Institute of Neuropathology

Chair of Neuropathology

Address
Schwabachanlage 6
91054 Erlangen
Phone: +49 9131 8526031
Fax: +49 9131 8526033
www.neuropathologie.uk-erlangen.de

Director
Prof. Dr. med. Ingmar Blümcke

Contact
Prof. Dr. med. Ingmar Blümcke
Phone: +49 9131 8526031
Fax: +49 9131 8526033
bluemcke@uk-erlangen.de

Research focus
- Neuropathological classification of focal epilepsies in humans
- Epigenetic mechanisms of epileptogenesis
- Molecular myopathology

Structure of the Institute

Professorships: 2
Personnel: 17
- Doctors (of Medicine): 3
- Scientists: 5 (thereof funded externally: 4)
- Graduate students: 2

Clinical focus areas
- European Reference Center for rare and complex epilepsies "EpiCare"
- Neuropathological reference center for epilepsy surgery and host of the European Epilepsy Brain Bank
- Member of the panel of the German reference center for brain tumors
- Disease of skeletal muscle (Member of the Muscle Research Center Erlangen)

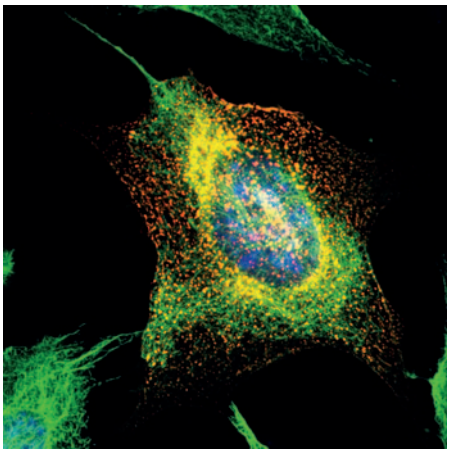
Research

The Institute of Neuropathology scientifically addresses diseases of the central nervous system and the skeletal musculature. Our internationally highly visible research expertise is in the area of human epilepsy and neuro-muscular disorders.
Our Institute welcomes visiting scientists to train them in studying human tissue samples for research purpose, but also for clinical diagnostics, e.g. from Australia (2018), Brazil (2017, 2018), Mexico (2018), and the Netherlands (2018).

Neuropathological classification of focal epilepsies in humans
PI: Prof. Dr. I. Blümcke
This research project is focused on drug-resistant focal epilepsies in humans to decipher pathomechanisms and clinically define brain lesions associated with chronic seizures, e.g. hippocampal sclerosis, glio-neuronal tumors, and focal cortical dysplasia. We perform systematic analysis in surgically resected human brain specimens in correlation with clinical histories and postsurgical follow-up data, and our work contributed in establishing new international standards for clinico-pathological diagnosis of focal cortical dysplasia (ILAE classification 2011) and hippocampal sclerosis (ILAE classification 2013).
Extensive collaboration with our clinical and neuropathology colleagues from Germany and many other European countries were helpful to establish the European Epilepsy Brain Bank, a reference and consultation center for neurosurgical epilepsy tissue specimen. The collection of more than 10.000 specimen and collaboration with 35 European centers will help us to target the integration of genetics and histopathology for a better understanding of etiology and pathogenesis of epilepsy-associated brain lesions and also a better disease classification in the near future (see the following research focus).
We are also in charge to develop a digital microscopy platform for the European Reference Network "EpiCare" (WP6), which will be based on whole slide imaging technology for microscopic review and semi-automated analysis with machine learning algorhythms.
Funding: EU

Epigenetic mechanisms of epileptogenesis
PI: Dr. K. Kobow
Our work specifically addresses methylation profiles and the epigenetic signaling machinery, i.e. histone code modifications, DNA methylation, or miRNA, in relation to epileptic neuronal activity using human surgical specimens and an experimental cell culture model. We also seek for new therapeutic strategies addressing the epigenetic signaling machinery, such as ketogenic diet. The integration of our data with histomorphological studies obtained from the European Epilepsy Brain Bank and the ERN "EpiCare" (see above) will help to develop new biomarker for disease mechanisms and successful new therapies.
Funding: EU

Molecular myopathology
PI: Prof. Dr. R. Schröder
The central research topic of this group is the pathogenesis of myofibrillar myopathies, which are morphologically characterized by the presence of pathological protein aggregation in cross-striated muscle cells. This group of often heritable myopathies and cardiomyopathies is clinically marked by a progressive course and premature death. To date, no specific treatment is available for these disorders. The main focus of our group is the generation and characterization of transgenic mouse and cell models for desmin-, VCP-, and filamin C-related myopathies and cardiomyopathies. The clinical, morphological, biochemical, and molecular analysis of these models provides deeper insights into the molecular "sequence" that leads to pathological protein aggregation and progressive muscle damage in these disorders. This work is the basis for the evaluation of novel targeted treatment strategies.
Funding: DFG, Deutsche Gesellschaft für Muskelkranke e.V.



Transfection of desmin into fibroblasts
The picture shows a 3T3 mouse fibroblast cell line transiently transfected with a cardiomyopathy causing human desmin mutant (desmin-R406W) 18 hours after transfection. The cell is stained with vimentin-specific (green) and desmin-specific (red) antibodies. Vimentin is building a filament network whereas desmin-R406W is only present as small dot-like aggregates.

Teaching

The Institute of Neuropathology offers lectures and teaching courses in histopathology for students in Medicine, Dentistry and Molecular Medicine. Comprehensive lectures (clinico-pathology conferences) are organized together with the Departments of Neurology and Neurosurgery.
In addition, we annually organize the International Summer School for Neuropathology and Epilepsy Surgery. The 6th Summer School took place from the 27 - 30 April 2017 at the Cleveland Clinic (USA), the 7th Summer School from 22 – 25 July 2017 in Campinas (Brazil), the 8th Summer School from 26 – 29 July 2018 in Erlangen and the 9th Summer School from 17 –

20 September 2018 in Beijing (China). In total, we have trained more than 300 participants from over 40 countries in our summer schools on the subject of epilepsy-associated brain lesions in hands-on workshops at the microscope and through innovative digital pathology platforms.

We supervise Bachelor's and Master's theses as well as doctoral theses of the Faculties of Medicine and Sciences, respectively.

Selected publications

Blümcke I et al. Histopathological findings in brain tissue obtained from epilepsy surgery. New England Journal of Medicine 2017 Oct 26;377(17):1648-1656

Capper D et al. DNA methylation-based classification of central nervous system tumours. Nature. 2018 Mar 22;555(7697):469-474

D'Gama AM, Woodworth MB, Hossain AA, Bizzotto S, Hatem NE, LaCoursiere CM, Najm I, Ying Z, Yang E, Barkovich AJ, Kwiatkowski DJ, Vinters HV, Madsen JR, Mathern GW, Blümcke I, Poduri A, Walsh CA. Somatic Mutations Activating the mTOR Pathway in Dorsal Telencephalic Progenitors Cause a Continuum of Cortical Dysplasias. Cell Rep. 2017 Dec 26;21(13):3754-3766

Kiese K, Jablonski J, Hackenbracht J, Wrosch JK, Groemer TW, Kornhuber J, Blümcke I, Kobow K. Epigenetic control of epilepsy target genes contributes to a cellular memory of epileptogenesis in cultured rat hippocampal neurons. Acta Neuropathol Commun. 2017 Oct 31;5(1):79

Di Liberto G et al. Neurons under T Cell Attack Coordinate Phagocyte-Mediated Synaptic Stripping. Cell. 2018 Oct 4;175(2):458-471.e19

Winter L, Unger A, Berwanger C, Spörrer M, Türk M, Chevessier F, Strucksberg KH, Schlötzer-Schrehardt U, Wittig I, Goldmann WH, Marcus K, Linke WA, Clemen CS, Schröder R. Imbalances in protein homeostasis caused by mutant desmin. Neuropathology Appl Neurobiol 2018 Sep 4

International cooperations

International League against Epilepsy

Prof. F. Cendes, Department of Neurology, UNICAMP, Campinas: Brazil

Prof. A. El-Osta, The Alfred Center, Monash University, Melbourne: Australia

Dra. I. Wang and L. Jehi; Epilepsy Center, Cleveland Clinic Foundation, Cleveland, Ohio: USA

Dr. J. Zurmanova, Dept. of Physiology, Charles University Prague: Czech Republic