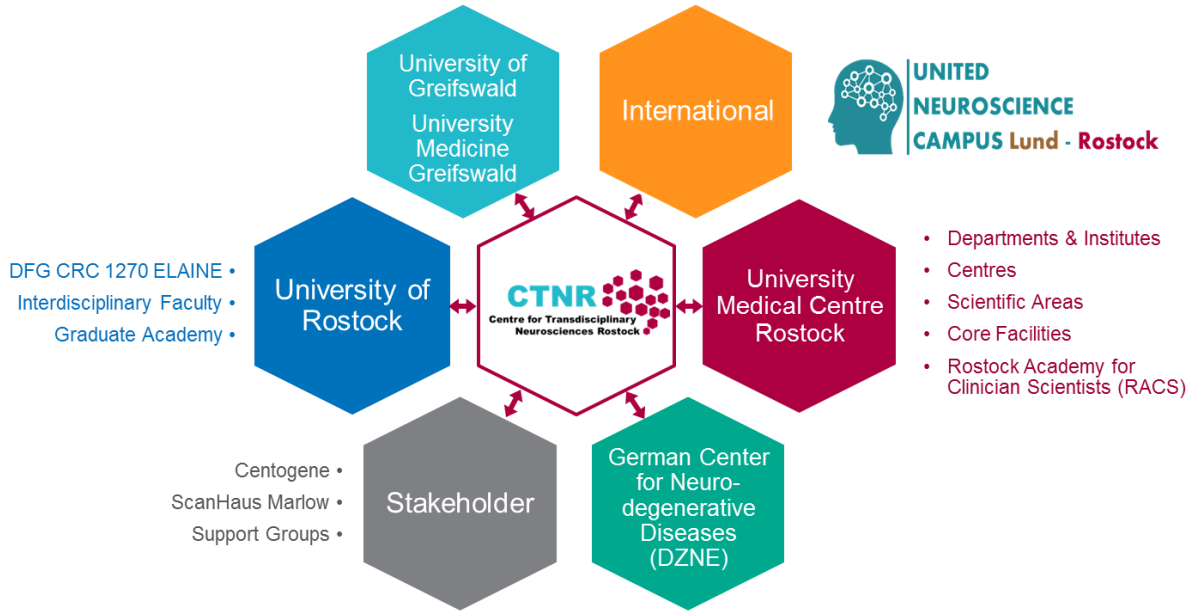


Figure 9: Network of the CTNR in 2020.

The CTNR with its members is particularly strong locally linked through research cooperation and activities with the German Center for Neurodegenerative Diseases (DZNE) - also with the Greifswald location - and the two departments of the interdisciplinary faculty of the University of Rostock ("Aging of the Individual and Society") and "Life, Light & Matter") networked.

In 2019, particular successes were the funding of a Schilling professorship and the associated establishment of the section for translational neurodegeneration "Albrecht Kossel" at the Department of Neurology as well as the BMBF funded project "Senescence-associated systems diagnostics kit for cancer and stroke (SASKit)" (see page 9) as a research network in systems medicine and the involvement of five CTNR members.

CTNR members are leaders of sub-projects at the DFG CRC 1270 ELAINE – “Electrically Active Implants” in the field of deep brain stimulation and of the integrated research training group (IRTG). Scientists from the fields of electrical engineering, computer science, mechanical engineering, material science, physics, biology, and medicine work together in an interdisciplinary manner.

www.elaine.uni-rostock.de

New international cooperation

Inspired by the worldwide unique idea of a transboundary TransCampus London-Dresden[4], the CTNR and MultiPark (Multidisciplinary research focused on Parkinson´s disease)[5] at the University of Lund (Sweden) are implementing a similar concept for neurosciences - a United Neuroscience Campus (UNC) Lund - Rostock.

The idea is the formal/institutional networking of two internationally excellent neuroscientific locations with a large translational focus in order to establish a virtual campus beyond the Lund and Rostock locations on key neuroscience topics. Through formal international cooperation beyond borders and standards, bilateral mobility and teaching programs for young scientists are to be established, innovative collaborative projects initiated and novel synergy effects used to increase scientific excellence in the long term.

The overarching strategic goals of the United Neuroscience Campus Lund - Rostock initiative are the promotion of young researchers, internationalisation, increasing the visibility of the community, and stimulating international collaborative research projects and publications, e.g. within the framework of the European Commission's "Horizon Europe - the next research and innovation framework programme", which starts in 2021.

Training Group: Basis for future education

In 2019, the CTNR received an intramural funding (Förderung der Vorbereitung von Anträgen der Verbundforschung) of the UMR to prepare an application for a DFG Research Training Group with the topic “Functional targets for strengthening resilience in neurodegeneration: regulation of excitability, protein clearance and sleep” (EXCITE).

Since the end of 2019, Luisa Müller summarised the current literature in a narrative review and in cooperation with the CTNR institutes Oscar Langendorff Institute of Physiology, Rudolf-Zenker-Institute for Experimental Surgery, and the Department of Psychosomatic and Psychotherapeutic Medicine. This work served creating a model for unravelling the multifactorial interactions of hyperexcitability in AD. She conducted several experiments on wildtype BL6J and transgenic APPswe/PS1dE9 mice, presenting with a phenotype of cerebral amyloidosis, to unravel the complex relationship between sleep-wake-rhythms and brain clearance. She established the method of intrahippocampal stereotactic injections in the cooperating working group of Angela Kuhla. This method will be used in future work on contrast agent based imaging to assess protein clearance from the brain. To investigate the influence of sleep-wake-rhythms on brain clearance a fluorescent dye was injected into the hippocampi of mice (wildtype and transgenic) at different times of the day (begin or end of the sleep period of the mice). At defined time points after injection brains were explanted and tissue dispersion of the dye was assessed histologically.

In 2020, the members of the EXCITE preparation group and first common topics for the doctoral training programme were defined. It is planned to present these results on the Alzheimer’s Association International Conference® 2021 and to publish them in a peer-reviewed journal. Due to the time delay caused by the corona pandemic in 2020, the described experiments and the histologic analysis are still going. Results will help to refine future experimental approaches, providing the methodological basis and documenting the close collaboration between CTNR institutes by linking preclinical and clinical groups.

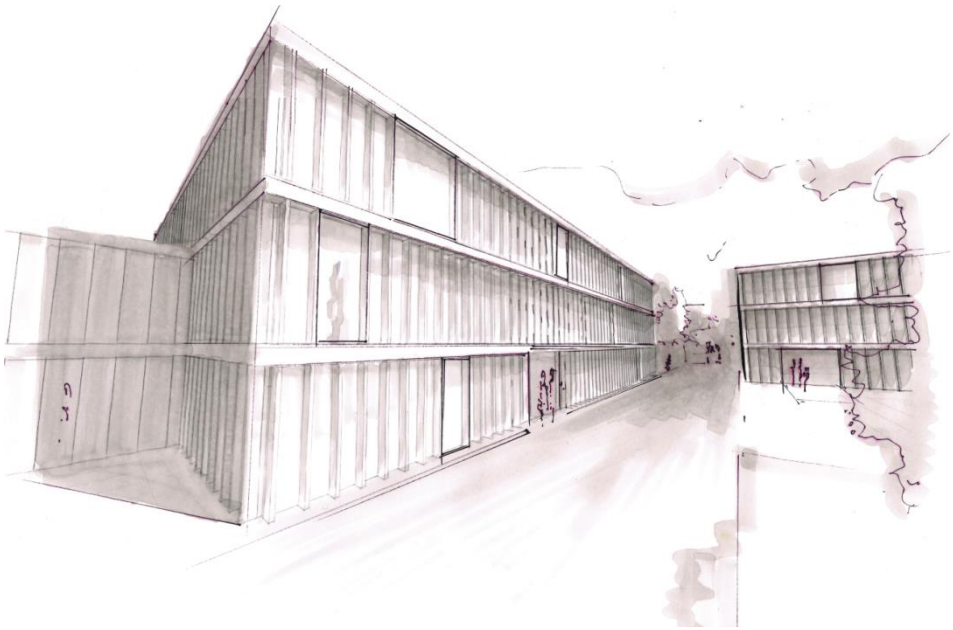
[4] See TransCampus TU Dresden–King’s College London: https://transcampus.eu/
[5] MultiPark: https://www.multipark.lu.se/

A lighthouse for participatory research

In 2019 and 2020, 12 CTNR members were part of a process for a concept of a research building application according to Art. 91b(1) GG at the German Council of Science and Humanities. 42 meetings for jour fixes, strategic discussions and project presentations took place under the head of a core group. Scientists, administrators, coordinators, consultants, companies (e.g. Centogene, ScanHaus Marlow), patients and politicians were involved in the process to design a research building for the scientific area “Neurosciences” of the UMR in Rostock: the “Centre for Participatory Neurosciences (NeuroPart)”.

Research in neurodegenerative diseases requires a consequent involvement of patients and stakeholders to integrate the needs and values of those concerned by the research into the research process. Therefore, the CTNR and the German Center for Neurodegenerative Diseases (DZNE) Rostock/Greifswald aim to develop participatory neurosciences as an integrative research program for neurodegenerative diseases. Participation brings together researchers with patients and other stakeholders to implement and achieve coproduction of knowledge on neurodegenerative diseases that balances scientific knowledge with patient and care-giver needs and public perspective. The new CTNR research building will allow development and implementation of participatory research methodology for the vulnerable group of older people with cognitive and physical impairments. At the same time NeuroPart will allow the integration of the public perspective in all stages of the translational research process. NeuroPart has the potential to become a lighthouse of participatory research with national and international visibility.

In November 2019, the proposal was rejected by the Science Council, but the Federal Ministry of Mecklenburg-Vorpommern announced interest and support for the realisation of NeuroPart. Therefore, in 2020 the main focus of the NeuroPart core group was to develop and present a new room concept in agreement with the Federal Ministry. Due to the corona pandemic, further joint steps with the Ministry were postponed to 2021.



Picture 2: Building sketch of the research building NeuroPart. It will allow the UMR and DZNE to create an internationally leading institution for the development, implementation and dissemination of methods of participatory research on resilience in neurodegenerative diseases.

Clinical research platform for neurosciences

In 2019, the CTNR started the initiation of a clinical research platform for neurosciences in Rostock. The platform contains the project management in the administrative planning and organisation of commercial and science-oriented clinical studies, taking into account the regulatory and site-specific academic constraints of the neuroscience research area. The definition and further development of the processes at the interfaces between scientists, the Coordination Centre for Clinical Studies (KKS) and the administration of the University Medical Centre Rostock will be important. A scientific manager was employed for six months to identify the essential requirements for an implementation of such a platform at the CTNR. It turned out that the most important thing is the development of the platform along a case study to identify the necessary structures. Thus since 2020, a project proposal for the Clinical Trials Programme at the German Research Foundation is in preparation by the Department of Psychosomatic Medicine and Psychotherapy in Rostock and in cooperation with the Coordination Centre for Clinical Studies Dresden.

Application initiatives

In addition to the joint interdisciplinary applications of the CTNR for the research building NeuroPart and the DFG GRK EXCITE, CTNR member's submitted further joint applications under the umbrella of the CTNR in 2019/2020 (see Tab. 2).

Table 2: Collaborative research applications (with applicants from more than one CTNR institute) prepared and submitted under the supervision of the CTNR.

Funding body	Funding initiative	Project title	Principal investigators
Else-Kröner-Fresenius Foundation	Else Kröner research college for young physicians	Neuroscience Research College for Clinician Scientists (NeuFoCS)	Andreas Hermann Rüdiger Köhling Angela Kuhla Alexander Storch Stefan Teipel
Else-Kröner-Fresenius Foundation	Else Kröner research training group	Structured Academic Research Training (START)	Hugo Murua Escobar Markus Kipp Angela Kuhla
Federal Ministry of Education and Research (BMBF)	Deep Learning in Biomedicine	Predicting delirium in elective hospitalization from heterogeneous hospital routine data (PREDEL)	Stefan Teipel Marc-André Weber Olaf Wolkenhauer
Federal Ministry of Education and Research (BMBF)	Concept development for a German Centre for Mental Health	Community Mental Health: Individualized prediction, prevention and treatment in rural areas	Michael Kölch Carsten Spitzer Birgit Völlm

In December 2020, the CTNR members Rüdiger Köhling (Experimental Models for the Understanding of Nervous System Diseases) and Olaf Wolkenhauer (Bioinformatics and Theoretical Biology) were elected by the German science community as DFG review board members for the next period 2020 – 2023.

The CTNR office regularly advises and supports CTNR members at the application of individual third-party funding projects (e.g. DFG research grants). The CTNR grant writing support includes the organisation of kick-off meetings for interdisciplinary applications, as well as individual consultation for formal reviews of the proposals and the calculation of project costs. In 2019 and 2020, 13 individual proposals have been supported by the CTNR coordination office (see Fig. 10). Please refer to Figure 17 for the total number of approved projects of all CTNR members.

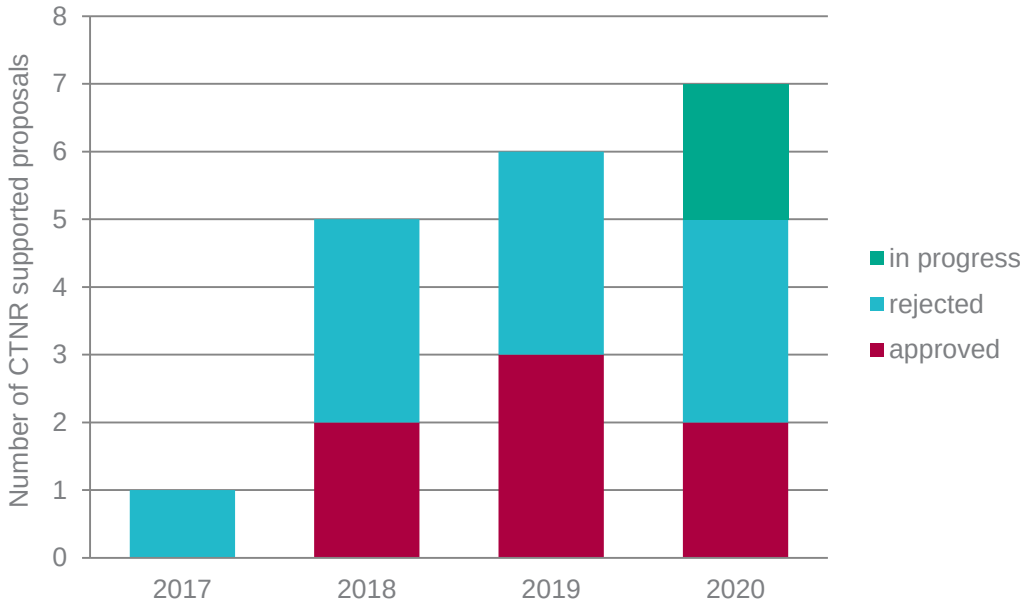


Figure 10: Number of individual proposals supported by the CTNR office.

Joint publications

Inter- and transdisciplinary publications are important to increase visibility, to define the unique selling point and to aim for excellence in the field of neurosciences. Thus, they are a main indicator for the evaluation and the success of the CTNR. Figure 11 shows the number of joint publications between CTNR members of more than one institution.

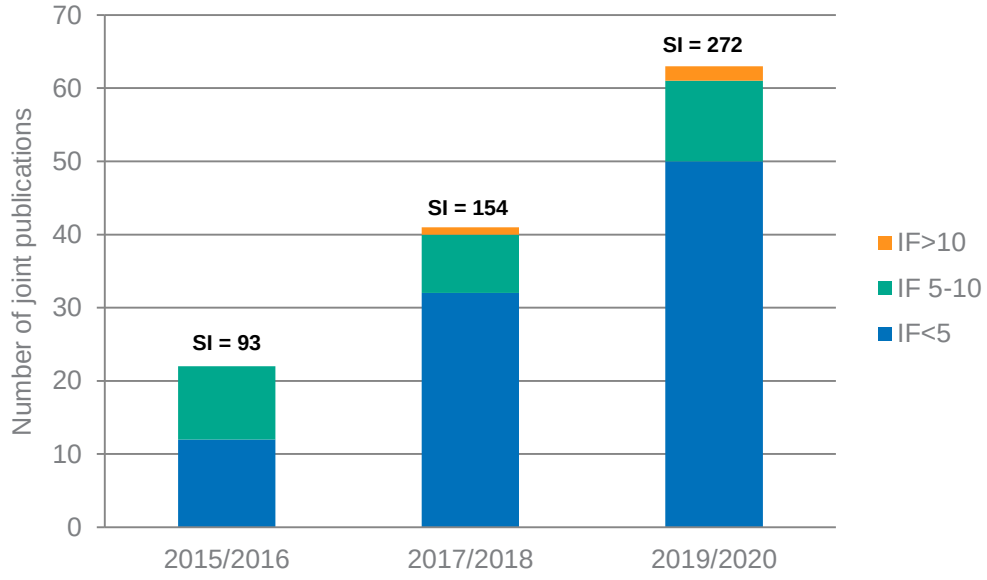


Figure 11: Number of joint publications between CTNR members (from different institutions) and the sum of the journal impact factors (SI) 2015/2015 (prior to CTNR foundation), 2017/2018 and 2019/2020.

The following illustrations (Fig. 12) show the increase in networking between CTNR members by joint publications. In comparison to 2017/2018, in 2019/2020 an increase in publications among members of three (green lines) different institutions can be observed.

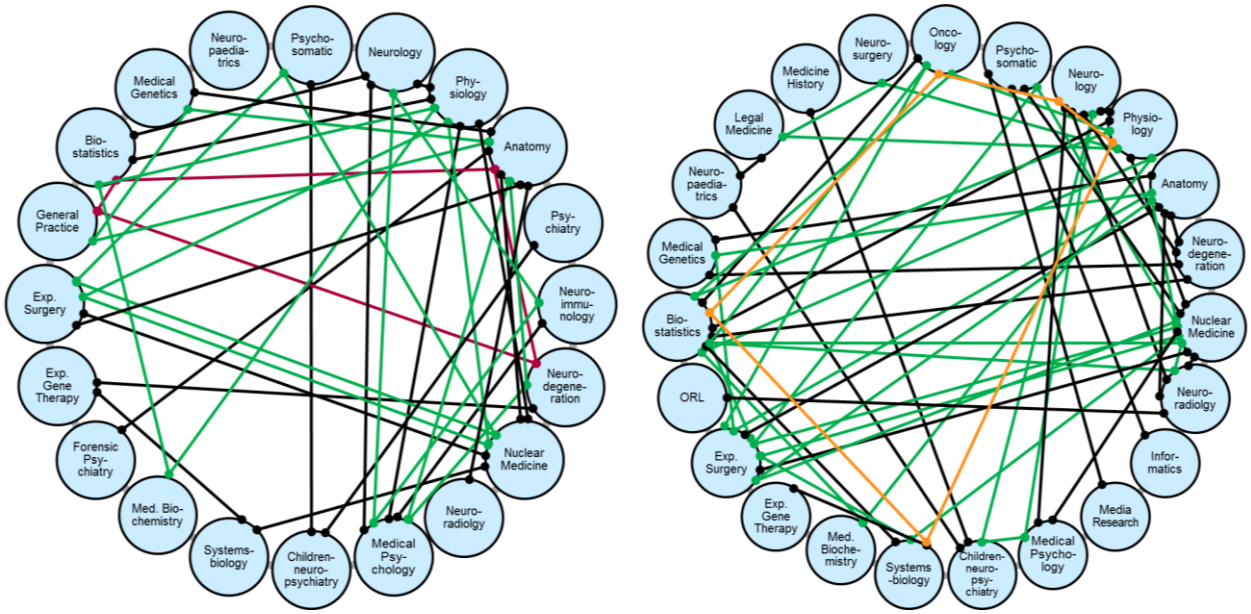


Figure 12: Interdisciplinary publication activities in 2017/2018 (left) and 2019/2020 (right) between CTNR members from two (black line), three (green line), four (red line) and five (orange line) different institutes.

Selected joint publications between CTNR members (bold) of more than one CTNR institution in 2019 and 2020:

Henze, L., **Walter, U.**, Murua Escobar, H., **Junghanss, C.**, Jaster, R., **Köhling, R.**, **Lange, F.**, Salehzadeh-Yazdi, A., **Wolkenhauer, O.**, Hamed, M., Barrantes, I., Palmer, D., Möller, S., Kowald, A., Heussen, N., & **Fuellen, G.** (2020). Towards biomarkers for outcomes after pancreatic ductal adenocarcinoma and ischaemic stroke, with focus on (co)-morbidity and ageing/cellular senescence (SASKit): protocol for a prospective cohort study. BMJ open, 10(12), e039560.

Kowe, A., Köhler, S., Klein, O. A., **Lüthje**, C., Kalzendorf, J., Weschke, S., & **Teipel,** S. (2020). Stakeholder involvement in dementia research: A qualitative approach with healthy senior citizens and providers of dementia care in Germany. Health & social care in the community, 10.1111/hsc.13238. Advance online publication.

Reichart, G., Mayer, J., Zehm, C., **Kirschstein, T**., Tokay, T., **Lange, F.**, **Baltrusch, S.**, **Tiedge, M.**, **Fuellen, G.**, Ibrahim, S., & **Köhling, R.** (2019). Mitochondrial complex IV mutation increases reactive oxygen species production and reduces lifespan in aged mice. Acta physiologica (Oxford, England), 225(4), e13214.

Madadi, A., Wolfart, J., **Lange, F.**, Brehme, H., Linnebacher, M., Bräuer, A. U., **Büttner, A.**, **Freiman, T.**, Henker, C., Einsle, A., Rackow, S., **Köhling, R., Kirschstein, T.**, & Müller, S. (2020). Correlation between Kir4.1 expression and barium-sensitive currents in rat and human glioma cell lines. Neuroscience letters, 741, 135481.

Kuhla, A., Meuth, L., Stenzel, J., Lindner, T., Lappe, C., Kurth, J., **Krause, B. J.**, **Teipel, S.**, Glass, Ä., Kundt, G., & **Vollmar, B.** (2020). Longitudinal [18F]FDG-PET/CT analysis of the glucose metabolism in ApoE-deficient mice. EJNMMI research, 10(1), 119.

Education and Events

The CTNR education and qualification programme is divided into activities and events organised by the CTNR community and by the CTNR office. A CTNR Lecture Series overlaps both areas. The CTNR office collects all information on the CTNR webpage to bundle the activities and to announce them. In addition, a CTNR newsletter (with 98 subscribers in 2020) about news, recent funding opportunities, training opportunities and events in the field of neurosciences is published monthly. Due to the corona pandemic the most planned events in 2020 were postponed to 2021, cancelled or held online/hybrid.

Neuroscience community

In 2019 and 2020, CTNR members organised many events for young clinical, medical and natural scientists to support them in the development of their careers, soft skills and networking. Following are some examples of the activities of CTNR institutes in 2019/2020:

56th annual meeting of the Society for Paediatric Radiology from September 18 to 21, 2019 in Rostock and Warnemünde

CTNR institute: Institute of Diagnostic and Interventional Radiology

13th Baltic Sea Summer School on Epilepsy from August 18 to 24, 2019 in Rostock

CTNR institute: Oscar-Langendorff-Institute of Physiology

Picture 3: 43 participants from 26 different countries at the summer school.

Seminar Series 2019/2020: Basic concepts of scientific working

The aim was to impart basic knowledge and skills in scientific work. An introduction to the statistical basics was given. At the end of the course, the young scientists acquired the basic knowledge to create their own scientific work. They learned to select and evaluate literature in order to formulate their research hypotheses based on this, to choose a design that is suitable for the research work and to apply appropriate procedures for evaluating the data.

Picture 4: Lecturer Jack Tomlin at the hybrid seminar.

CTNR institute: Forensic Psychiatry (host)

Neuroanatomy for PhD-students, 2019

A neuroanatomical advanced training as a two-day course with the human specimen to explain how the human brain is structured and which regions are affected by various neuronal diseases such as Alzheimer's disease, Parkinson's disease or amyotrophic lateral

sclerosis. The preparation took place in small groups (maximum 8 people) on palatinates and fixed human brains. The latest 3D projector technology was used in order to be able to convey the anatomy of very small brain structures.

CTNR institute: Anatomy

First Motor Neuron Diseases Update 2019 & Neuropalliative Update, 2020

Further education programmes on the subject of motor neuron diseases to show current innovations and overview of current developments in neuropalliative medicine and legal aspects relevant to everyday life.

CTNR institute: Translational Neurodegeneration Section "Albrecht Kossel"

Minisymposia on Health and Senescence, 2019

Talks about biomarkers and interventions towards "Healthy Aging", and the mechanisms of cellular senescence, in the cancer/cardio/neuro fields were held. Handling cellular senescence in patients as well as in healthy people is an emerging key topic: latest research shows that doing it right can decide about disease progression, and may stop or reverse aging processes in skin and other organs.

CTNR institutes: Biostatistics and Informatics in Medicine and Ageing Research, Oscar-Langendorff-Institute of Physiology

Stakeholder Workshop - Participation for better solutions in dementia, 2019

In November 2019, the CTNR and the Department "Ageing of Individuals and Society" of the Interdisciplinary Faculty organised a stakeholder workshop in the field of neurodegenerative diseases. Affected persons, researchers and other representatives of care and society exchanged experiences and opinions about risks and benefits of participative research. With the method of a “World Café” the participants worked out how active cooperation should be designed and what kind of research questions could be relevant.

Picture 5: Stakeholders discussing about participation in research.

Palliative Care Course for Nurses, 2019

Seriously ill people who no longer have any prospect of a cure require special care and attention. Palliative medicine has specialized in this. The course like to pass on the palliative medical knowledge and the many years of experience and offer nursing staff from hospitals, retirement homes, outpatient care facilities, hospices and all other professional groups in the health sector a palliative care course every year. Participation in the course is certified with the certificate "Palliative Care - treatment, care and support for critically ill and dying people" from the Bonn Palliative Center according to the curriculum of the German Society for Palliative Medicine.

CTNR institutes: Department of Internal Medicine, Medical Clinic III

Qualification programme

In 2019 and 2020, the qualification programme realised by the CTNR office and in cooperation with the Graduate Academy of the University of Rostock contained (online) seminars about grant writing and funding opportunities for young scientists:

Lectures: Funding Opportunities for young scientists

The talks provide an overview of the third party funding system in Germany and the EU, introduce the most important funding bodies and give advices on how to apply.

CTNR institute: CTNR office

Picture 6: Lecturer Virginia Bolowski and participants.

Seminars: DFG Research Grants - structure, content and submission

The (virtual) seminars on how to write DFG grant proposals (Sachbeihilfe) were given by the coordinator Virginia Bolowski.

CTNR institute: CTNR office

Picture 7: Online seminar with virtual participants.

Seminar: Successful writing of grant proposals

Olaf Wolkenhauer shared his experiences as an applicant and reviewer for DFG, BMBF and EU funding. The seminar was therefore aimed at all those for whom writing applications for third-party funding.

CTNR institute: Systems Biology & Graduate Academy

Online Seminar: Productivity, Project and Time Management for Scientists

The seminar looked at well-established and widely used strategies for productivity, project and time management and gave an overview of productivity tools. By having a common system, combining personal and work-related interest and activities, across tools, and devices, productivity can significantly be improved.

CTNR institute: Systems Biology & Graduate Academy

Lecture Series

In 2020, the CTNR implemented a monthly lectures series with financial and organisational support for members to initiate talks, workshops and symposia with national and international guest speakers in the field of neurosciences. Due to the corona pandemic most speakers were invited but their lectures postponed to 2021 (see Tab. 3).

Table 3: Topics of the CTNR lecture series 2020

Date 2020	Speaker and topic	CTNR host institution
April (postponed)	Manuela Neumann (Tübingen): Clinical Neuropathology	Translational Neurodegeneration Section "Albrecht Kossel"
May (postponed)	Frederike D. Hanke (Rostock): Seal vision – from the periphery to the central nervous system	Anatomy
June (postponed)	Armin Nagel (Erlangen): Challenges and opportunities of ultra-high field (7 Tesla) magnetic resonance imaging	Diagnostic and Interventional Radiology
July (postponed)	Thomas Hummel (Dresden): Smell better	Anatomy
August	Josanne Van Dongen (Rotterdam): Forensic Neuroscience: How neuroscientific insights can add to forensic psychology	Forensic Psychiatry
September	Welf Wustlich (Rostock): Doctor AI: Artificial Intelligence in Medicine	CTNR

Lecture of Excellence: Pioneers in Neurosciences

The 600th birthday of the oldest university in the Baltic Sea region was an important event beyond national borders in 2019. As part of this university anniversary, the CTNR founded the lecture series “Lectures of Excellence: Pioneers in Neurosciences". Under the patronage of the Rector of the University of Rostock, Wolfgang Schareck, excellent scientists who have made significant discoveries in the field of life sciences are invited annually to provide insights into their research. These include, above all, Nobel Prize winners, Leibniz Prize winners and other excellent awards. The lectures are aimed at a scientific plenum consisting of scientists, physicians and young researchers. The Lecture of Excellence is sponsored by the Else Kröner-Fresenius-Foundation.

Picture 8: Christiane Nüsslein-Volhard at the Aula of the University of Rostock. Photo: Thomas Mandt

On 20th March 2019, the CTNR "Lectures of Excellence: Pioneers in Neurosciences" took place for the first time. The Nobel laureate Christiane Nüsslein-Volhard gave a lecture on "The stripes of Zebrafish: Development and evolution of biological aesthetics". The biochemist Christiane Nüsslein-Volhard deals with genetic research and developmental biology and was director of the genetics department at the Max Planck Institute for Developmental Biology in Tübingen from 1985 to 2014. She has received numerous awards for her discoveries of genes that control the development of animals and humans, as well as the evidence of shape-forming gradients in the fly embryo, 1995 the Nobel Prize in Medicine or Physiology.

Picture 9: Rüdiger Köhling, Emil Reisinger, Christiane Nüsslein-Volhard, Alexander Storch and Udo Kragl (left to right) at the Lecture of Excellence. Photo: Thomas Mandt

About 200 participants visited the lecture in the Aula of the Universities main building and used the opportunity to get in close contact with the excellent scientist. The Pro-Rector of Research and Transfer of Knowledge of the University of Rostock, Udo Kragl opened the event and handed over the jubilee medal of the University (Jubiläumstaler). The CTNR speaker, Alexander Storch introduced Christiane Nüsslein-Volhard.

In the evening there was a joint dinner with representatives of the CTNR Board. On the following day, the CTNR coordinator Virginia Bolowski took Christiane Nüsslein-Volhard through the Rostock city centre and showed her the treasure chamber of the University of Rostock and the astronomical clock of the St. Mary's Church.

Masters Course: Clinical and Translational Neurosciences

In 2019, a concept for a CTNR Master's programme in “Clinical and Translational Neurosciences” was developed by members of the CTNR Board and the Office. The main objectives are the early practical involvement and connection of students to neuroscientific research and research groups. After a planned initial and orientation phase, semester-long, practice-oriented project work, which is continued over the following semesters, is intended to impart the academic practice required. In this context, the essential scientific exchange between students and between students and tutors takes place in accompanying method colloquia and progress seminars. The focus of teaching is on clinical relevance, which includes a high level of bedside teaching. This enables the focus on clinical as well as translational research and unmet medical needs. Teaching content includes basic subjects in neuroanatomy and neurophysiology, neurology and psychiatry including their history and ethics, neurodegeneration, aspects of diagnostics in particular imaging and cerebrospinal fluid diagnostics, pharmacology and other neurotherapies, as well as methods of neuroscience, experimental animal science and soft skills in the natural sciences.

In 2020, an initial study programme concept was created and presented to the Office for Higher Education & Quality Development (HQE) of the University of Rostock and the Dean of Studies of the UMR. An important step was the acquisition of more than 30 lecturers, which enabled a complex spectrum of courses for the conception of the module plan and the first outline of the timetable. Furthermore, a Reform Commission was initiated from representatives of the participating institutes to create the curriculum. The following work steps are planned for 2021: (i) the initial meeting of the Reform Commission, (ii) the draft of the Module Handbook and the Examination Regulations and the submission to the Dean of Studies Office and the Capacity Officer, (iii) presentation and approval in the Faculty Council, (iv) the first reading in the Senate Commission for Studies, Teaching and Evaluation, and (v) at the end of the year, the dispatching of the documents to the expert group. The publication of the study and examination regulations is planned for June 2022 and the start of the CTNR Masters Course for the winter term 2022/2023.

TAC Programme

From November 2020 on, the CTNR provides the framework for an educational programme for doctoral candidates of CTNR members. Doctoral researchers get the possibility to be supervised by a Thesis Advisory Committee (TAC). The TAC aims to provide guidance for both the doctoral candidate and their supervisors, in order for them to reach a successful end of the project. The CTNR provides a pool of members as potential TAC supervisors.

Picture 10: TAC meeting.

- ✓ The TAC consists of 3 CTNR members (supervisors).
- ✓ The TAC Meetings will be organised by the doctoral candidates.
- ✓ Typically, the TAC meets twice in the 1st year and once per year thereafter (initial and annual report meetings).
- ✓ For each TAC meeting, a written report and an oral presentation has to be prepared by the doctoral candidate.
- ✓ The meetings focus on the evaluation of the report, presentation, research performance and theoretical knowledge, the evaluation of the thesis project and work done so far, and recommendations for the following year.

The CTNR office developed an information guideline for the CTNR TAC programme and an information platform on the website[6].

Neuro Medical Scientist Programme

The reasons for the necessity of structured career paths differ fundamentally between clinical and scientific young researchers. While for physicians during specialist/subspecialist training the lack of time is the main reason why it is more difficult to carry out one's own research project, in the non-clinical natural/life sciences, the uncertain contractual situation and the salary level are the decisive factors in declining an academic career. The CTNR funding programmes must also meet the subject-specific needs in order to keep and recruit young scientists at the location.

Picture 11: Medical Scientist.

In the Neuro Medical Scientist Programme, medical scientists, i.e. (non-physician) medical researchers in theoretical, preclinical and clinical subjects, as well as non-medical researchers in other natural / life / engineering / social science fields with a neuroscientific focus are funded who planning to submit or already completed their doctoral thesis. Based on the recommendations of the Science Council, the CTNR thus promotes the early career phase before and after the doctorate.

[6] See CTNR TAC programme: https://ctnr.med.uni-rostock.de/career#tab-content-154406

As part of the Neuro Medical Scientist Programme, a scientific position is offered for a period of max. 12 months (the position can be split up depending on incoming applications). The financial support is used to give young scientists the opportunity to apply for third-party funds ("Anschubfinanzierung") or to complete the doctorate ("Überbrückungsfinanzierung"). The proposed project should contribute to the strategic aims of the CTNR (e.g. initiation of cooperative research projects). The first position was advertised at the end of 2020 and will be occupied in 2021.

The Medical Scientist Programme is embedded in the existing structures of the CTNR and the Rostock Academy for Clinician Scientists (RACS, see below). The programme thus benefits from the focus-specific advanced training curriculum, which contains both clinical-specialist and clinical-scientific content in a balanced ratio. The curriculum also includes faculty-wide measures, among others offered by the CTNR, to impart general key qualifications (e.g. seminars on applying a DFG research grant). The aim is to integrate the curricular offers of the pre-existing training structures such as the Graduate Academy of the University of Rostock, the Collaborative Research Centre SFB 1270 "ELAINE" and its integrated graduate school (IRTG) and the interdisciplinary faculty, as optional modules.

In addition, the programme includes a mentoring and an evaluation scheme, the opportunity to participate in CTNR events (e.g. lecture series) and the support of networking and knowledge transfer through laboratory visits and retreats.

The CTNR office developed an information guideline for the programme and an information platform on the website[7].

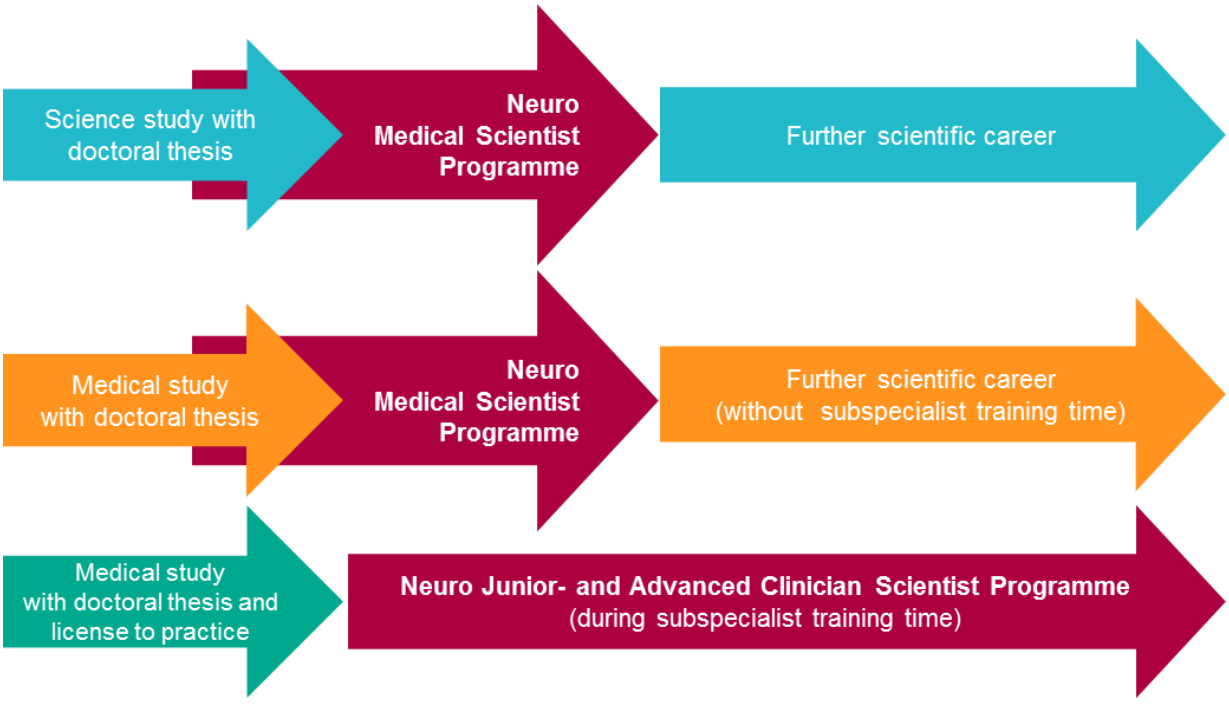


Figure 13: CTNR Medical and Clinician Scientist Programmes.

The CTNR programme for supporting young researchers started in 2019 with a Clinician Scientist Programme in order to enable physicians in the field of neurosciences a research protected time (see below). Both programs currently enable structured career path opportunities for the different needs of young researchers (see Fig. 13).

[7] See CTNR Medical Scientist Programme: https://ctnr.med.uni-rostock.de/career#tab-content-154299

Neuro Clinician Scientist Programme

To improve the recruiting of young clinical scientific researchers and to support their specific challenges concerning compatibility of research and clinical work, in 2018 the University Medicine Rostock (UMR) established a Rostock Academy for Clinician Scientists (RACS)[8]. In order to create efficient incentives for an academic/research career besides medical training, several positions for an advanced training in a clinical specialty/subspecialty (ärztliche Weiterbildungsstellen) are advertised. The key element of the program is the research protected time of two years within the specialist/subspecialist training time to conduct a theoretical research project.

Since 2019, the CTNR offers in addition to RACS regularly two Clinician Scientist positions for the research protected time of two years within the specialist/subspecialist training time to conduct a theoretical research project in the field of Neurosciences. The programme consists of an individual clinical, scientific and soft skill educational curriculum under the umbrella of the Rostock Academy for Clinician Scientists.

In October 2020, the 10 Clinician Scientists of the Rostock Academy for Clinician Scientists (RACS) and of the Clinician Scientists Programs of the three scientific priority areas Biomedical Engineering / Biomaterials, Neurosciences and Oncology met the first time on a scientific retreat at the Ostseehotel Dierhagen. In addition to lectures by the young scientists, their evaluations and meetings of the steering committee, a workshop on the subject of research funding and third-party funding applications was held by the CTNR coordinator Virginia Bolowski.

Picture 12: Seminar on the 1st Clinician Scientist retreat in 2020.

Since October 2019, Maxi Kersten is the first Clinician Scientist of the CTNR Clinician Scientist Program for Neurosciences. Since 2015, she is a resident at the Department of Neurology and member of a clinical research group for movement disorders and deep brain stimulation. As a Neuro Clinician Scientist, she is working on "Functional characterization of the basal ganglia-cortex network to improve individual clinical efficacy of deep brain stimulation in movement disorders". The clinical mentor of Maxi Kersten is Alexander Storch (Department of Neurology) and the scientific mentor is Rüdiger Köhling (Oscar-Langendorff-Institute of Physiology). For a detailed research profile please see below.

Starting in August 2020, Felix Streckenbach is a Clinician Scientist of the CTNR Clinician Scientist Program for Neurosciences. Since 2018, he is a resident at the Institute of Diagnostic and Interventional Radiology, Paediatric Radiology and Neuroradiology and member of the clinical research group in Neuroradiology. As a Neuro Clinician Scientist, he is working on the “development of a biodegradable stent for intracranial aneurysms”. The clinical mentor of Felix Streckenbach is Marc-André Weber (Institute of Diagnostic and Interventional Radiology, Paediatric Radiology and Neuroradiology) and the scientific mentors are Nils Grabow and Klaus-Peter Schmitz (Institute for Biomedical Engineering). For a detailed research profile please see below.

[8] See Rostock Academy for Clinician Scientists: https://www.med.uni-rostock.de/forschung-lehre/forschung/clinician-scientists-entwurf

Intraoperative target determination in deep brain stimulation

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State-of-the Art

Deep brain stimulation (DBS) in basal ganglia (BG) structures, namely the subthalamic nucleus (STN) or Globus pallidus internus (GPi), is an established therapy to treat motorsymptoms in Parkinson's disease (PD) and dystonia. Nevertheless, the pathophysiologies of these diseases as well as the mechanisms underlying the effects of DBS are still incompletely understood. In this view, individual target determination for DBS therapy in the BG remains a major challenge. The staged procedure of preoperative anatomical and intraoperative clinical and electrophysiological targeting currently used in clinical routine may only insufficiently anticipate the efficacy of DBS therapy in the individual patient.

Overall Scientific Aim

We evaluate methods which could be promising to improve the intraoperative individual selection of the target for DBS therapy in Parkinson´s disease and dystonia patients. Moreover, two genetic rat models of dystonia will be characterized according to the in vivo basal ganglia and DBS functioning to further understand the pathophysiology of dystonia and to improve DBS therapy in human dystonia.

Projects, Methods & Technologies

DBS effects are mainly thought to be mediated by fibre connections and in this context the so called hyperdirect pathway (HDP) could be a structure of particular interest. This structure monosynaptically connects cortex and STN and STN-DBS may act by retrograde disruption of the cortical drive (from mesial premotor cortical area) to STN in lower and higher beta frequency band oscillations in PD. It has repeatedly been demonstrated that cortical potentials evoked by STN stimulation and recorded by scalp electrodes can functionally characterize the HDP which leads us to the hypothesis that these potentials may be a suitable marker to intraoperatively determine STN areas anatomically and functionally connected with fronto-mesial cortex areas. In this context we assume that electrode contacts of chronic stimulation in STN areas that have been intraoperatively determined of high functional connectivity with fronto-mesial cortex may be of outstanding clinical efficacy.

Curriculum Vitae
2007 – 2014 University Medical Centre Rostock, University of Rostock
since 2015 Resident physician at the Department of Neurology, University Medical Centre Rostock
2017 Doctorate in Medicine, Oscar-Langendorff-Institute of Physiology, University Medical Centre Rostock
Since 2019 Member of the research group for movement disorders and deep brain stimulation, Department of Neurology, University Medical Centre Rostock
Since 2019 Neuro Clinician Scientist of the Centre for Transdisciplinary Neurosciences Rostock (CTNR)

In the ongoing project we could already show technical feasibility during DBS surgery. We are currently analysing our first cohort correlating postoperative clinical efficacy of STN-DBS with intraoperatively determined potentials in fronto-mesial cortical areas evoked by stimulation of STN areas corresponding to the respective contact of the electrode for chronic stimulation.

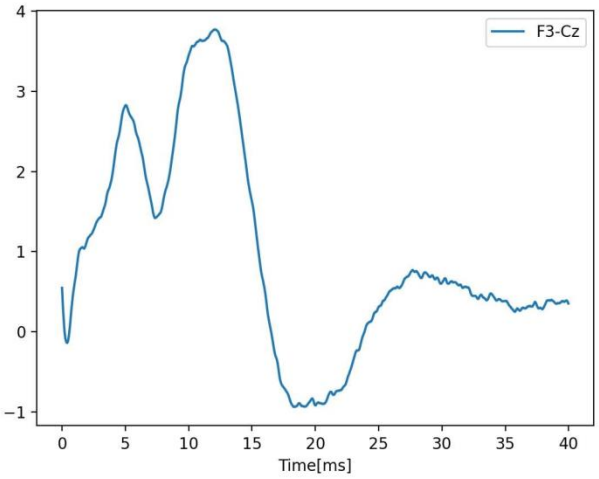

Figure 14: Example of a multiphasic cortical potential evoked by stimulation in the STN at the anatomically determined target for STN-DBS.

This project is a collaboration of the Department of Neurology, University Medical Centre Rostock, Germany (clinical DBS programme leader PD Dr. med. René Reese), the Department of Neurosurgery, University Medical Centre of Rostock (Dr. med. Thomas Kriesen) and the SFB1207 “ELAINE” B03 (M.Sc. Jakob Heller; project leader Prof. Dr. D. Timmermann).This project is financially supported by the FORUN programme of the University of Rostock (889010).

In a further planned work our hypothesis will be tested in a reciprocal translational approach in two genetically dystonic rat models (DYT1 and DYT6). STN and the internal pallidum (GPi) may, similar to PD, serve as targets for DBS in the dystonias, a hyperkinetic movement disorder. Clinical effects of DBS however are much more heterogeneous than in PD at least partly due to the fact that the pathophysiology of the dystonias is much less understood than of PD. In this context we are about to investigate two genetic rat models of human dystonia. We will characterize basal ganglia signalling by in vivo extracellular recordings of axonal activity and oscillatory activity and will correlate these data with local and remote neuronal effects of DBS. Potentials evoked by DBS within the stimulated nucleus, in nuclei of the basal ganglia circuit and in remote cortical areas will be characterized in view of somatotopical properties and compared to human data of the project illustrated above.

This project is a collaboration of the Department of Neurology, University Medical Centre Rostock, Germany (clinical DBS programme leader PD Dr. med. René Reese), the CRC 1207 “ELAINE” C04 (project leader Dr. med. Mareike Fauser and Prof. Dr. med. Alexander Storch) and C03 (project leader Prof. Dr. med. vet. A. Richter and Prof. Dr. med. R. Köhling) and the Institute of Medical Genetics, University of Tubingen, Germany (Dr. med. Fubo Cheng).

Selected Publications

Kersten M, Rabbe T, Blome R, Porath K, Sellmann T, Bien CG, Köhling R, Kirschstein T (2019). Novel Object Recognition in Rats with NMDAR Dysfunction in CA1 After Stereotactic Injection of Anti-NMDAR Encephalitis Cerebrospinal Fluid. Frontiers in Neurology, 10:586.

Walter U, Tsiberidou P, Kersten M, Storch M, Löhle M (2018). Atrophy of the Vagus Nerve in Parkinson’s Disease Revealed by High-Resolution Ultrasonography. Frontiers in Neurology 9:805.

Würdemann T, Kersten M, Tokay T, Guli X, Kober M, Rohde M et al. (2016). Stereotactic injection of cerebrospinal fluid from anti-NMDA receptor encephalitis into rat dentate gyrus impairs NMDA receptor function. Brain Research 1633, S. 10–18.

Bioresorbable intracranial stent for endovascular therapy

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State-of-the Art

Major indications for the implantation of an intracranial stent are the treatment of intracranial arterial stenosis and reconstruction of the parent vessel as part of endovascular aneurysmal therapy.

However, with the results of the SAMMPRIS-trail ("Stenting and aggressive medical management for preventing recurrent stroke in intracranial stenosis"), which demonstrated superiority of best medical treatment (BMT) compared to endovascular therapy in intracranial arterial stenosis, the number of implanted stents for this indication declined. However, stent-assisted percutaneous angioplasty remains the main therapeutic option for patients under BMT with recurrent ischemic events. Therefore new therapeutic approaches with drug eluting balloons or other stents are part of current studies.

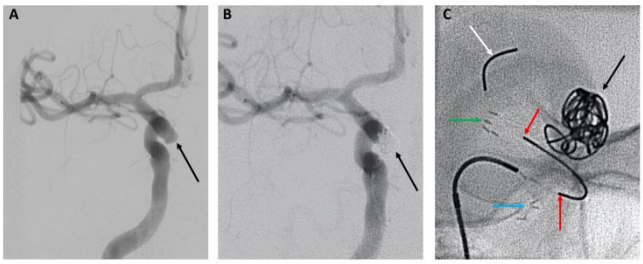

Figure 15: Digital subtraction angiography (a.-p. view) of an internal carotid artery paraophthalmic wide-neck aneurysm (black arrow) before (A) and after (B) stent-assisted coil embolization. Non-subtracted imaging (lateral view) (C) after stent deployment; carrier system of the stent with distal tip (white arrow); effective zone (red arrows) of the stent, which secures the coils (black arrow) inside the wide-neck aneurysm; proximal (blue arrow) and distal (green arrow) markers indicating the total length of the stent.

Endovascular coil embolization of intracranial aneurysms is an established neuroradiological procedure. A particular challenge for endovascular therapy is wide-neck aneurysms, in which the coils cannot be fixated securely within the aneurysmal sac. For this purpose, intracranial stents have been established since the mid-1990s, which reconstruct the course of the parent vessel and thus allow the coil package to be anchored in the aneurysm. One major drawback of stent implantation is the need for permanent platelet inhibition with subsequently increased risk of hemorrhagic complications. Platelet inhibition is usually performed during the first year after implantation as a dual therapy. Furthermore, there is no long-term experience for implanted intracranial stents.

Overall Scientific Aim

Bioresorbable stents offer a new therapeutic approach in the treatment of intracranial aneurysms and stenoses and are part of many current studies. In contrast to conventional stents, they dissolve after some time into their main components water and carbon dioxide, which are then metabolized by the body. Therefore, platelet inhibition to prevent thromboembolic complications might not be necessary after the bioresorbable stents is resolved thus decreasing the risk of hemorrhagic complications.

Curriculum Vitae
2011-2018 State exam in Medicine, University of Rostock
2018 Doctorate in Medicine, Department of Ophthalmology, University Medical Centre Rostock
Since 2018 Resident physician at the Institute of Diagnostic and Interventional Radiology, Paediatric Radiology and Neuroradiology, University Medical Centre Rostock
Since 2020 Neuro Clinician Scientist at Centre for Transdisciplinary Neurosciences Rostock (CTNR)

Furthermore, these types of stents may have a decreased risk for neo-intimal hyperplasia with subsequent stenosis. This will reduce the risk of recurrent ischemic events and may facilitate the endovascular access to the vessel when treatment distal to the implanted stent is necessary. Finally, bioresorbable stents have fewer artefacts in CT and MRI and therefore follow-up imaging will be facilitated. Our aim is to investigate and test a suitable bioresorbable intracranial stent that is fully resorbed after implantation and therefore requires dual platelet aggregation inhibition only for a limited period of time.

Projects, Methods & Technologies

Various established vascular models for in vitro research are described in previous studies. Usually, these models are based on 3D rotational angiography datasets, which offer highest spatial resolution. CT and especially MRI datasets provide significantly less spatial resolution. The majority of reports describe vascular models for intracranial aneurysms, literature for vascular models of intracranial stenosis is sparse and there is no established model so far.

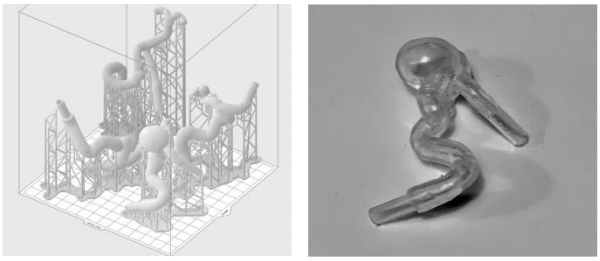

Figure 16: Individualised model of an internal carotid artery paraophthalmic aneurysm of a patient based on an individual 3D-CT-angiography data set using a 3D stereolithography printing process.

In previous works, we established an in vitro vascular flow model for intracranial aneurysms based on high-resolution CT angiography datasets at Institute of Diagnostic and Interventional Radiology, Paediatric and Neuroradiology. This model allows us, to create an individualized model of the intracranial circulation and the intracranial aneurysm from a single patient 3D-CT-angiography data set using a 3D printing process. These models can then be integrated in the flow model which allows us to perform angiographic diagnostics and interventions as well as CT and MR imaging.

In cooperation with the Institute of Biomedical Engineering already available lasercut bioresorbable stents (polylactide, PLLA) will be modified to fit the needs for an intracranial stent. Furthermore, the delivery device will be optimized to fit to the intracranial and supra-aortic vasculature. These modified stents will then be evaluated regarding the physical and hemodynamic characteristics in the vascular model. Using the established model, these examinations can be performed under fluoroscopy or high-definition video imaging. After this process is finished, the newly developed stent will be transferred to the in vivo model of the New Zealand Rabbit.

The following requirements are necessary for a bioresorbable intracranial stent: a) small access system; usually, intracranial stents are delivered via a 1.7F (0.6mm) microcatheter, b) self-expansive, c) minimal mechanical load on the adjacent tissue and thus low radial force, the stent should only reconstruct the vessel in its course and must be formable by using balloon PTA d) a narrow curve radius for optimal intravascular application and control, e) successful resorption of the stent after 6 months.

Selected Publications

Keiler J, Meinel FG, Ortak J, Weber MA, Wree A, Streckenbach F (2020). Morphometric characterization of human coronary veins and subvenous epicardial adipose tissue – implications for cardiac resynchronization therapy devices, Front. Cardiovasc. Med., 8;7:611160.

Ammermann F, Meinel FG, Beller E, Busse A, Streckenbach F, Teichert C, Weinrich M, Neumann A, Weber MA, Heller T (2020). Concomitant chronic venous insufficiency in patients with peripheral artery disease: insights from MR angiography, European Radiology, 30(7):3908-3914.

Langer S, Beller E, Streckenbach F (2020). Artificial Intelligence and Big Data, Klinische Monatsblätter Augenheilkunde, 237(12):1438-1441.

Streckenbach F, Klose R, Langner S, Langner I, Frank M, Wree A, Neumann AM, Glass Ä, Stahnke T, Guthoff RF, Stachs O, Lindner T (2019). Ultrahigh-Field Quantitative MR Microscopy of the Chicken Eye In Vivo Throughout the In Ovo Period. Molecular Imaging Biology. 21(1):78-85.

Streckenbach F, Stachs O, Langner S, Guthoff RF, Meinel FG, Weber MA, Stahnke T, Beller E (2020). Age-Related Changes of the Human Crystalline Lens on High-Spatial Resolution Three-Dimensional T1-Weighted Brain Magnetic Resonance Images In Vivo, Investigative Ophthalmology & Visual Science, 1;61(14):7.

Members' outcomes

The third-party funding and publication outcomes are significantly improved in 2019/2020 also by strategic recruitments of excellent young researchers and professors to the University Medicine Rostock in the field of neurosciences.

Members' third-party funding

During 2019 and 2020, the CTNR members submitted several third-party fund proposals. Figure 17 shows the number of approved projects by funding bodies. The approved total funding amounts are shown in Figure 18.

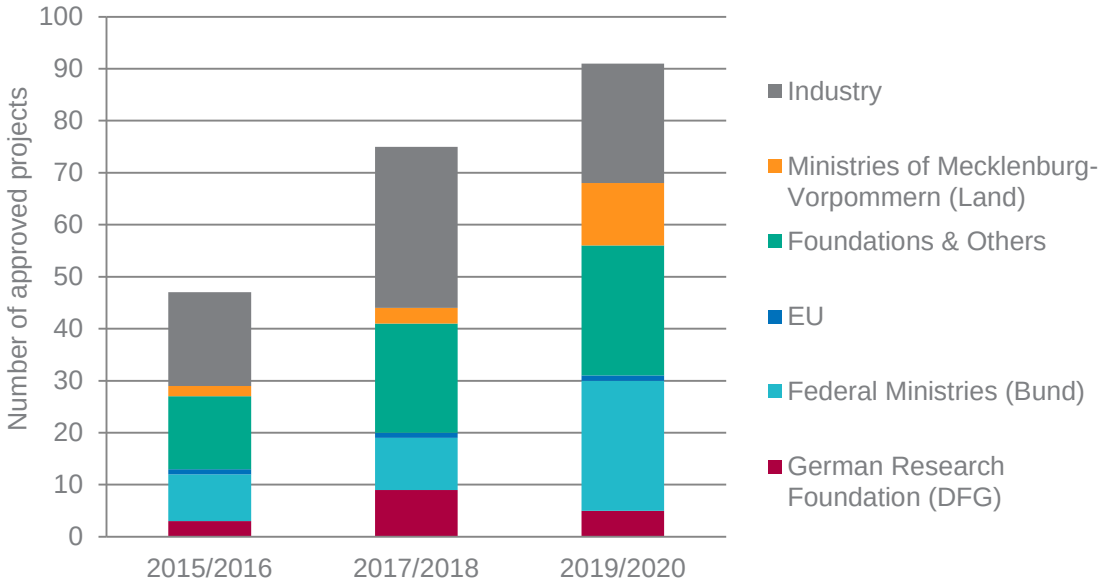

Figure 17: Number of approved third-party projects in 2015/2016 (prior to CTNR foundation), 2017/2018 and 2019/2020 by funding bodies.

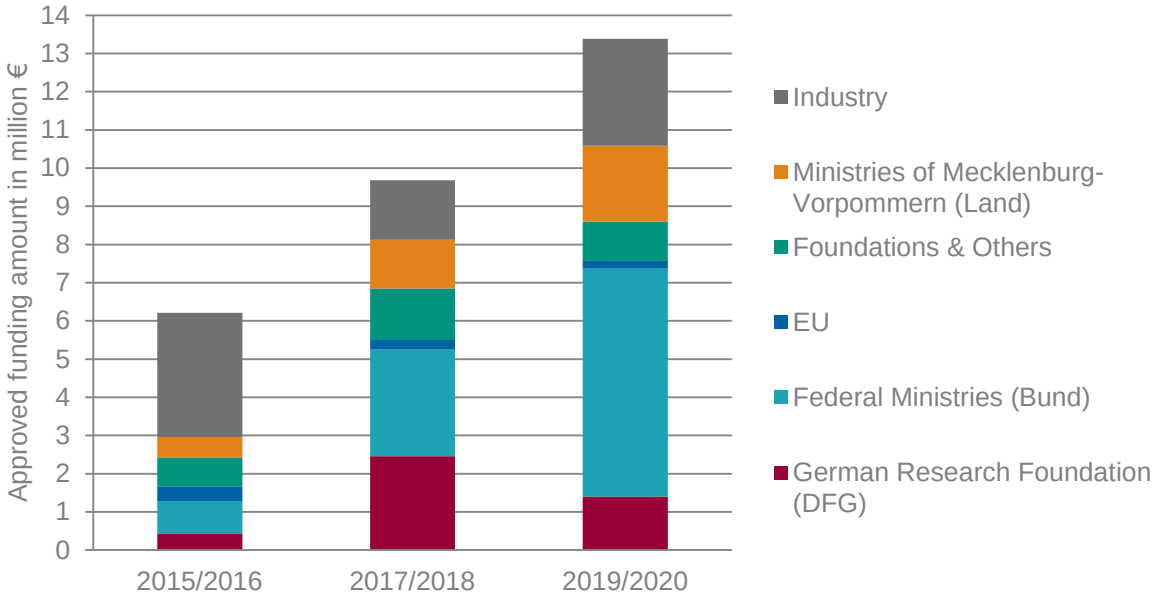

Figure 18: Approved funding amounts (in Mio. €) of all CTNR members in 2015/2016 (prior to CTNR foundation), 2017/2018 and 2019/2020 by funding bodies.

Members' publications

Figure 19 shows the number of publications of the CTNR members by impact factors (IF) and the total sum of journal impact factors (SI) calculated from the publication record for the years 2015-2020.

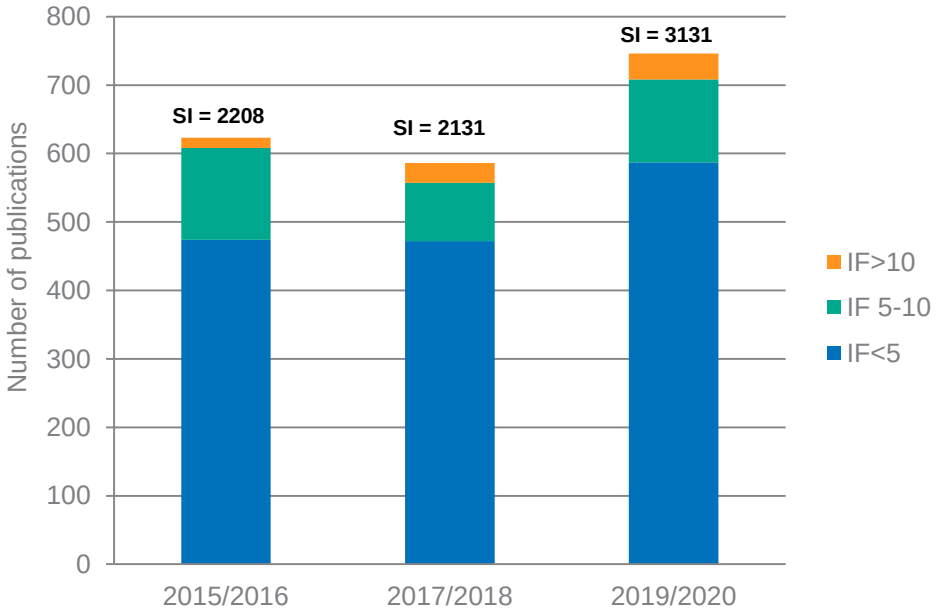

Figure 19: Number of publications of CTNR members by impact factors (IF) and the sum of impact factors (SI) 2015/2016, 2017/2018 and 2019/2020. Journal impact factors for publications in 2020 based on 2019.

Selected publications of CTNR members (bold) in 2019 and 2020 in the field of neurosciences:

Uyar, B., Palmer, D., Kowald, A., Murua Escobar, H., Barrantes, I., Möller, S., Akalin, A., & **Fuellen, G.** (2020). Single-cell analyses of aging, inflammation and senescence. Ageing research reviews, 64, 101156.

Baumgarten, P., Sarlak, M., Monden, D., Spyrantis, A., Bernatz, S., **Gessler, F.**, Dubinski, D., Hattingen, E., Marquardt, G., Strzelczyk, A., Rosenow, F., Harter, P.N., Seifert, V., **Freiman, T.M.** (2020). Early and Late Postoperative Seizures in Meningioma Patients and Prediction by a Recent Scoring System. Cancers (Basel), 13(3):450.

Goerss, D., Hein, A., Bader, S., Halek, M., Kernebeck, S., Kutschke, A., Heine, C., Krueger, F., **Kirste, T.**, & **Teipel, S.** (2020). Automated sensor-based detection of challenging behaviors in advanced stages of dementia in nursing homes. Alzheimer's & dementia : the journal of the Alzheimer's Association, 16(4), 672–680.

Spittau, B., Dokalis, N., & Prinz, M. (2020). The Role of TGFβ Signaling in Microglia Maturation and Activation. Trends in immunology, 41(9), 836–848.

Walter, U., Mühlenhoff, C., Benecke, R., Dressler, D., Mix, E., Alt, J., Wittstock, M., Dudesek, A., **Storch, A.**, & Kamm, C. (2020). Frequency and risk factors of antibody-induced secondary failure of botulinum neurotoxin therapy. Neurology, 94(20), e2109–e2120.

Research profiles of new members

In 2019 and 2020 twelve new members joined the CTNR. The following pages introduce the research of the new members by their individual research profiles.

Innate immunity in acute and chronic inflammation in the CNS

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State-of-the Art

The CNS does exhibit features of inflammation in response to injury, infection or disease. We distinguish here between acute and chronic diseases. Altogether, resident CNS cells generate inflammatory mediators, including proinflammatory cytokines, prostaglandins, free radicals and complement, which in turn induce chemokines and adhesion molecules, recruit immune cells, and activate glial cells. The glial activation and subsequent release of neurotoxic proinflammatory factors are assumed to play an important role in the pathogenesis of the different neurological disorders and are critically involved in pathogen recognition and are considered to represent the innate immune system of the CNS. The pattern recognition receptors (PRRs) are responsible for the activation of glial cells in response to so-called danger- or pathogen-associated molecular patterns (DAMPs or PAMPs). These include Toll-like receptors (TLRs) and formyl peptide receptors (FPRs).

Overall Scientific Aim

The focus of our scientific work is on the role of the innate immune system in CNS inflammation. In the case of acute inflammations, we are investigating the connection between the innate immune system and bacterial meningitis. Bacterial meningitis is a severe disease of the CNS which, despite rapid antibiotic therapy, still leads to the death of the patient in many cases. Furthermore, many formerly ill patients suffer from neurological late damage such as cognitive and motor impairments or hearing loss. In the context of the disease, we are investigating the role of important components of the innate immune response. The second research focus of our scientific work deals with the role of the innate immune system in chronic, degenerative inflammations such as Alzheimer's disease or multiple sclerosis (MS). The focus here is also on the G-protein-coupled formyl peptide receptors, but also on the Toll-like receptors.

Projects, Methods & Technologies

The first focus of our research is on bacterial meningitis. In the context of the disease, we are investigating the role of important components of the innate immune response in the CNS. Our focus is on the acute phase, but also on neuroregeneration after bacterial meningitis. For the investigations, I use established infection and inflammation models as well as corresponding deficient or transgenic mouse models and primary cell cultures. As a model of bacterial meningitis, we use the intracranial injection of Streptococcus pneumoniae through the cranial skull. In particular, our work focuses on the function and effect of antimicrobial peptides (AP) as so-called endogenous antibiotics. In addition to their antimicrobial activity, APs also have important immunomodulatory functions. Our results showed that the AP cathelin-releated antimicrobial peptide deficiency led to a higher mortality rate that was associated with increased bacterial titers as well as decreased meningeal neutrophil of glial cell activation that was accompanied by a more pronounced proinflammatory response.

Curriculum Vitae
1995 – 2000 University studies at the Ernst-Moritz-Arndt-University Greifswald
2001 – 2004 PhD thesis, Institute for Pharmacology and Toxicology, Otto-von-Guericke-University Magdeburg
2010 Venia legendi for Anatomy at the RWTH Aachen University
2011 "Fachanatom" (professional anatomist) by the “Anatomische Gesellschaft”
2019 Appointment as Associate Professor at the Medical Faculty of RWTH Aachen University
Since 2019 Research assistant at the Institute of Anatomy at the University Medical Centre Rostock

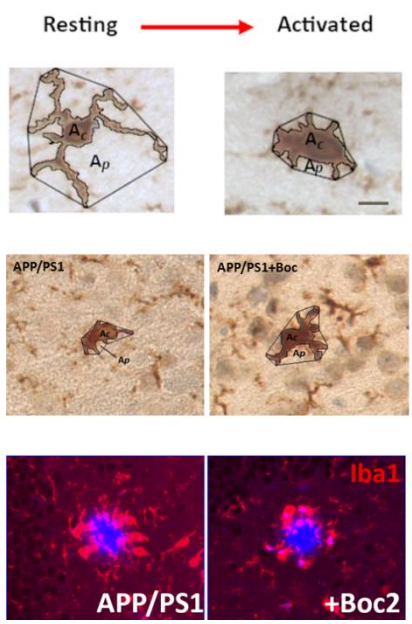

Figure 20: Microglia reactivity determined by detailed morphological analysis (i.e., ramification index, RI). Analysis of the RI (Ap/Ac) as a subtle indicator for microglia activation revealed a decrease of RI in APP/PS1 double-transgenic compared to WT mice (first row), which was less severe in Boc2-treated APP/PS1 doubletransgenic mice (second row). Representative image of a plaque stained with anti-IBA-1 (red) and anti-beta-Amyloid 1-42 (blue; third row). [from Schröder et al. (2020) J Neuroinflammation. 17(1), 131].

In addition to the AP, we are interested to investigate the influence of other important components of the innate immune system, such as the so-called pattern recognition receptors, on the inflammatory response and neuroregeneration after bacterial meningitis. The focus here is on the formyl peptide receptors, among others. The chemotactic G-protein-coupled formyl peptide receptors (FPRs) are characterised by a broad ligand spectrum of bacterial, but also non-bacterial agonists. This includes pro- as well as anti-inflammatory ligands. Based on our work, we were able to show the importance of the receptors for the inflammatory response after bacterial meningitis. In another study, we investigate the influence of a modulation of the inflammatory reaction by anti-inflammatory ligands of the FPR on the acute reaction as well as the late effects after meningitis (DFG BR3666/6-1). The application of the anti-inflammatory agonist für the FPRs Ac2-26 improves the course of pneumococcal meningitis. Ac2-26-treated wild-type mice showed less neutrophil infiltration and, in parallel, reduced induction of pro-inflammatory glial cell responses in the hippocampal formation and cortex.

The second focus of our research is on the role of the innate immunity in chronic, degenerative inflammations such as Alzheimer's disease or multiple sclerosis (MS). The focus here is also on the G protein-coupled formyl peptide receptors, but also on the Toll-like receptors. Using a mouse model for Alzheimer disease, FPR antagonism by Boc2-treatment significantly improved spatial memory performance, reduced neuronal pathology, induced the expression of homeostatic growth factors, and ameliorated microglia, but not astrocyte, reactivity. Furthermore, the elevated levels of amyloid plaques in the hippocampus were reduced by Boc2-treatment, presumably by an induction of amyloid degradation.

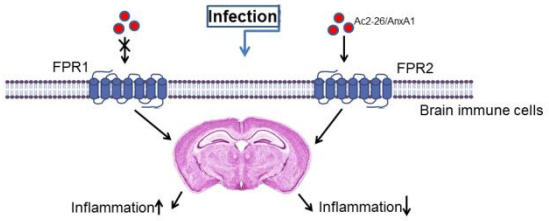

Figure 21: Schematic model of Ac2-26/AnxA1 peptide mechanism of action in the pneumococcal meningitis. Ac2-26 mediated about FPR2 expressed by the brain immune cells the anti-inflammatory response after pneumococcal infection. This results in an improvement in the inflammatory reaction. The activation of the FPR1 during the infection tends rather to an increase of the inflammatory response. [from Rüger et al. (2020) J Neuroinflammation. 17(1), 325].

Selected Publications

Schloer S, Hübel N, Masemann D, Pajonczyk D, Brunotte L, Ehrhardt C, Brandenburg LO, Ludwig S, Gerke V, Rescher U. (2019) The annexin A1/FPR2 signaling axis expands alveolar macrophages, limits viral replication, and attenuates pathogenesis in the murine influenza A virus infection model. FASEB J. 33(11), 12188-12199.

Abazid A, Martin B, Choinowski A, McNeill RV, Brandenburg LO, Ziegler P, Zimmermann U, Burchardt M, Erb H, Stope MB. (2019) The androgen receptor antagonist enzalutamide induces apoptosis, dysregulates the heat shock protein system, and diminishes the androgen receptor and estrogen receptor β1 expression in prostate cancer cells. J. Cell. Biochem. 120(10), 16711-16722.

Blume C, Geiger MF, Brandenburg LO, Müller M, Mainz V, Kalder J, Albanna W, Clusmann H, Mueller CA. (2020) Patients with degenerative cervical myelopathy have signs of blood spinal cord barrier disruption, and its magnitude correlates with myelopathy severity: a prospective comparative cohort study. Eur. Spine J. 29(5), 986-993.

Schröder N, Schaffrath A, Welter JA, Putzka T, Griep A, Ziegler P, Brandt E, Samer S, Heneka MT, Kaddatz H, Zhan J, Kipp E, Pufe T, Tauber SC, Kipp M, Brandenburg LO (2020) Inhibition of formyl peptide receptors improves the outcome in a mouse model of Alzheimer disease. J. Neuroinflammation. 17(1), 131.

Rüger M, Kipp E, Schubert N, Schröder N, Pufe T, Stope MB, Kipp E, Blume C, Tauber SC, Brandenburg LO (2020) The Formyl peptide receptor agonist Ac2-26 alleviates neuroinflammation in a mouse model of pneumococcal meningitis. J. Neuroinflammation. 17(1), 325.

Cellular pathology of Temproal Lobe Epilepsy

Freiman, Thomas

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Department of Neurosurgery
University Medical Centre Rostock
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State-of-the Art

Epileptic seizures are one of the most prevalent neurological symptoms; nearly 1% of the world population suffers therefrom. Whereas most epilepsy can be treated well with anti-epileptic drugs, about one third of epilepsy shows pharmacoresistance. The most frequent form of pharmacorresistant epilepsy is temporal lobe epilepsy (TLE), which shows hippocampal sclerosis (HS) as the pathological correlate. In these cases selective removal of the epileptic focus in the brain can give the patient seizure freedom and remaining the brain function intact. It has been shown, that patients been treated surgical in pharmacoresistant epilepsy, live longer than non-surgically treated patients. The Pathology of HS is characterised by selective neuronal death in the hippocampal subregions of the cornu ammonis (CA)1, CA3 and CA4. Granule cells (GC) and CA2 neurons are less affected but GC axons, the mossy fibers (MF), lose their target cells in CA3 and CA4 and sprout to the surviving GC layer (GCL). We have recently shown that MFs is not only present in the GCL but extents even into CA1 and CA2.

Overall Scientific Aim

We are interested in the cellular neuronal pathology, neuronal migration and axonal sprouting and reconnection, as well as its possible extracellular steering mechanism.

Projects, Methods & Technologies

We examine hippocampal specimens of patients with TLE, undergoing epilepsy surgery. Specimen were cept vivable, sliced a processed for immunohistochemistry, neuronal tracing and electron micrography. Cell death was analysed according to two HS classifications (Wyler grade and International League against Epilepsy (ILAE) types) and clinical patient records were compared. In addition an elaborated animal model, the intrahippocampal kainate-injection, to compare the results operated and injected transgenic Thy1-eGFP mice intrahippocampally with kainate to induce TLE.

Curriculum Vitae
1991 - 1997 Medical study at the Goethe-University Frankfurt am Main, Ruprechts-Kars-University Heidelberg, Harvard-University Boston.
1997 German- and U.S. American (USMLE)- Medical Licensing Examination
1997 - 2013 Neurosurgical Residency, -Registrar- and -Consultant-Position, University Medical Centre Freiburg im Breisgau
2000 - 2008 Principal Investigator, German Research Council (Sonderforschungsbereich) "Temporal Lobe Epilepsy"
2006, 2009 German- and European (EANS)-Neurosurgical Board Examination
2012 Habilitation in Neurosurgery, Albert-Ludwig-University Freiburg
2013 - 2020 Chief-Consultant, University Hospital Frankfurt am Main
2018 - 2020 Principal Investigator Research Council of the State of Hesse "Center for Personalised Translational Epilepsy Research (CePTER)"
since 2020 Full-Professor and Chairman of the Department of Neurosurgery, University Medical Centre Rostock

In the future we will cooperate with the Departments of Anatomy and Physiology to perform our basic research und with the Department of Neurology and Paediatrics. Our aim is to show the effect of axonal reorganisation on the electrophysiological properties of granule- and basket cells as well as immunological steering mechanisms of cell death and axonal sprouting.

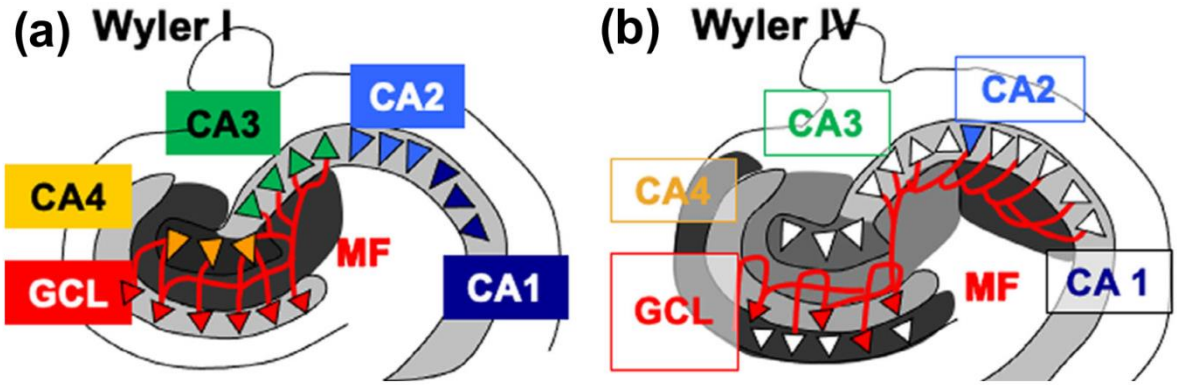

Figure 22: Schematic of cellular death and axonal reorganisation in the human hippocampus in TLE.

Selected Publications

Freiman TM, Häussler U, Zentner J, Doostkam S, Beck J, Scheiwe C, Brandt A, Haas CA, Puhahn-Schmeiser B (2021). Mossy fiber sprouting into the hippocampal region CA2 in patients with temporal lobe epilepsy. Hippocampus. 10.1002/hipo.23323.

Baumgarten P, Sarlak M, Monden D, Spyrantis A, Bernatz S, Gessler F, Dubinski D, Hattingen E, Marquardt G, Strzelczyk A, Rosenow F, Harter PN, Seifert V, Freiman TM (2021). Early and Late Postoperative Seizures in Meningioma Patients and Prediction by a Recent Scoring System. Cancers (Basel) 13(3):450.

Melzer L, Freiman TM, Derouiche A (2021). Rab6A as a Pan-Astrocytic Marker in Mouse and Human Brain, and Comparison with Other Glial Markers (GFAP, GS, Aldh1L1, SOX9). Cells. 10(1):72.

Madadi A, Wolfart J, Lange F, Brehme H, Linnebacher M, Bräuer AU, Büttner A, Freiman T, Henker C, Einsle A, Rackow S, Köhling R, Kirschstein T, Müller S (2021). Correlation between Kir4.1 expression and barium-sensitive currents in rat and human glioma cell lines. Neurosci Lett. 2021 Jan 10;741:135481. Epub 2020 Nov 5.

Spyrantis A, Cattani A, Woebbecke T, Konczalla J, Strzelczyk A, Rosenow F, Wagner M, Seifert V, Kudernatsch M, Freiman TM. Electrode placement accuracy in robot-assisted epilepsy surgery: A comparison of different referencing techniques including frame-based CT versus facial laser scan based on CT or MRI. Epilepsy Behav. 2019 Feb;91:38-47.

Understanding mechanisms regulation glioma cell migration/invasion

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State-of-the Art

Gliomas are the most common primary brain tumours and can be classified into different grades (grades I-IV) and histopathological subgroups. Ependymomas account for less than 10% of all gliomas, whereas oligodendrogliomas (10%-30%) and astrocytomas (60%- 70%) are more common. A characteristic feature and major obstacle to the treatment of malignant gliomas is their diffuse infiltrative growth into the surrounding brain tissue, which makes efficient tumour resection very difficult.

Overall Scientific Aim

Tissue factor (TF) is a 47 kDa type I transmembrane protein that belongs to the cytokine receptor superfamily. TF is transcriptionally induced by epidermal growth factor receptor (EGFR) activation, loss of phosphatase and tensin homolog (PTEN), and hypoxia and its expression positively correlates with histological grading of gliomas and the extent of necrosis (Hamada et al., 1996). Hypoxia-induced expression of TF has been shown to be largely dependent on the transcription factor early growth response gene-1 (Egr-1). TF is known to exert multiple effects on cancer cell autonomic functions and the tumour microenvironment. Increased expression of TF correlates with a hypercoagulative state of tumours, including malignant gliomas, and intravascular thrombosis plays an important role in the formation of hypoxic regions within the tumour. The formation of pseudopalisades likely represents active migration of glioma cells away from the necrotic core, and hypoxia is thought to be a driving force for the increased migratory and invasive behaviour of glioma cells. Normal interstitial oxygen concentration in the mammalian brain ranges from 1% to 5% (Silver and Erecinska, 1998). The main features of glioblastoma multiforme (GBM), the most malignant glioma that allows differentiation from lower grade tumours, include tumour hypoxia and pseu- dopalizing necrosis. Severe hypoxia/anoxia (0.1% O2) is observed in a significant number of GBMs and may be associated with their aggressiveness.

Projects, Methods & Technologies

In addition to its pro-thrombotic role, TF may act as a transmembrane receptor, and the intracellular domain of TF is involved in the modulation of several intracellular signaling pathways relevant to tumour growth, angiogenesis, and metastasis, such as the p44/p42

Curriculum Vitae
2004-2010 State exam in Medicine, Goethe University Frankfurt
2012 Doctorate in Molecular Neurooncology, Department of Neurosurgery, Goethe University Frankfurt
2019 Habilitation in Neurosurgery, Medical Faculty, Goethe University Frankfurt
2020 Doctorate in Clinical Neurosciences, Cambridge University (Gates Scholar)
2018-2020 Senior neurosurgeon, Department of Neurosurgery, Goethe University Frankfurt
Since 2020 Vice Chairman, Department of Neurosurgery, University Medical Centre Rostock

MAP kinase (MAPK) pathway, the p38 MAPK pathway, and the PI3K/Akt pathway. Several studies also suggest that intracellular signaling triggered by the TF-FVIIa (tissue factor VIIa) complex involves FVIIa-mediated cleavage and activation of protease-activated receptor 2 (PAR-2), a member of the PAR family of G-protein-coupled seven-transmembrane receptors consisting of four members (PAR-1-4), leading to subsequent activation of small GTPase pathways. In addition, TF is also known to regulate integrin function, particularly integrin 31. Er previously presented evidence that TF/FVIIa signaling plays an important role in cell growth, migration, and invasion of glioma cells downstream. Our data also suggest that these effects of TF/FVIIa are mediated by downstream activation of PAR-2 and the p44/42 MAP kinase/extracellular regulated kinase (ERK) signaling pathway.

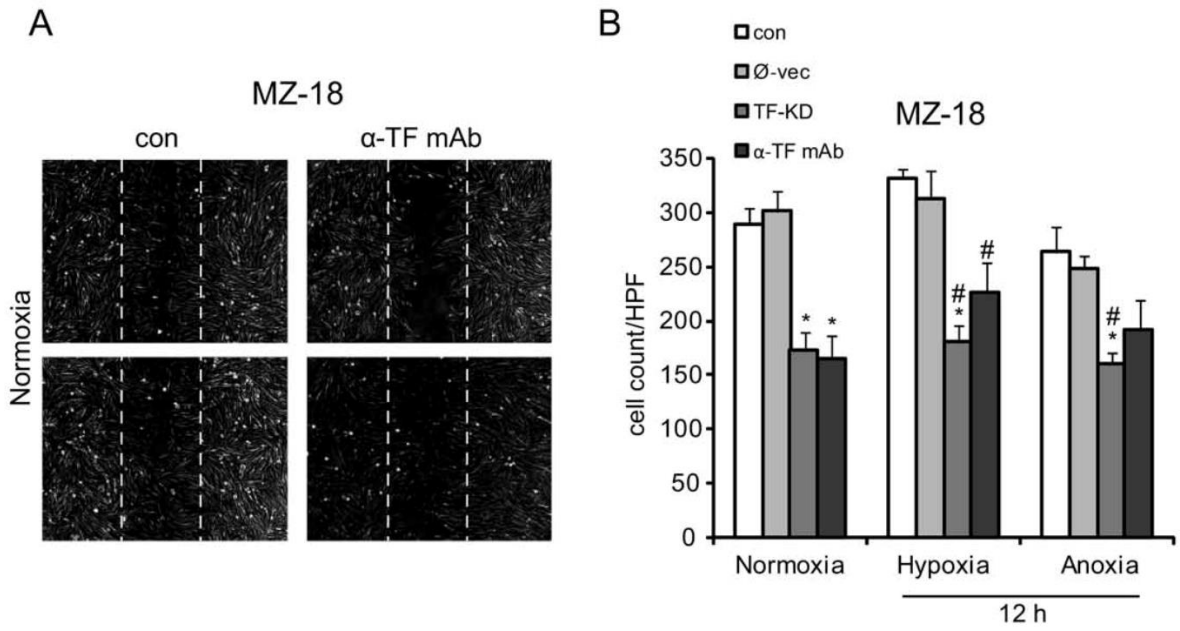

Figure 23: Glioma cell migration is mediated by TF signaling. MZ-18 cells with or without TF signaling inhibition were seeded and cultivated to optical confluence. The subsequently performed scratch was followed by a medium change after which mAb TF9-10H10 was added where indicated. (A) Representative microscopic images of migrated MZ-18 cells after inhibition of TF signaling by mAb TF9-10H10 or by knockdown of TF (TF-KD). Untreated cells (con) and cells treated with an empty control vector were used as controls. Images are taken after 12 h of normoxia, hypoxia (1% O2) or anoxia (0.1% O2). The dimensions of the scratch are indicated by white bars. (B) Cell count quantification of cells remigrated into the scratch. After 12 h of normoxia, hypoxia (1% O2) or anoxia (0.1% O2) treatment, remigrated cells were counted as described in Experimental procedures. * P<0.05 compared to normoxic controls. # P<0.05 compared to untreated control cells cultivated under identical oxygen concentrations.

Selected Publications

Gessler, F., Bernstock, J. D., Braczynski, A., Lescher, S., Baumgarten, P., Harter, P. N., Mittelbronn, M., Wu, T., Seifert, V., & Senft, C. (2019). Surgery for Glioblastoma in Light of Molecular Markers: Impact of Resection and MGMT Promoter Methylation in Newly Diagnosed IDH-1 Wild-Type Glioblastomas. Neurosurgery, 84(1), 190–197.

Gessler, F., Bernstock, J. D., Behmanesh, B., Brunnberg, U., Harter, P., Ye, D., Friedman, G. K., Hansmann, M. L., Wagner, M., Seifert, V., Weise, L., & Marquardt, G. (2019). The Impact of Early Corticosteroid Pretreatment Before Initiation of Chemotherapy in Patients With Primary Central Nervous System Lymphoma. Neurosurgery, 85(2), 264–272.

Bernstock, J. D., Vicario, N., Li, R., Nan, L., Totsch, S. K., Schlappi, C., Gessler, F., Han, X., Parenti, R., Beierle, E. A., Whitley, R. J., Aban, I., Gillespie, G. Y., Markert, J. M., & Friedman, G. K. (2020). Safety and efficacy of oncolytic HSV-1 G207 inoculated into the cerebellum of mice. Cancer gene therapy, 27(3-4), 246–255.

Bernstock, J. D., Vicario, N., Rong, L., Valdes, P. A., Choi, B. D., Chen, J. A., DiToro, D., Osorio, D. S., Kachurak, K., Gessler, F., Johnston, J. M., Jr, Atkinson, T. P., Whitley, R. J., Bag, A. K., Gillespie, G. Y., Markert, J. M., Maric, D., & Friedman, G. K. (2019). A novel in situ multiplex immunofluorescence panel for the assessment of tumor immunopathology and response to virotherapy in pediatric glioblastoma reveals a role for checkpoint protein inhibition. Oncoimmunology, 8(12), e1678921.

Won, S. Y., Dubinski, D., Behmanesh, B., Bernstock, J. D., Seifert, V., Konczalla, J., Tritt, S., Senft, C., & Gessler, F. (2020). Management of hydrocephalus after resection of posterior fossa lesions in pediatric and adult patients-predictors for development of hydrocephalus. Neurosurgical review, 43(4), 1143–1150.

Aging and neurodegeneration: from basic science to clinical translation

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State-of-the Art

Neurodegenerative diseases are a major burden of the aging society. Currently disease mechanisms are often solely investigated from the side of the degenerative insults. However, the main risk factor for neurodegenerative diseases is aging. Much attention is drawn to understand the respective underlying mechanisms. A major need is to combine these two worlds with the understanding how the organisms or the brain can escape such insults (resilience).

Overall Scientific Aim

The section for “Translational Neurodegeneration” will uniquely combine these two strategies to ultimately find causative therapies for neurodegenerative diseases. Main strategies for therapeutic interventions in neurodegeneration are:

1) Strengthening healthy aging processes to improve resilience against neurodegeneration
2) Reduction or attenuation of pathological aging
3) Therapy of neurodegenerative diseases by specific intervention of the respective pathophysiology

These three strategies must not be viewed on their own, but particularly the combination of these three approaches harbours large potentials in the field of neurodegeneration. This is especially true since many if not all currently accused mechanisms for neurodegeneration increase with aging (reduced clearance of proteins, reduced efficacy in DNA damage repair and so on).

Curriculum Vitae
1999 - 2005 MD-PhD-student, Technische Universität Dresden and University of Ulm, State exam
2005 - 2013 Resident in the Department of Neurology, Medical Faculty Carl Gustav Carus at the Technische Universität Dresden
2014 Habilitation, Dept. Neurology, Technische Universität Dresden
2013 - 2018 Senior neurologist, Department of Neurology, Technische Universität Dresden
2016 - 2018 Full professor (W2) Neurology with focus on Neurodegenerative Diseases, University Medical Centre Rostock, Technische Universität Dresden
2016 - 2018 Deputy Director, Center for Healthy Aging, Technische Universität Dresden
Since 2019 Full professor (W2), Neurology and Neurodegenerative Diseases and Head of the Translational Neurodegeneration Section „Albrecht-Kossel“ (Schilling Professor), Department of Neurology, University Medical Centre Rostock

Projects, Methods & Technologies

Neuroresilience: Physiological vs. Pathological aging

We try to identification and use of intrinsic (e.g. REST, GATA4, and novel candidates) and extrinsic (serum, and novel candidates) factors of pathological aging and how to use them in the overall strategy of novel treatments in neurodegeneration.

Disease modelling: from pathophysiology to individualised causal therapy

We intend to understand the molecular pathophysiology of neurodegeneration including work on protein clearance machinery, resilience against DNA damage and axonal degeneration, cell nuclear integrity and disease spreading.

Clinical science: bidirectional clinical translation

One of our main strategies is the bidirectional clinical translation. This will include anterograde translation of novel concepts (e.g. DNA damage), novel biomarkers or novel treatment strategies (e.g. lipoic acid, fampyra, dasatinib, which are already novel targets ready for clinical translation) using both observational studies and clinical trials. The second approach is to continuously retrogradely translate clinical data/established and novel clinical markers into basic scientific models and approaches. These strategies also will ultimatively help to overcome translational roadblocks.

The main models used:

The main model used in the new section will be human cell models of pathological aging (progeria infantilis and adultorum, down syndrome) and neurodegeneration (main focus on ALS/FTD, but including also old age neurodegeneration [ALS/FTD] and young age neurodegeneration [Chorea-Acanthocytosis, Nieman pick type C, NCL]). These include mainly human induced pluripotent stem cells and their derivatives as well as directly programmed human cells.

Selected Publications

Glaß H, Neumann P, Pal A, Reinhardt P, Storch A, Sterneckert J, Hermann A. (2020). Combined Dendritic and Axonal Deterioration Are Responsible for Motoneuronopathy in Patient-Derived Neuronal Cell Models of Chorea-Acanthocytosis. Int J Mol Sci., 21(5).

Kuta R, Larochelle N, Fernandez M, Pal A, Minotti S, Tibshirani M, St Louis K, Gentil BJ, Nalbantoglu JN, Hermann A, Durham HD.(2020). Depending on the stress, histone deacetylase inhibitors act as heat shock protein co-inducers in motor neurons and potentiate arimoclomol, exerting neuroprotection through multiple mechanisms in ALS models. Cell Stress Chaperones. 25, 173–191.

Hagenacker T, Wurster CD, Günther R, Schreiber-Katz O, Osmanovic A, Petri S, Weiler M, Ziegler A, Kuttler J, Koch JC, Schneider I, Wunderlich G, Schloss N, Lehmann HC, Cordts I, Deschauer M, Lingor P, Kamm C, Stolte B, Pietruck L, Totzeck A, Kizina K, Mönninghoff C, von Velsen O, Ose C, Reichmann H, Forsting M, Pechmann A, Kirschner J, Ludolph AC, Hermann A, Kleinschnitz C. (2020). Nusinersen in adults with 5q spinal muscular atrophy: a non-interventional, multicentre, observational cohort study. Lancet Neurol. 19(4), 317-325.

Naumann M, Peikert K, Günther R, van der Kooi AJ, Aronica E, Hübers A, Danel V, Corcia P, Pan-Montojo F, Cirak S, Haliloglu G, Ludolph AC, Goswami A, Andersen PM, Prudlo J, Wegner F, Van Damme P, Weishaupt JH, Hermann A. (2019). Phenotypes and malignancy risk of different FUS mutations in genetic amyotrophic lateral sclerosis. Ann Clin Transl Neurol. 6(12), 2384–2394.

Naumann M, Pal A, Goswami A, Lojewski X, Japtok J, Vehlow A, Naujock M, Günther R, Jin M, Stanslowski N, Reinhardt P, Sterneckert J, Frickenhaus M, Pan-Montojo F, Storkebaum E, Poser I, Freischmidt A, Weishaupt JH, Holzmann K, Troost D, Ludolph AC, Boeckers TM, Liebau S, Petri S, Cordes N, Hyman A, Wegner F, Grill S, Weis J, Storch A, Hermann A. (2018). Impaired DNA damage response signaling by FUS-NLS mutations leads to neurodegeneration and aggregation formation. Nature Communucations, 9:335.

Computational State Space Models and Sensor-Based Behaviour Analysis

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State-of-the Art

The objective of computational behaviour analysis is the reconstruction of hidden state variables of human behaviour from sensor data. Technological advances in wearable sensors make it possible to monitor human activity in everyday life – for instance, by using smart watches, fitness trackers, etc. Such systems are able to provide data on motor activity, location, and vital signs.

From a medical care perspective, the ability to obtain data from everyday situations creates the opportunity to understand how clinical status manifests itself in everyday behaviour. This allows a behaviour-based detection of change in status, assessing the effect of therapeutic interventions based on behaviour measurement, and also real-time intervention in reply to specific behavioural phenomena, such as disorientation.

The focus of our research are methods for recursive Bayesian state estimation and probabilistic artificial intelligence for providing the state estimation algorithms that turn sensor data into information on behaviour. With respect to the estimation target, we specifically look at cognitive function and at the ability to perform structured, goal-directed activities, such as given by the instrumental activities of daily living.

Overall Scientific Aim

From a state-estimation perspective, cognitive status includes long-term variables, such as presence of dementia, as well as short-term variables, such as acute disorientation. It is not known, if these variables have an effect on everyday behaviour that can be detected – possibly in real time – in the signals of wearable sensors. Specifically, the ability for a real-time detection of state changes in short-term variables would allow providing just-in-time assistive interventions effectively and with minimal intrusion on self-efficacy.

With respect to structured, goal-directed activities, it turns out that the reconstruction of composite everyday activities poses a substantial challenge to current technology for the real time analysis of structured time series. Neural methods – such as LSTM – require massive amounts of labelled training data, which is not available in this setting. On the other hand, knowledge-based Bayesian methods struggle with the complex non-metric and discrete state space created by everyday activities. Specifically, state-of-the-art mechanisms for nonlinear non-Gaussian sequential state estimation, based on particle filters and Markov-Chain Monte-Carlo, show a very high variance and low recognition performance.

Curriculum Vitae
1983 - 1988 Dipl.-Ing. (MSc) Computer Science, Darmstadt Technical University
1989 - 1995 Doctorate (scl) in Computer Science, Darmstadt Technical University
1995 - 2002 Head of Department, “Mobile Multimedia Technologies”, Fraunhofer IGD Rostock
2002 - 2004 Head of Department, “Interactive Multimedia Appliances”, Fraunhofer IGD Darmstadt
2005 Full Professor (C3), Mobile Multimedia Systems, University of Rostock
2006 - 2015 Speaker, DFG RTG 1424 MuSAMA
2007 - 2011 Founding Chairman, Interdisciplinary Department “Aging of the Individual and Society” (AGIS), University of Rostock, since 2011 Member of the Board
2016 - 2018 Director, Institute for Computer Science, University of Rostock
Since 2019 Founding Director, Institute for Visual and Analytic Computing, Rostock University

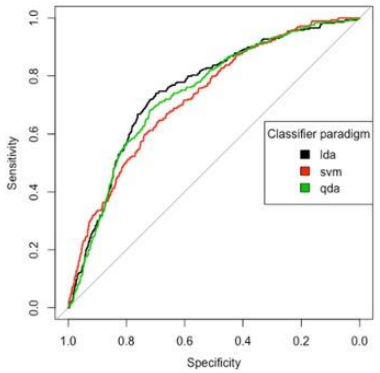

Figure 24: Way-finding study: (top) route. (bottom) AUC for detecting disorientation on accelerometer signals using different classifiers. Note the superior performance of LDA, indicating that crucial factor here is the choice of features.

In cooperation with the DZNE Rostock / Greifswald we have been able to establish two important results on the detectability of the effect of cognitive states in everyday behaviour. Based on a study with n=46 subjects we found that the presence of clinically probable Alzheimer's dementia was detectable in an individual with an accuracy of 91% (AUC=.96) in accelerometric protocols of unrestricted everyday motion behaviour. In a recent study with n=13 subjects, we were able to show that acute disorientation in outdoor wayfinding has a significant effect on specific features of accelerometric sensor signals (AUC=.75). This finding is interesting, as the target was substantially more challenging than in the above investigation: it was real-time detection (i.e., classification of a 10 second signal window) of a cognitive state prior to its manifestation in action (such as taking a wrong turn). Thus an AUC of .75 is an encouraging result. Both results suggest that long- and short-term variables of cognitive state have an effect on signal features of wearable sensors that can be exploited in state estimation and behaviour reconstruction.

For addressing the complexity of inference, we have introduced the methods of Computational State Space Models (CSSMs) and the Marginal Filter (MF).

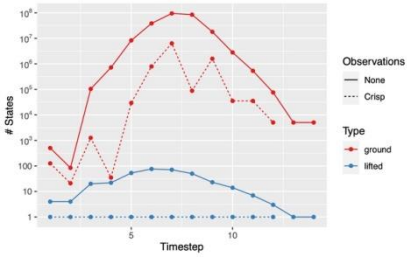

Figure 25: Example of state space reduction by the Lifted Marginal Filter, for a simple multi-agent action sequence. Red ("ground"): marginal filter, Blue ("lifted"): lifted marginal filter.

CSSMs enable the construction of transition models for Bayesian filters using knowledge-based techniques by exploiting prior knowledge on the causal structure of everyday actions to formulate elements of a probabilistic model. The MF provides an efficient Bayesian filter for these models that is 80–125 times more efficient than a particle filter. We were able to show that with this method it becomes possible to create a detailed reconstruction of an important instrumental activity of daily living, preparing and taking a meal, which so far has not been achieved with conventional Bayesian filter methods.

Recently, we introduced the Lifted Marginal Filter (LMF), an improvement to the MF that combines maximally parallel probabilistic multiset rewriting systems with techniques from statistical relational learning to address the state-space explosion caused by multi-person settings. The LMF achieves a factorial reduction in the effective number of MF states, potentially enabling state estimation in correlated multi person environments – such as geriatric wards or nursing homes – without requiring ethically controversial privacy compromising tracking technology.

Selected Publications

Lüdtke, S., Schröder, M., Bader, S., Kersting, K., & Kirste, T. (2018). Lifted Filtering via Exchangeable Decomposition. Proceedings of the 27th International Joint Conference on Artificial Intelligence. IJCAI-ECAI 2018, Stockholm.

Lüdtke, S., Schröder, M., Krüger, F., Bader, S., & Kirste, T. (2018). State-Space Abstractions for Probabilistic Inference: A Systematic Review. Journal of Artificial Intelligence Research, 63, 789–848.

Schaat, S., Koldrack, P., Yordanova, K., Kirste, T., & Teipel, S. (2019). Real-Time Detection of Spatial Disorientation in Persons with Mild Cognitive Impairment and Dementia. Gerontology, 1–10.

Lüdtke, S., Gehrke, M., Braun, T., Möller, R., & Kirste, T. (2020, Juni). Lifted Marginal Filtering for Asymmetric Models by Clustering-based Merging. Proceedings of the 24th European Conference on Artificial Intelligence (ECAI). ECAI, Santiago de Compostela, Spain.

Lüdtke, S., & Kirste, T. (2020). Lifted Bayesian Filtering in Multiset Rewriting Systems. Journal of Artificial Intelligence Research, 69, 1203–1254.

Risk factors and therapeutic approaches for psychiatric disorders in childhood

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State-of-the Art

Mental health problems are a major health issue for child and adolescent health. Psychiatric disorders in children and adolescents are severe disorders with life-long impact on mental (and physical) health. Several risk factors are identified: genetic and biological but also social and environmental factors contribute to the development of psychiatric and neurodevelopmental disorders in early life. Transgenerational aspects of transmission are of high interest for prevention. A high variety of evidence based treatments are available, including psychotherapy, pharmacotherapy and innovative interventions like bright-light therapy (BLT), transcranial direct current stimulation (tDCS) etc. There is a lack of knowledge about stepped care interventions, personalized interventions and risk adapted prevention and interventions.

Overall Scientific Aim

We focus both on prevention and intervention in at risk populations for child and adolescent psychiatric disorders. Psychopathology in childhood and adolescence shows high variability. Symptoms changes over time. Therefore, trajectories of externalizing as well as internalizing symptoms and transdiagnostic entities are of main interest to identify specifiers of psychopathology. Affective dysregulation (AD) with anger, irritability, impulsivity and emotional symptoms is such a transdiagnostic category. In the international context AD is studied as a core symptom in childhood which leads to severe psychopathology and limited social participation in later life.

Second focus lies on environmental risk factors: at risk populations are characterized by several factors, like experience of early adversities, intellectual deficits and social characteristics. Low SES, parental mental health problems or low educational levels are main risk factors for psychopathology in off-springs. Combining research on specifiers of psychopathology (phenotypes, biomarkers and neurobiological aspects) with prevention and intervention research we want to improve early intervention and therapy outcomes.

Curriculum Vitae
1992 - 1999 Medical studies at Universities of Rostock, Vienna and Free University Berlin
2001 Medical Thesis at Institute of History of Medicine Free University Berlin
2010 Habilitation in Child and Adolescent Psychiatry University of Ulm
2006 - 2011 senior consultant and Deputy Head of the Department for Child and Adolescent Psychiatry University of Ulm
2011 - 2019 Research group leader Department for Child and Adolescent Psychiatry University of Ulm
2011 - 2016 Head of Department for Child and Adolescent Psychiatry, Vivantes Berlin
2016 Full Professor Brandenburg Medical School
Since 2019 Full Professor (W3) for Child and Adolescent Psychiatry and Psychotherapy at University Rostock and Head of Department for Child and Adolescent Psychiatry, Neurology, Psychosomatics and Psychotherapy, University Medical Centre Rostock

Projects, Methods & Technologies

Studies and projects at the Department Child and Adolescent Psychiatry (CAP) at UMR within the field of prevention and intervention are e.g. the Rostock Longitudinal Study (ROLS, funded by DFG) which is running over 50 years and identifies risk factors, environmental factors for mental health as well resilience factors. The CAP UMR is partner site of several BMBF-funded prevention and intervention trials on affective dysregulation (ADOPT study, BMBF 01GL1741F), non-suicidal self-injuring behaviour (NSSI) (STAR study, BMBF 01GL1747A), sleep and depression (Delight study, BMBF 01KG1713). Interventions in these studies consist by comprehensive assessment including neurobiological parameters combined with either stepped care interventions (online and intensified treatment) or innovative interventions like BLT.

We are involved in the multicentre CHIMPS-study (Federal Joint Committee 01NVF18003) which aims to prevent transgenerational risk of children with mentally ill parents by stratified prevention strategies. Children with intellectual disabilities or learning disorders at special risk both for physical as well as for mental health and adverse childhood experiences (ACE). ACE are the strongest predictors for poor health outcome also in later life with an increased risk for cardiovascular, metabolic and psychiatric disorders and substance abuse. We developed within the study “Emma-Untouchable” (BMBF, FKZ: 1KR1206) a training for prevention of sexual abuse tailored for girls with intellectual disabilities. Early substance abuse increases the risk for severe comorbid psychiatric disorders as well as psychiatric disorders in adolescence are accompanied with increased risk for substance abuse. The study IMAC-Mind (BMBF FKZ: 01GL1745E) also targets adolescents with intellectual impairment. Boys with mild to borderline intellectual disability are educated with a combination of drug education and mindfulness. Neurobehavioral regulation is modelled as a biopsychological factor moderating the effectivity of prevention. The dependent variable is the time between the end of the intervention and the first event of drunkenness. The study is part of the IMAC-consortium (https://imac-mind.de/) examining conditions of abuse among youth.

Further studies are running on telemedical and e-health applications combined with EEC for identification of biomarkers (eMICHI) and pain and tDCS. The latter study is based on the new established comprehensive centre for pain in children at UMR in cooperation with the Department of Paediatrics: here we will focus on neurobiological mechanisms of pain, experimental treatments (e.g.t-DCS) and coping mechanisms of patients.

Selected Publications

Dueck A, Reis O, Bastian M, van Treeck L, Weirich S, Haessler F, Fiedler A, Koelch M, Berger C (2020). Feasibility of a Complex Setting for Assessing Sleep and Circadian Rhythmicity in a Fragile X Cohort. Front Psychiatry 11, 361.

Koelch MG, Döpfner M, Freitag CM, Dulz B, Rösler M. (2019). Störung des Sozialverhaltens und Antisoziale Persönlichkeitsstörung - Herausforderungen in der Transition vom Jugend- zum Erwachsenenalter. Fortschr Neurol Psychiatr. 87(11), 634-637.

Jurek B, Chayka M, Lang K, Kreye J, Kraus L, Fidzinski P, Kornau HC, Dao LM, Wenke N, Long M, Rivalan M, Winter Y, Leubner J, Herken J, Mayer S, Mueller S, Boehm-Sturm P, Dirnagl U, Schmitz D, Kölch M, Prüss H (2019). Maternal human NMDA receptor NR1 autoantibodies impair neonatal brain function and behavior in a murine model of gestational transfer. Ann Neurol. 86(5), 656-670.

Cunitz K, Bühler A, Willmund GD, Ziegenhain U, Fegert JM, Zimmermann P, Kölch M (2019). Interventionsprogramme bei psychischen Belastungen von Kindern von Angehörigen des Militärs in den USA – Ergebnisse eines systematischen Literaturreviews hinsichtlich der Übertragbarkeit auf Deutschland. Z Kinder- und Jugendpsychiatrie 7(6), 503-526.

Döpfner M, Katzmann J, Hanisch C, Fegert JM, Kölch M, Ritschel A, Treier AK, Hellmich M, Roessner V, Ravens-Sieberer U, Banaschewski T, Görtz-Dorten A; ADOPT Consortium (2019). Affective dysregulation in childhood - optimizing prevention and treatment: protocol of three randomized controlled trials in the ADOPT study. BMC Psychiatry.19(1), 264.

Psychiatry and Neurology after 1945 in Germany

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Fundamental questions about the role of psychiatry and neurology in the GDR still unanswered. A system of basic structures is largely missing. Psychiatry and neurology were also part of the state-controlled health system of the German Democratic Republic (GDR).

In the project "Psychiatry in the GDR between help, custody and abuse?" we investigate in cooperation with the Clinic of Psychiatry, University Medical Centre Greifswald, within the research network "Seelenarbeit im Sozialismus - SiSaP" the structural anchoring and social status of psychiatric care after 1945 in the Soviet Occupation Zone and GDR. We are also interested in the structures relevant for psychiatry within the GDR health care system in the period from 1945 to 1990. This project is funded by the Federal Ministry of Education and Research.

Qualitative interviews with contemporary witnesses who were confronted with psychiatry in the GDR in some form between 1945 and 1989 will be used to support this goal. The specialist publications published in the GDR are systematized and analysed in terms of content. By means of a critical comparison with "the everyday experiences" it will be examined to what extent these were an expression of the respective research and practice. The main focus will be on interview-related work with contemporary witnesses (former actors and patients) and on archival studies. In addition to focusing on the patient perspective, the aim is to identify the links between those responsible and the Ministry for State Security.

The results are made available in the form of bibliographies and literature collections as well as an online database on archival records of psychiatry in the GDR for future scientific projects. An important concern is to inform the public about the results via a homepage, through regular events, information brochures, the design of a travelling exhibition.

The project "Provenance Research on the Non-European Anthropological Collection of the University Medical Center Rostock" is funded by the Stiftung Deutsches Zentrum Kulturgutverluste. The Department of the History of Medicine and the Institute of Anatomy at the Rostock University Medical Centre are investigating the collection of non-European human skulls that are currently housed in the Institute of Anatomy. Around 150 years ago, the physician Friedrich Merkel (1845-1919) brought these to the Institute of Anatomy "Race-skull collection" in order to expand his teaching areas, to include anthropology.

Curriculum Vitae
1990–1996 State exam in Medicine, Martin-Luther-University of Halle-Wittenberg
1999 Doctorate in obstetric and perinatology care from the perspective of the woman in childbirth, Medical Faculty, Martin-Luther-University of Halle-Wittenberg
2002 Specialist in Psychiatry and Psychotherapy
2011 Habilitation in Psychiatry, Medical Faculty, University of Rostock
2007–2018 Senior psychiatrist, Department of Psychiatry and Psychotherapy, University of Rostock
Since 2012 Speaker of the Section History, German Association for Psychiatry, Psychotherapy and Psychosomatics (DGPPN)
Since 2018 Associate Professor of Psychiatry, University Medical Centre Rostock
Since 2018 Head of Department of the History of Medicine, University Medical Centre Rostock

Picture 13: Project poster "Psychiatry in the GDR between help, custody and abuse?"

Selected Publications

Kumbier E (2019). Gift im Filter: der Einsatz von „Detoxikationsverfahren" bei Schizophrenien. Nervenarzt 90: 1135–1143.

Kumbier E, Karenberg A (2019). „Einen Lehrauftrag für Neurologie hat Herr C. ja nicht" – Die schwierige Disziplingenese der Neurologie zwischen Innerer Medizin und Psychiatrie. In: Reisinger EC, Haack K (Hrsg.) Die Medizinische Fakultät der Universität Rostock – 600 Jahre im Dienst der Menschen. Böhlau, Köln, Wien, Weimar, S. 145–159.

Kumbier E, Haack K (2019). Spezialisierung und Professionalisierung – Die Herausbildung der modernen Medizin an der Universität Rostock unter besonderer Berücksichtigung der Psychiatrie. In: von der Höh M (Hg.) Traditionen, Zäsuren, Dynamiken: 600 Jahre Universität Rostock. Böhlau, Köln, Wien, Weimar, S. 287–312.

Kumbier E (2020, Hg.). Psychiatrie in der DDR II. Weitere Beiträge zur Geschichte. Schriftenreihe zur Medizin-Geschichte, Bd. 27, be.bra wissenschaft verlag, Berlin.

Kumbier E, Haack K (2020): Die Therapeutische Gemeinschaft und das Arzt-Schwester-Patient-Verhältnis in der Psychiatrie zwischen therapeutischem Anspruch und sozialistischer Realität. In: Wahl M (Hg), Volkseigene Gesundheit: Reflexionen zur Sozialgeschichte des Gesundheitswesens der DDR. Franz Steiner, Stuttgart, S. 111–134.

Neurobiology and physics of locomotor systems in insects

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State-of-the Art

Locomotion is a key for survival in nature and has thus shaped the neural and biomechanical apparatus in humans and animals. Complex locomotor behaviors result from rules with which sensory information is encoded into muscle commands. High temporal precision and signal-to-noise ratio is typically needed in feedback control loops and any imprecision or loss of neural feedback limits posture stability and propulsion efficiency. These constraints are most relevant in systems with small locomotor cycle duration of few milliseconds (Fig. 26).

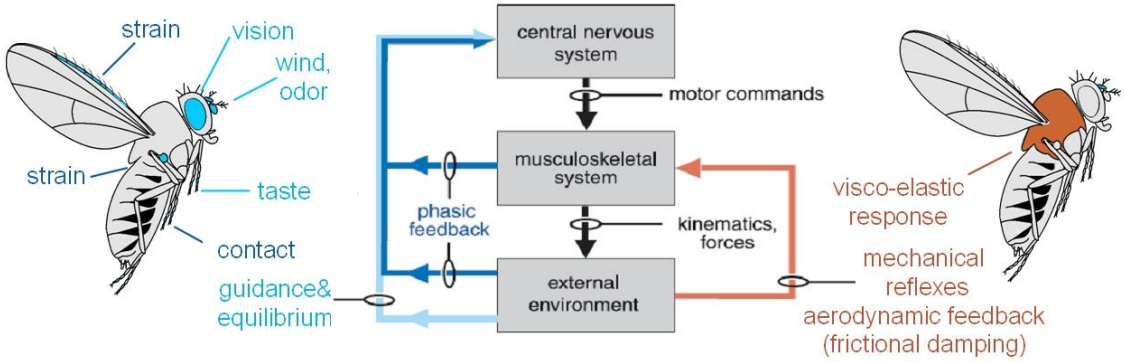

Figure 26: Principles of locomotion. Propulsion systems in humans and animals require the interaction of various components covering neurobiological and biomechanical structures.

Oscillatory motion of fins and wings in animals may reach frequency of up to 800 Hz and thus cycle times below the duration of single action potentials. Compared to human locomotor behaviour, this requires specialized concepts for both muscle contraction and neural feedback control.

Overall Scientific Aim

Discovering the cascade of locomotor control is a key for understanding posture balance and propulsion and tightly links scientific concepts from Neurobiology, Biomechanics and

Curriculum Vitae
1994 - 1996 Research associate at University of Chicago, USA
1996 - 1997 Postdoc at University of California at Berkeley, USA
1997 - 1999 Postdoc at the biocenter of the University of Würzburg, Germany
1999 - 2001 Research associate at the biocenter of the University of Würzburg, Germany
2001 - 2007 Assistant professor and head of a BioFuture research group, University of Würzburg, Germany
2008 - 2012 Assistant professor and head of a Heisenberg research group, University of Ulm
2013 - 2021 Full Professor, chair of the department of Animal Physiology, University of Rostock

Mathematics. My lab investigates the neurobiology and physics of this process in flight of the model system Drosophila, using wildtype and transgene animals. Main goal is to understand how animals perceive and process visual information and how sensory feedback from the environment interferes with the biomechanical limits of the locomotor system.

Projects, Methods & Technologies

Our methods cover electrophysiological recordings of flight muscle activity, behavioural genetics using GAL4/UAS tools, live cell recording of calcium activation during manoeuvring flight, locomotor essays for assessing locomotor limits, numerical simulations of air flows around the wings and robotics as physical test beds. Respiratory measurements and genetically induced expression of ion channels in locomotor muscles allows estimating propulsive efficiency and how animals control and balance power output during locomotion (Fig. 27). As the typical duration of muscle contraction in vertebrate skeletal muscles is up to 100-times longer than needed in flight of insects, the asynchronous insect flight muscle employs calcium- and strain-dependent troponin isoforms that allows high contraction frequencies without synchronized neural activation by motoneurons. Numerical simulations of neural integration in flies show that the temporal precision of sensory feedback is due to electrical synapses and synaptic integration at the level of motoneurons in the periphery - not the central nervous system (CNS). By circumventing higher brain structures, this concept increases neural computing speed and highlights local neural circuits for locomotor control in general. The combined bionic knowledge of our research impacts other scientific fields and also contributes to the development of small man-made flight devices using biological principles for propulsion.

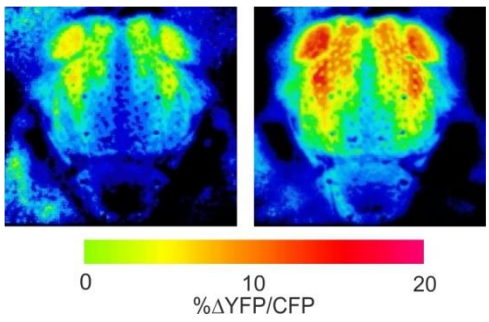

Figure 27: In vivo calcium imaging of flight power muscles in flying Drosophila. Color-coded calcium activity at rest (left) and flight (right). Calcium probe is Cameleon 2.1 expressed by Mef2. Top view on thorax. YFP, yellow fluorescent protein; CFP, cyan fluorescent protein.

Selected Publications

Lehmann, F.-O. and Wehmann, H.-N. (2019). Aerodynamic interference depends on stroke plane spacing and wing aspect ratio in damselfly model wings. Internat. J. Odonatology.

Wehmann, H.-N., Heepe, L., Gorb, S. N., Engels, T. and Lehmann, F.-O. (2019). Local deformation and stiffness distribution in fly wings. Biology Open 8(1), bio038299.

Krishna, S., Cho, M., Wehmann, H.-N., Engels, T. and Lehmann, F.-O. (2020). Wing design in flies: properties and aerodynamic function. Insects11(8), 466.

Farisenkov, S., Kolomenskiy, D., Engels, T., Lapina, N., Petrov, P., Lehmann, F.-O., Onishi, R., Liu, H., and Polilov, A. (2020). Aerodynamic performance of a bristled wing of a very small insect. Exp. Fluids 61, 194.

Engels, T., Wehmann, H.-N., and Lehmann, F.-O. (2020). Three-dimensional wing structure attenuates aerodynamic efficiency in flapping fly wings. J. R. Soc. Interface 17, 20190804.

Impact of traumatic stress on mental and physical health

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State-of-the Art

Traumatic stress in general and childhood maltreatment (CM) in particular are among the most important psychosocial factors impacting on mental and physical health identified so far. This is particularly true for those involving inflammatory processes. Moreover, traumatic experiences and related phenomena (e.g. dissociation) contribute to symptom severity, chronicity, treatment resistance, and thus poor overall prognosis. Traumatic stress exerts its devastating effects by severely impairing personality functioning (PF), a trans-diagnostic construct important for psychosocial functioning and in the vast majority of mental disorders. Treatment approaches to improve PF and to overcome the sequelae of traumatic experiences comprise different psychotherapeutic methods.

Overall Scientific Aim

Improving the detailed assessment of exposure to traumatic stress across the lifespan, particularly with respect to CM, has the potential to contribute to individualized diagnostic, preventive and treatment strategies by identifying people at risk for its devastating effects on both mental and physical health. Likewise, assessing personality dysfunctions in both general population and clinical samples, their developmental antecedents, and their evolution over the lifespan may guide the improvement of psychotherapeutic strategies and to develop novel approaches.

Projects, Methods & Technologies

Our primary research methods are clinical approaches aiming to develop and improve diagnostic methods and psychotherapeutic interventions. We predominantly apply diagnostic procedures carried out by clinical experts, self-report measures, as well as state of the art methods for the evaluation of treatment programs. These do not only include up-to-date measures, but also elaborated statistical approaches (e.g. multilevel random effects models). For further in-depth analyses, we have adopted sophisticated paradigms from social psychology (i.e. the Implicit Association Test).

Moreover, our research group has expertise in standardized laboratory stress paradigms (Trier Social Stress Test and its placebo variant) and neuroendocrine tests (e.g. the dexamethasone/ corticotropin-releasing hormone [DEX/CRH] test).

Our psychotherapy research focuses predominantly on naturalistic and effectiveness studies using large, real-world treatment samples of inpatients with high external validity and an emphasis on

Curriculum Vitae
1988 - 1995 State exam in Medicine, RWTH Aachen and Medical University Lübeck
1995 Doctoral thesis on psychiatric comorbidity in neurologic inpatients with conversion disorders
1995 - 2001 Residency in psychiatry and psychotherapy, University Medicine Greifswald
1995 - 2001 Residency in psychiatry and psychotherapy, University Medicine Greifswald
2001 - 2007 Senior psychiatrist, Department of Psychiatry and Psychotherapy, University Medicine Greifswald
2005 Habilitation in Psychiatry, Psychotherapy and Psychosomatic Medicine, University Medicine Greifswald
2008 - 2011 Senior and Deputy, Department of Psychosomatic Medicine and Psychotherapy, University Medical Center Hamburg
2012 - 2019 Medical Director Fachklinikum Tiefenbrunn (Göttingen)
Since 2019 Full Professor (W3) for Psychosomatic Medicine and Psychotherapy and Director of the Department of Psychosomatic Medicine and Psychotherapy, University Medical Centre Rostock

personality functioning. Additionally, the identification of psychosocial factors positively or negatively predicting treatment outcome is a major interest, alongside with a focus on negative or side effects of psychotherapy. We are currently planning a randomized controlled trial (RCT) for the psychotherapeutic treatment of patients with psychogenic, non-epileptic seizures (PNES), a largely understudied stress-related mental disorder.

Corresponding to our major research interest we have focused on stress-related mental disorders including dissociative, conversion, somatoform, depressive and borderline personality disorders. Moreover, we are familiar with anxiety, other personality disorders and severe mental illness (i.e. schizophrenia spectrum disorders) as well.

Having implemented the assessment of potentially traumatic experiences and their most prototypical sequelae, i.e. posttraumatic stress disorder (PTSD) in the 1st follow-up of the "Study of Health in Pomerania" (SHIP), we demonstrated the utmost relevance of traumatic stress and PTSD for mental health in specific age groups and their impact on somatic morbidity in the general population.

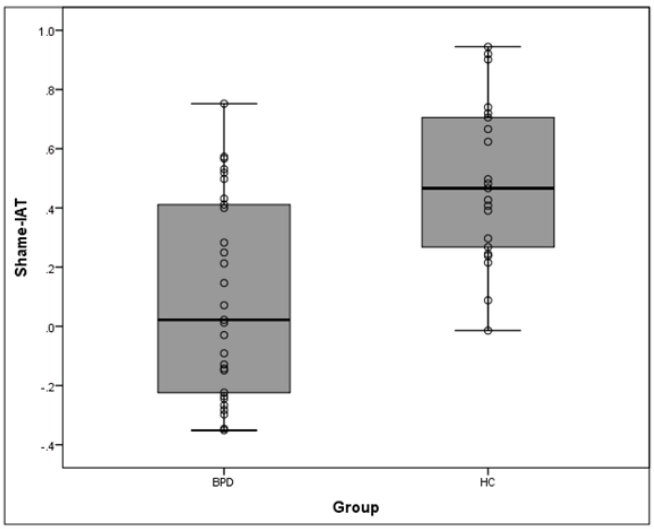

Figure 28: Boxplots including single case values of Shame-IAT for patients with BPD and healthy controls (HC).

The integration of biomarkers, genetic polymorphisms and objective (subclinical) disease markers (e.g. data from carotid ultrasound or spirometric lung function) into our analyses allowed gaining further insights into the mechanisms and pathways, by which traumatic stress 'translates' into somatic pathology and physical illness. Moreover, having developed and evaluated psychometrically sound and feasible methods for the retrospective assessment of the various dimensions of childhood maltreatment (CM) including the different types of abuse and neglect to be used in both epidemiological and clinical studies, we were able to analyse the deleterious effects of these specific forms of traumatic stress occurring early in life. Based on the epidemiological data of SHIP, we demonstrated their negative consequences on both mental and physical health in a detailed and nuanced way by integrating genetic, biological and objective disease markers. In addition to this general population approach, we have extensively investigated the differential impact of traumatic stress in general and of CM in particular on mental health and various dimensions of psychosocial functioning in diverse populations like patients with severe mental disorders, forensic inpatients, criminal offenders, former child soldiers and people exposed to political persecution.

Selected Publications

Hellmann-Regen J, Spitzer C, Kuehl LK, Schultebraucks K, Otte C, Wingenfeld K (2019). Altered cellular immune reactivity in traumatized women with and without major depressive disorder. Psychoneuroendocrinology 101, 1-6.

Zimmermann J, … Spitzer C, Wright AGC (2019). Integrating structure and dynamics in personality assessment: First steps toward the development and validation of a Personality Dynamics Diary. Psychol Assess 31, 516-31.

Leichsenring F, Jaeger U, … Spitzer C (2019). Changes in personality functioning after inpatient pschodynamic therapy: A dimensional approach to personality disorders. Psychodyn Psychiatry 47, 183-96.

Baumann E, Schmidt AF, Jelinek L, Benecke C, Spitzer C (2020). Implicitly measured aggressiveness self-concepts in women with borderline personality disorder as assessed by an Implicit Association Test. J Behav Ther Exp Psychiatry 66, 101513.

Spitzer C, Klinger-König J, … Grabe HJ (2020). Association of traumatic stress and posttraumatic stress disorder with carotid atherosclerosis: Findings from the general population. Eur J Psychotraumatol 11:1, 1815280.

Appendix

Publications 2019 – 2020

(Only PubMed-listed publications of CTNR members)

Baltrusch, Simone

Walckling, M., Waterstradt, R., & Baltrusch, S. (2020). Collagen Remodeling Plays a Pivotal Role in Endothelial Corneal Dystrophies. Investigative ophthalmology & visual science, 61(14), 1.

Schultz, J., Warkus, J., Wolke, C., Waterstradt, R., & Baltrusch, S. (2020). MiD51 Is Important for Maintaining Mitochondrial Health in Pancreatic Islet and MIN6 Cells. Frontiers in endocrinology, 11, 232.

Langer, S., Hofmeister-Brix, A., Waterstradt, R., & Baltrusch, S. (2019). 6-Phosphofructo-2-kinase/fructose-2,6-bisphosphatase and small chemical activators affect enzyme activity of activating glucokinase mutants by distinct mechanisms. Biochemical pharmacology, 168, 149–161.

Niemann, J., Zehm, C., Waterstradt, R., Tiedge, M., & Baltrusch, S. (2019). Cytosolic and mitochondrial Ca2+ concentrations in primary hepatocytes change with ageing and in consequence of an mtDNA mutation. Cell calcium, 82, 102055.

Reichart, G., Mayer, J., Zehm, C., Kirschstein, T., Tokay, T., Lange, F., Baltrusch, S., Tiedge, M., Fuellen, G., Ibrahim, S., & Köhling, R. (2019). Mitochondrial complex IV mutation increases reactive oxygen species production and reduces lifespan in aged mice. Acta physiologica (Oxford, England), 225(4), e13214.

Berger, Christoph

Dueck, A., Reis, O., Bastian, M., van Treeck, L., Weirich, S., Haessler, F., Fiedler, A., Koelch, M., & Berger, C. (2020). Feasibility of a Complex Setting for Assessing Sleep and Circadian Rhythmicity in a Fragile X Cohort. Frontiers in psychiatry, 11, 361.

Koo, P. C., Berger, C., Kronenberg, G., Bartz, J., Wybitul, P., Reis, O., & Hoeppner, J. (2019). Combined cognitive, psychomotor and electrophysiological biomarkers in major depressive disorder. European archives of psychiatry and clinical neuroscience, 269(7), 823–832.

Marx, I., Reis, O., & Berger, C. (2019). Perceptual timing in children with attention-deficit/hyperactivity disorder (ADHD) as measured by computer-based experiments versus real-life tasks: protocol for a cross-sectional experimental study in an ambulatory setting. BMJ open, 9(4), e027651.

Bertsche, Astrid

Neininger, M. P., Woltermann, S., Jeschke, S., Herziger, B., Müller, R. M., Kiess, W., Bertsche, T., & Bertsche, A. (2020). How do pediatric patients perceive adverse drug events of anticonvulsant drugs? A survey. European journal of pediatrics, 179(9), 1413–1420.

Jeschke, S., Woltermann, S., Neininger, M. P., Pauschek, J., Kiess, W., Bertsche, T., & Bertsche, A. (2020). Why do children and adolescents with epilepsy disclose or not disclose their condition to their friends?. European journal of pediatrics, 179(10), 1627–1633.

Harsanyi, J., Bertsche, T., Kiess, W., Bertsche, A., & Neininger, M. P. (2020). Final-year pharmacy and medical students do not recognise "red flags" in childhood fever. Acta paediatrica (Oslo, Norway : 1992), 109(12), 2717–2718.

Lademann, H., Bertsche, A., Petzold, A., Zack, F., Büttner, A., Däbritz, J., Hauenstein, C., Bahn, E., Spang, C., Reuter, D., Warnke, P., & Ehler, J. (2020). Acute Disseminated Encephalomyelitis with Seizures and Myocarditis: A Fatal Triad. Medicina (Kaunas, Lithuania), 56(6), 277.

Harsanyi, J., Bertsche, T., Kiess, W., Bertsche, A., & Neininger, M. P. (2020). The aim of our feverish child simulation was to identify shortcomings in university training. Acta paediatrica (Oslo, Norway : 1992), 109(12), 2826.

Kakkassery, V., Koschmieder, A., Walther, F., Lehbrink, R., Bertsche, A., Wortmann, S. B., Buchmann, J., Jäger, M., Friedburg, C., Lorenz, B., & Jünemann, A. (2020). Chorioretinale Atrophie bei kindlichem zerebralem Folatmangel – eine vermeidbare Erkrankung? [Chorioretinal atrophy in pediatric cerebral folate deficiency-a preventable disease?]. Der Ophthalmologe : Zeitschrift der Deutschen Ophthalmologischen Gesellschaft, 10.1007/s00347-020-01126-1. Advance online publication.

Woltermann, S., Jeschke, S., Herziger, B., Müller, R. M., Kiess, W., Bertsche, T., Bertsche, A., & Neininger, M. P. (2020). Anticonvulsant long-term and rescue medication: The children's perspective. European journal of paediatric neurology : EJPN : official journal of the European Paediatric Neurology Society, 28, 180–185.

Döring, J. H., Saffari, A., Bast, T., Brockmann, K., Ehrhardt, L., Fazeli, W., Janzarik, W. G., Kluger, G., Muhle, H., Møller, R. S., Platzer, K., Santos, J. L., Bache, I., Bertsche, A., Bonfert, M., Borggräfe, I., Broser, P. J., Datta, A. N., Hammer, T. B., Hartmann, H., … Syrbe, S. (2020). The Phenotypic Spectrum of PRRT2-Associated Paroxysmal Neurologic Disorders in Childhood. Biomedicines, 8(11), 456.

Mewes, S., Jeschke, S., Bertsche, T., Neininger, M. P., & Bertsche, A. (2020). Knowledge of and attitudes towards epilepsy among first- and second-year students at a German university. Epilepsy & behavior : E&B, 112, 107490.

Jeschke, S., Woltermann, S., Neininger, M. P., Pauschek, J., Kiess, W., Bertsche, T., & Bertsche, A. (2020). Interviews with patients aged 6-17 years provide valuable insights for physicians who need to deliver an epilepsy diagnosis. Acta paediatrica (Oslo, Norway : 1992), 10.1111/apa.15672. Advance online publication.

Schnabel, S., Neininger, M. P., Bernhard, M. K., Merkenschlager, A., Kiess, W., Bertsche, T., & Bertsche, A. (2019). Epilepsy: a cross-sectional study of paediatricians and general practitioners on their experiences, knowledge and handling of the disease. Epileptic disorders : international epilepsy journal with videotape, 21(2), 197–205.

Neininger, M. P., Buchholz, P., Frontini, R., Kiess, W., Siekmeyer, W., Bertsche, A., Siekmeyer, M., & Bertsche, T. (2019). Incompatible intravenous drug combinations and respective physician and nurse knowledge: a study in routine paediatric intensive care. European journal of hospital pharmacy : science and practice, 26(4), 214–217.

Hackel, K., Neininger, M. P., Kiess, W., Bertsche, T., & Bertsche, A. (2019). Epilepsy: knowledge and attitudes of physiotherapists, occupational therapists, and speech therapists. European journal of pediatrics, 178(10), 1485–1491.

Bertsche A. (2019). Wieviel MRT braucht der Neuropädiater?. RoFo : Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin, 191(S 02), S105–S106.

Brandenburg, Lars-Ove (member since 2020)

Schröder, N., Schaffrath, A., Welter, J. A., Putzka, T., Griep, A., Ziegler, P., Brandt, E., Samer, S., Heneka, M. T., Kaddatz, H., Zhan, J., Kipp, E., Pufe, T., Tauber, S. C., Kipp, M., & Brandenburg, L. O. (2020). Inhibition of formyl peptide receptors improves the outcome in a mouse model of Alzheimer disease. Journal of neuroinflammation, 17(1), 131.

Rüger, M., Kipp, E., Schubert, N., Schröder, N., Pufe, T., Stope, M. B., Kipp, M., Blume, C., Tauber, S. C., & Brandenburg, L. O. (2020). The formyl peptide receptor agonist Ac2-26

alleviates neuroinflammation in a mouse model of pneumococcal meningitis. Journal of neuroinflammation, 17(1), 325.

Blume, C., Geiger, M. F., Brandenburg, L. O., Müller, M., Mainz, V., Kalder, J., Albanna, W., Clusmann, H., & Mueller, C. A. (2020). Patients with degenerative cervical myelopathy have signs of blood spinal cord barrier disruption, and its magnitude correlates with myelopathy severity: a prospective comparative cohort study. European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society, 29(5), 986–993.

Buchmann, Johannes

Weirich, S., Reinhardt, M., Buchmann, J., Dück, A., Höppner, J., Hofmockel, R., Grözinger, M., & Häßler, F. (2020). Elektrokonvulsionstherapie – bei Kindern und Jugendlichen mit Schizophrenie wirksam und gut verträglich [Electroconvulsive Therapy - A beneficial and well tolerated therapy in children and adolescents with schizophrenia]. Fortschritte der Neurologie-Psychiatrie, 88(8), 495–499.

Büttner, Andreas

Kolbe V, Büttner A. Domestic Violence Against Men-Prevalence and Risk Factors. Deutsches Ärzteblatt International 117:534-541, 2020.

Kolbe, V., Rentsch, D., Boy, D., Schmidt, B., Kegler, R., & Büttner, A. (2020). The adulterated XANAX pill: a fatal intoxication with etizolam and caffeine. International journal of legal medicine, 134(5), 1727–1731.

Koehn, K., Buettner, A., & Lindner, I. (2020). Effect of sodium hypochlorite decontamination on the DNA recovery from human teeth. International journal of legal medicine, 134(1), 93–99.

Lademann, H., Bertsche, A., Petzold, A., Zack, F., Büttner, A., Däbritz, J., Hauenstein, C., Bahn, E., Spang, C., Reuter, D., Warnke, P., & Ehler, J. (2020). Acute Disseminated Encephalomyelitis with Seizures and Myocarditis: A Fatal Triad. Medicina (Kaunas, Lithuania), 56(6), 277.

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Tischer, T., Bebersdorf, A., Albrecht, C., Manhart, J., Büttner, A., Öner, A., Safak, E., Ince, H., Ortak, J., & Caglayan, E. (2020). Deactivation of cardiovascular implantable electronic devices in patients nearing end of life : Reality or only recommendation?. Deaktivierung kardiovaskulärer implantierbarer elektronischer Systeme bei Patienten am Lebensende : Realität oder nur Empfehlung?. Herz, 45(Suppl 1), 123–129.

Zack, F., Schau, H., Dalchow, A., Rock, M., Blaas, V., & Büttner, A. (2020). Lesions and characteristic injury patterns caused by high-voltage fault arcs. International journal of legal medicine, 134(4), 1353–1359.

Jonitz-Heincke, A., Klinder, A., Boy, D., Salamon, A., Hansmann, D., Pasold, J., Buettner, A., & Bader, R. (2019). In Vitro Analysis of the Differentiation Capacity of Postmortally Isolated Human Chondrocytes Influenced by Different Growth Factors and Oxygen Levels. Cartilage, 10(1), 111–119.

Jürs, A. V., Völkner, C., Liedtke, M., Huth, K., Lukas, J., Hermann, A., & Frech, M. J. (2020). Oxidative Stress and Alterations in the Antioxidative Defense System in Neuronal Cells Derived from NPC1 Patient-Specific Induced Pluripotent Stem Cells. International journal of molecular sciences, 21(20), 7667.

Völkner, C., Liedtke, M., Petters, J., Lukas, J., Escobar, H. M., Knuebel, G., Bullerdiek, J., Holzmann, C., Hermann, A., & Frech, M. J. (2020). Generation of an iPSC line (AKOSi004-A) from fibroblasts of a female adult NPC1 patient, carrying the compound heterozygous mutation p.Val1023Serfs*15/p.Gly992Arg and of an iPSC line (AKOSi005-A) from a female adult control individual. Stem cell research, 50, 102127. Advance online publication.

Völkner, C., Liedtke, M., Petters, J., Huth, K., Knuebel, G., Murua Escobar, H., Bullerdiek, J., Lukas, J., Hermann, A., & Frech, M. J. (2020). Generation of an iPSC line (AKOSi006-A) from fibroblasts of an NPC1 patient, carrying the homozygous mutation p.I1061T (c.3182 T > C) and a control iPSC line (AKOSi007-A) using a non-integrating Sendai virus system. Stem cell research, 49, 102056.

Petters, J., Cimmaruta, C., Iwanov, K., Chang, M. L., Völkner, C., Knuebel, G., Murua Escobar, H., Frech, M. J., Hermann, A., Rolfs, A., & Lukas, J. (2020). Generation of induced pluripotent stem cell lines AKOSi002-A and AKOSi003-A from symptomatic female adults with Wilson disease. Stem cell research, 43, 101708.

Petters, J., Völkner, C., Krohn, S., Murua Escobar, H., Bullerdiek, J., Reuner, U., Frech, M. J., Hermann, A., & Lukas, J. (2020). Generation of two induced pluripotent stem cell lines from a female adult homozygous for the Wilson disease associated ATP7B variant p.H1069Q (AKOSi008-A) and a healthy control (AKOSi009-A). Stem cell research, 49, 102079.

Gläser, A., Hammerl, F., Gräler, M. H., Coldewey, S. M., Völkner, C., Frech, M. J., Yang, F., Luo, J., Tönnies, E., von Bohlen Und Halbach, O., Brandt, N., Heimes, D., Neßlauer, A. M., Korenke, G. C., Owczarek-Lipska, M., Neidhardt, J., Rolfs, A., Wree, A., Witt, M., & Bräuer, A. U. (2020). Identification of Brain-Specific Treatment Effects in NPC1 Disease by Focusing on Cellular and Molecular Changes of Sphingosine-1-Phosphate Metabolism. International journal of molecular sciences, 21(12), 4502.

Rabenstein, M., Murr, N., Hermann, A., Rolfs, A., & Frech, M. J. (2019). Alteration of GABAergic Input Precedes Neurodegeneration of Cerebellar Purkinje Cells of NPC1-Deficient Mice. International journal of molecular sciences, 20(24), 6288.

Völkner, C., Peter, F., Liedtke, M., Krohn, S., Lindner, I., Murua Escobar, H., Cimmaruta, C., Lukas, J., Hermann, A., & Frech, M. J. (2019). Generation of the Niemann-Pick type C2 patient-derived iPSC line AKOSi001-A. Stem cell research, 41, 101606.

Lukas, J., Pospech, J., Oppermann, C., Hund, C., Iwanov, K., Pantoom, S., Petters, J., Frech, M., Seemann, S., Thiel, F. G., Modenbach, J. M., Bolsmann, R., de Freitas Chama, L., Kraatz, F., El-Hage, F., Gronbach, M., Klein, A., Müller, R., Salloch, S., Weiss, F. U., … Sendler, M. (2019). Role of endoplasmic reticulum stress and protein misfolding in disorders of the liver and pancreas. Advances in medical sciences, 64(2), 315–323.

Feng, X., Yang, F., Rabenstein, M., Wang, Z., Frech, M. J., Wree, A., Bräuer, A. U., Witt, M., Gläser, A., Hermann, A., Rolfs, A., & Luo, J. (2020). Stimulation of mGluR1/5 Improves Defective Internalization of AMPA Receptors in NPC1 Mutant Mouse. Cerebral cortex (New York, N.Y. : 1991), 30(3), 1465–1480.

Feng, X., Cozma, C., Pantoom, S., Hund, C., Iwanov, K., Petters, J., Völkner, C., Bauer, C., Vogel, F., Bauer, P., Weiss, F. U., Lerch, M. M., Knospe, A. M., Hermann, A., Frech, M. J., Luo, J., Rolfs, A., & Lukas, J. (2019). Determination of the Pathological Features of NPC1 Variants in a Cellular Complementation Test. International journal of molecular sciences, 20(20), 5185.

Freiman, Thomas (member since 2020)

Dubinski, D., Won, S. Y., Miesbach, W., Keil, F., Behmanesh, B., Baumgarten, P., Raimann, F. J., Bernstock, J. D., Senft, C., Seifert, V., Freiman, T. M., & Gessler, F. (2020). Direct oral anticoagulants for therapeutic anticoagulation in postoperative pulmonary embolism after meningioma resection. Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia, 81, 265–269.

Won, S. Y., Dubinski, D., Freiman, T., Seifert, V., Gessler, F., Strzelczyk, A., & Konczalla, J. (2020). Acute-on-chronic subdural hematoma: a new entity for prophylactic anti-epileptic treatment?. European journal of trauma and emergency surgery : official publication of the European Trauma Society, 10.1007/s00068-020-01508-9. Advance online publication.

Conradi, N., Behrens, M., Hermsen, A. M., Kannemann, T., Merkel, N., Schuster, A., Freiman, T. M., Strzelczyk, A., & Rosenow, F. (2020). Assessing Cognitive Change and Quality of Life 12 Months After Epilepsy Surgery-Development and Application of Reliable Change Indices and Standardized Regression-Based Change Norms for a Neuropsychological Test Battery in the German Language. Frontiers in psychology, 11, 582836.

Won, S. Y., Freiman, T. M., Reif, P. S., Dubinski, D., Hattingen, E., Herrmann, E., Seifert, V., Rosenow, F., Strzelczyk, A., & Konczalla, J. (2020). DIagnostic Subdural EEG electrodes And Subdural hEmatoma (DISEASE): a study protocol for a prospective nonrandomized controlled trial. Neurological research and practice, 2, 50.

Won, S. Y., Kilian, A., Dubinski, D., Gessler, F., Dinc, N., Lauer, M., Wolff, R., Freiman, T., Senft, C., Konczalla, J., Forster, M. T., & Seifert, V. (2020). Microsurgical Treatment and Follow-Up of KOOS Grade IV Vestibular Schwannoma: Therapeutic Concept and Future Perspective. Frontiers in oncology, 10, 605137.

Fuellen, Georg

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