Institute of Anatomy

Chair of Anatomy and Cell Biology

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Research focus
- The role of B cells in the immunopathogenesis of MS
- Development of neuroprotective treatment options for patients with MS
- The ENS as autoimmune target in MS
- Extrinsic and intrinsic innervation of the esophagus as targets of the autoimmune response in MS
- The human ENS
- Cell biology of the NF2 tumorsuppressor protein
- Vagal innervation studies
- Intrinsic choroidal neurons (ICN)
- Innervation of brown adipose tissue (BAT)

Structure of the Chair

Professorships: 3
Personnel: 24
- Scientists: 4 (thereof funded externally: 0)
- Graduate students: 11

Special structural feature
Both chairs collegially lead the Institute of Anatomy.

Research

The main research focus evolves around the immunopathology of multiple sclerosis (MS), which also comprises the development of new diagnostic tools and innovative therapeutic strategies. An additional major research interest is the enteric nervous system (ENS), in particular its morphology, function, and involvement in neurodegenerative diseases.

The role of B cells in the immunopathogenesis of MS
PI: Prof. Dr. S. Kürten, Dr. R. Chunder
MS is a chronic autoimmune disease of the central nervous system (CNS). The role of B cells in the immunopathogenesis of MS has increasingly attracted attention over the last years. Next to the production of autoantibodies and the presentation of autoantigens, B cells can also be involved in the formation of tertiary lymphoid organs in the CNS. Our aim is to decipher the mechanisms of B cell contribution to MS immunopathology by using animal models. In particular we are employing experimental autoimmune encephalomyelitis (EAE) as a B cell-dependent mouse model, which relies on the active immunization with a fusion protein of myelin basic protein and proteolipid protein. Using this model we aim to identify key molecules, which are involved in tertiary lmyphoid organ formation. These molecules are also analyzed in patients with MS and set in relation to the course and severity of the disease. In addition, we focus on the development of novel therapeutic strategies and biomakers that can be used towards individual and patient-based treatment decisions.

Development of neuroprotective treatment options for patients with MS
PI: Prof. Dr. S. Kürten
All of the currently available drugs for the treatment of MS target the inflammatory component of the disease. Yet, already with the onset of the disease, neurodegeneration is evident, which progresses over time and is responsible for the irreversible loss of nerve fibers. Studying mouse models of MS we were able to show that treatment with the L-type calcium channel antagonist nimodipine leads to a decrease in axonal damage and demyelination, accompanied by an increase in remyelation. Here, we would like to study the underlying mechanisms in detail.

The ENS as autoimmune target in MS
PI: Prof. Dr. S. Kürten, Dr. R. Chunder
We have previously shown the degeneration of the ENS in a mouse model of MS. Here we aim to provide an in-depth analysis of the morphological and functional alterations of the ENS as a result of MS immunopathology. We also strive to identify potential target antigens and to determine the kinetics of ENS degeneration to understand whether the process is causative or rather an epiphenomenon of the disease. The results will be of major clinical importance for both, the diagnostics and therapy of MS, and may provide a completely new view on the etiology of the disease.

Extrinsic and intrinsic innervation of the esophagus as targets of the autoimmune response in MS
PI: Prof. Dr. J. Wörl, Prof. Dr. S. Kürten, Prof. Dr. W. L. Neuhuber
Based on detailed knowledge of the innervation of the esophagus, in particular of the so-called enteric co-innervation, we are using a mouse model of MS to investigate whether glial or neuronal structures in the esophagus are damaged by autoimmune processes in MS. The aim of the project is to figure out whether swallowing disorders in patients suffering from MS are caused by morphological alterations in the esophagus. Dysphagia is frequently observed in patients with MS, while its pathogenesis is still unkown.

The human ENS
PI: Prof. Dr. A. Brehmer, PD Dr. S. Jabari
Our current knowledge on human neuroenteric structures and functions is fragmentary, and a neuropathology of the ENS underdeveloped. Our main task is the morphological-immunohistochemical classification of enteric neurons in both, health and disease (e.g. in megasyndromes of Chagas and Hirschsprung diseases). Besides, interactions between the ENS and the intestinal epithelium (including its enteroendocrine cells) and the development of a digital pathology are in the focus.

Cell biology of the NF2 tumor-suppressor protein
PI: PD Dr. M. Kressel
The neurofibromatosis type 2 (NF2) protein merlin is a classical tumor suppressor protein. Loss of function, e.g. through inherited NF2 gene mutations, characteristically leads to tumors of Schwann cell origin of the eighth cranial nerve. Merlin is a constituent of a protein complex at the plasma membrane, which inhibits cell proliferation cell-density dependent inducing effects of the Hippo signal transduction pathway. Protein isoforms created by alternative splicing of a NF2 binding partner were identified and the effects on the subcellular localization studied. As a prerequisite for further studies, the extent to which these isoforms can be expressed in bacterial hosts was investigated.

Vagal innervation studies
PI: PD Dr. M. Kressel
Because of their eminent functional significance for the entire organism, intense research efforts are directed towards the course of terminal fibers of the vagus nerve and their microscopic architecture. By neuronal tract-tracing methods, the course of not yet known vagal terminal endings in the abdomen was mapped and their connection to the surrounding tissues studied.

Intrinsic choroidal neurons (ICN)
PI: Prof. Dr. W. Neuhuber
The choroid of higher primates, in particular humans, and of birds harbors several thousands of

intrinsic neurons, the so-called ICN. They form an intrinsic network similar to the ENS and innervate choroidal blood vessels and non-vascular smooth muscle. On the other hand, ICN are contacted by postganglionic sympathetic and parasympathetic as well as trigeminal peptidergic afferent neurons. The functional significance of ICN is still enigmatic, however, they likely play a role in ocular homeostasis. This is suggested by circadian changes of vasoactive intestinal polypeptide (VIP), one of the vasodilatative transmitters of ICN. The project is a collaboration with the Department of Ophthalmology and PMU Salzburg.

Innervation of brown adipose tissue (BAT)

PI: Prof. Dr. W. Neuhuber

Brown adipose tissue is important not only for thermogenesis in newborns, but occurs also in adults in supraclavicular and paravertebral regions. It plays a still poorly investigated metabolic role. Using immunohistochemical and molecular biological techniques, BAT and sympathetic ganglia are studied in mouse and human. The project is a collaboration with Baton Rouge, USA.

Teaching

The Chair of Anatomy and Cell Biology contributes to the curriculum of Medicine and Dentistry with obligatory courses and electives. In particular, the Chair is responsible for all lectures and seminars in neuroanatomy and is instrumental in organizing and conducting the dissection course, which is of central importance for the preclinical teaching curriculum and attended by approximately 230 students of medicine and dentistry each semester. In addition, the Chair offers the elective "Applied Anatomy (EMPTY course)" and „Palpatory Surface Anatomy". Interdisciplinary preclinical and clinical lectures as well as seminars are provided in collaboration with the departments of Neurology, of Obstretics and Gynecology, (Neuro)Surgery, the Institute of Radiology and the Division of Neuroradiology.

In addition, MD, PhD, Bachelor's and Master's theses are supervised.

Selected publications

Wunsch M et al. The enteric nervous system is a potential autoimmune target in multiple sclerosis. Acta Neuropathol. 2017 Aug;134(2):281-295

Schampel A, Volovitch O, Koeniger T, Scholz CJ, Jörg S, Linker RA, Wischmeyer E, Wunsch M, Hell JW, Ergün S, Kuerten S. Nimodipine fosters remyelination in a mouse model of multiple sclerosis and induces microglia-specific apoptosis. Proc Natl Acad Sci U S A. 2017 Apr 18;114(16): E3295-E3304

Zetzmann K, Strehl J, Geppert C, Kuerten S, Jabari S, Brehmer A. Calbindin D28k-Immunoreactivity in Human Enteric Neurons. Int J Mol Sci. 2018 Jan 8;19(1)

Simon M, Ipek R, Homola GA, Rovituso DM, Schampel A, Kleinschnitz C, Kuerten S. Anti-CD52 antibody treatment depletes B cell aggregates in the central nervous system in a mouse model of multiple sclerosis. J Neuroinflammation. 2018 Aug 11;15(1):225

Hohberger B, Jessberger C, Hermann F, Zenkel M, Kaser-Eichberger A, Bergua A, Jünemann AG, Schrödl F, Neuhuber W. VIP changes during daytime in chicken intrinsic choroidal neurons. Exp Eye Res. 2018 May;170:8-12

International cooperations

Prof. P. V. Lehmann, MD, PhD, Cellular Technology Limited, Shaker Heights: USA

Prof. C. Linington, PhD, University of Glasgow, Glasgow: UK

Prof. ABM da Silveira, PhD, Federal University of Uberlandia, Uberlandia: Brazil

Prof. J. Shimizu, DVM, PhD, Gifu University, Gifu City: Japan

Prof. L. Steinman, MD, PhD, Stanford University, Stanford: USA