INSTITUTO CAJAL

**SEMINARIO PRESENCIAL**

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# Reprogramming reactive glial cells into GABAergic neurons: A new avenue for reducing epileptic seizures


## Abstract

The mammalian CNS lacks intrinsic regenerative capacity to replace lost neurons and induce functional recovery after injury/diseases. Reprogramming brain-resident glial cells into clinically-relevant induced neurons (iNs) is an emerging strategy towards replacing lost neurons and restoring lost brain functions. A fundamental question is whether iNs can promote functional recovery in pathological contexts. We addressed this question in the context of therapy-resistant Mesial Temporal Lobe Epilepsy (MTLE), which is associated with hippocampal seizures and degeneration of hippocampal GABAergic interneurons. Using a MTLE mouse model, we show that retrovirus-driven expression of Ascl1 and Dlx2 in reactive hippocampal glia *in situ,* or in cortical astroglia grafted in the epileptic hippocampus, causes efficient reprogramming into iNs exhibiting hallmarks of interneurons. These induced interneurons functionally integrate into epileptic networks and establish GABAergic synapses onto dentate granule cells. MTLE mice with GABAergic iNs show significant reduction in both number and duration of spontaneous recurrent hippocampal seizures. Thus glia-to-neuron reprogramming is a potential disease-modifying strategy to reduce seizures in therapy-resistant epilepsy.


## Affiliation and short bio

Christophe Heinrich received a PhD in Neuropharmacology from the University of Strasbourg (France), where he studied the role of BDNF and adult hippocampal neurogenesis in Mesial-Temporal Lobe Epilepsy. Afterwards, he joined the lab of Prof. Magdalena Götz at the Ludwig-Maximilian University of Munich (Germany) for his postdoctoral training. He focused on direct lineage reprogramming of glial cells into induced neurons as a promising cell-based strategy for brain repair. He showed that astroglia from the cerebral cortex can be reprogrammed into functional, synapse-forming neurons of distinct phenotypes by forced expression of specific neurogenic transcription factors. After his postdoc, he moved back to France where he was recruited as assistant professor at CNRS (National Centre for Scientific Research). He was awarded in 2017 the Attraction Package from the Laboratory of Excellence (LabEx) CORTEX at the University of Lyon, where he has now established his own research group at the Stem Cell and Brain Research Institute (SBRI, INSERM). His lab is currently exploring the functional impact of *in vivo* lineage reprogramming as a promising cell-replacement strategy in regenerative medicine to induce functional recovery in neurological disorders.