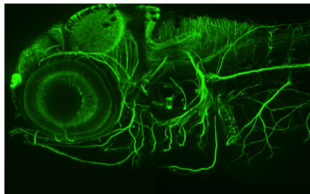


Thursday October 11th 2018– 12:15
Department of Physiology, Bugnon 7, 1005 Lausanne
Seminar room, 6th floor

Modeling genetic epilepsies in zebrafish to unveil the underlying mechanisms and pave the way for new treatments



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Host: Prof. F. Amati and P. Gut



Epilepsy is a widespread neurological disorder characterized by recurrent seizures corresponding to episodes of synchronized over-excitation of various neuronal populations. While epilepsy is a major public health issue affecting more than 50 million people worldwide, classic anti-epileptic drugs are inefficient in approximately one third of the patients, highlighting the need for novel therapies. In the last decades, much effort has been deployed in trying to unravel the genetic origins of idiopathic forms of epilepsy, which represent more than two thirds of all epilepsies. At this juncture, we aimed at functionally characterizing in vivo the pathogenicity of different class of epilepsy-causing genes that have been identified. To do so, we take advantage of the zebrafish as a convenient vertebrate model to study neurodevelopment. We investigated the consequences loss-of-function mutations in ion channel genes (GABRA1, GABRG2) as well as non-ion channel genes (DEPDC5, PCDH19) and showed that the pathogenic disorder can be accurately phenocopied in zebrafish. Moreover, through unbiased transcriptomic analysis and in vivo immunolabeling, we dug into the underlying pathogenic molecular mechanisms and showed that these mutations lead to specific neurodevelopmental defects. Importantly, we also identified an unexpected new role played by DEPDC5 apart from its canonical function. In sum, our work shed new light on the pathogenic mechanisms associated with neurodevelopmental disorders and paves the way for the identification of new therapies

Éric Samarut gained his PhD degree in Molecular Aspects of Life Sciences in 2013 from the Université de Strasbourg. In 2014, he started a postdoc in Pierre Drapeau's laboratory where he established a new line of research performing functional genomics of neurological disorders using zebrafish. He recently published his work as first or senior author in Current Biology, Epilepsia and JCI Insights. Eventually, by identifying new mechanisms of the disease, his work could pave the way for the design of new therapeutical strategies.