Department für Neurowissenschaften

INSTITUT FÜR BIOLOGIE
UND UMWELTWISSENSCHAFTEN

Invitation to a Guest Lecture
at the joint colloquium of the Institute of Biology and Environmental Sciences and the Department of Neuroscience

Module bio890: Current topics in biology

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Antrittsvortrag mit anschließendem Sektempfang

Molecular and evolutionary insights into the structural organization of the Cation Chloride Cotransporter Family

Brain function relies on a fine-tuned balance between excitation and inhibition. In most parts of the nervous system, the interplay of NKCC1 and KCC2 is key to inhibitory neurotransmission as it determines the intracellular chloride concentration ($[Cl^-]_i$). In mature neurons, KCC2 lowers $[Cl^-]_i$ and is hence required for fast inhibitory neurotransmission mediated by GABA or glycine. By contrast, NKCC1 is more active in immature inhibitory neurons to increase $[Cl^-]_i$ resulting in depolarizing action of GABA or glycine. Dysregulation of either of the two cotransporters impairs the delicate balance between excitation and inhibition in the nervous system causing several neurological and psychiatric disorders such as epilepsy, schizophrenia and autism spectrum disorders. NKCC1 and KCC2 are both members of the secondary active CCC membrane protein family. Gene duplication events at the base of archaeans and eukaryotes led to diversification and neofunctionalization of the paralogous CCC subfamilies: Na^+ K^+ $2Cl^-$ inward cotransporters (NKCCs) and Na^+ Cl^- inward cotransporters (NCC), K^+ Cl^- outward cotransporters (KCCs), a polyamine inward transporter (CCC9), and the transport-inactive CCC interacting protein (CIP1). Single particle cryo-EM based structures of KCCs, NKCC1 and NCC showed that these transporters consists of intracellularly located termini and twelve transmembrane domains (TMs), that are essential for ion translocation. The termini are important for trafficking, basolateral and apical sorting in polarized cells, dimerization, and regulation via posttranslational modifications. In this talk, I will show which structural elements are important for ion translocation in KCC2. In addition, I will discuss the posttranslational regulation of KCC2 and NKCC1. Both, the understanding of the operating mode and the regulatory mechanisms of these transporters are a prerequisite for the development of rational designed pharmaceuticals.

30.05.2023, 4 pm (s.t.), W04 1-162

Host: Prof. Dr. Gabriele Gerlach (Animal Biodiversity and Evolutionary Biology), IBU

Members of all institutes are cordially invited to join the lecture.