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Editorial

<https://doi.org/10.1515/nf-2019-0019>

Dear reader,

This special edition of the Neuroforum is dedicated “Neuroinflammation”. What does inflammation mean? The definition of the term ‘inflammation’ has changed significantly throughout the years. Initially, Celsus defined inflammation based on the clinical cardinal signs “*tumor, rubor, calor et dolor*”, that was found later to be accompanied by histological signs of extravasation of blood cells such as granulocytes and lymphocytes in the tissues including the brain. Nowadays, the term “neuroinflammation” is used in many cases to describe totally different and diverse CNS diseases. While viral, bacterial and autoimmune diseases as well as the acute ischemic stroke are histopathologically characterized by extravasation of hematopoietic cells, the concept of neuroinflammation has also expanded to neurodegenerative diseases, e.g. Alzheimer’s disease, Parkinson’s disease, and Huntington’s disease. From a neuropathological perspective though, these diseases are rather neurodegenerative instead of inflammatory pathologies because one can’t find immune cells of the adaptive (that blood-derived) rather than of the innate immune system (that is yolk sac-derived) in the CNS. Consequently, in classic neuroinflammatory diseases the blood-brain barrier is destroyed and in this case transmigration of hematopoietic cells takes place. In general, all these inflammatory diseases show an activation of the innate immune system, especially of myeloid cells, for instance in microglia.

This special edition aims to address some of the currently most important questions in the field of neuroinflammation and to pose central questions about the pathogenesis and treatment of neuroinflammatory diseases. It includes contributions from members of the Collaborative

Research Centre/Transregio (CRC/TRR) 167 (“Development, function and potential of myeloid cells in the central nervous system”, NeuroMac). Research within this CRC/TRR is supposed to contribute significantly to a better understanding of inflammatory CNS diseases.

The review article by Chotima Böttcher, Roman Sankowski, Josef Priller and Marco Prinz deals with the characterization of myeloid cells in CNS diseases on single-cell level. By the recent development of new methods such as single-cell PCR and antibody-based single-cell flow cytometry (CyTOF) it is now possible to define new subpopulations of myeloid cells during homeostasis as well as during inflammatory CNS diseases. Henceforth, these new techniques allow now a precise definition of new context-associated subpopulations of myeloid cells and lead us to expect a better targeted therapy of CNS diseases in the future.

Charlotte Mezö, Omar Mossad, Daniel Erny and Thomas Blank give an overview about the interaction of the microbiome with the innate immune system in the CNS. Their article is based on the idea that the human body contains trillions of microorganisms that play a vital role for human health: the host microbiota that are important for the development and function of the immune system inside and outside of the CNS. Recent studies of the gut-brain axis give reasons to hope that the interactions of both organs will be better understood in the future, thus, achieving a therapeutic intervention of CNS diseases such as Alzheimer’s or Parkinson’s through modification of the digestive system.

In their article, Maximilian Lenz and Andreas Vlachos focus on the neuro-immunological synapse in the CNS. The topic is based on several recent studies which have shown that microglia as tissue macrophages of the CNS, are paramount for the neuronal development and the homeostasis of neurons in the adult brain as well as for the modulation of the synapses. Moreover, it was shown before that a neuro-immunological synapse exists in the CNS and that microglial factors such as the tumor necrosis factor alpha can significantly shape the plasticity of the neuronal synapses together with astrocytes.

Philipp Henneke and Seja Lehnardt give an overview about molecular mechanisms through which viruses, bacteria, fungi and parasites are sensed by CNS cells during infections of the central nervous system. So-called Toll-like Receptors (TLRs) play an important role in detecting

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those pathogens that can be found on different CNS cells. Aside from pathogens also destroyed neurons can secrete RNAs which can activate also endosomal Toll-like receptors through endosomes. These processes can contribute to neuroinflammation, too, and these possibilities are discussed in their review article.

The final review article by Daniel Berchthold, Luise Weitbrecht, Christian Meisel and Andreas Meisel focuses on another hematopoietic cell within the diseased CNS: the B cell. The authors discuss in depth the role of B cells for the acute ischemic stroke. For a long time, only certain cells of the adaptive immune response, the T cells, were the focus of most research activities. Just recently, it was shown that also B cells are important in acute and chronic phases of ischemic stroke. In their review article the authors describe the role of B cells in brain ischemia and possible antibody-dependent and independent mechanisms for the development of a cognitive impairment after a stroke.

We hope that these contributions will not only increase the knowledge about mechanisms during neuroinflammation of neuroscientists, but will hopefully convince the reader that a deeper understanding of the underlying pathomechanisms of CNS inflammation is urgently needed in order to help us to successfully treat these diseases in the future.

We sincerely thank the Society for Neuroscience and the editorial team of the Neuroforum for selecting the above-mentioned scientifically valuable and clinically relevant topics and, of course, all authors for their willingness to participate.

Yours faithfully,
Josef Priller and Marco Prinz

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