Introductory Remarks to Symposium 12

Epileptogenesis in mouse models of genetic epilepsies

Holger Lerche, Tuebingen

Epilepsy is a common and disabling disorder that represents a significant disease burden worldwide. Gene discovery and functional analysis of genetic defects have been instrumental in deciphering disease mechanisms and developing first personalized treatments. However, most of the genetic alterations underlying epilepsy remain to be elucidated. Genetic epilepsies exhibit a typical age-dependency, the cause of which is largely unknown. It is therefore likely that developmental factors play a central role in the epileptogenesis of genetic epilepsies. In addition, specific seizure phenotypes are frequently accompanied by comorbid neurodevelopmental phenotypes with potentially overlapping vulnerable periods that include motor and language delays, intellectual disability, attention-deficit/hyperactivity disorder, and autism spectrum disorder. Mouse models can be used to investigate whether and how genetic mutations trigger epileptogenic processes and how these interact with developmental processes that likely contribute to the age-dependent manifestation of seizure phenotypes in genetic epilepsies. The developing brain is particularly vulnerable to disruption and insults, but its plasticity also offers significant preventive and therapeutic potential. Using genetic mouse models, treatment of channel variants identified in humans has been shown to prevent epileptogenesis and neurodegeneration early in development (e.g., inducible KCNQ2 model of developmental and epileptic encephalopathy). Several other genes such as SCN2A or KCNA2 have been identified to be involved in severe genetic epilepsies accompanied by developmental delays. However, to develop targeted treatment options for these syndromes, it is important to know when and how to use them most effectively.

In this symposium, we will address the general concept of vulnerable periods in genetic mouse models and will show that brain-region specific vulnerability, miswiring in developing neural networks, and altered dendritic integration are involved in epileptogenesis and specific seizure types in genetic epilepsies. Possible treatment options targeting the disease cause and clinical data will be discussed.

Symposium 12, Thursday, March 23, 11:00 - 13:00

Symposium 12

Thursday, March 23, 2023
11:00 - 13:00, Lecture Hall 103

Chair: Holger Lerche, Tuebingen

11:00 **Opening Remarks**

11:05 Andrea Merseburg, Cologne
DEVELOPMENTAL WINDOWS OF OPPORTUNITY IN MOUSE MODELS OF GENETIC EPILEPSIES (S12-1)

11:25 Thomas Wuttke, Tuebingen
BRAIN-REGION SPECIFIC EPILEPTOGENESIS IN DRAVET SYNDROME (S12-2)

11:45 Tony Kelly, Bonn
ABERRANT DENDRITIC HYPEREXCITABILITY AND DENDRITIC MATURATION OF CA3 PYRAMIDAL CELLS IN THE SCN2A^{A263V} GENETIC EPILEPSY MODEL (S12-3)

12:05 Ulrike Hedrich, Tuebingen
KCNA2-ENCEPHALOPATHY: FROM BENCH TO BEDSIDE (S12-4)

12:25 Eleonora Anna Loi, Jena
NMDA-RECEPTOR-FC-FUSION CONSTRUCTS NEUTRALIZE ANTI-NMDA RECEPTOR ANTIBODIES (S12-5)

12:35 **Discussion and Concluding Remarks**

Symposia