PostDoctoral position

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Neuroglial Interactions in Cerebral Physiopathology team
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We are looking for motivated post-docs to join Gilles Huberfeld's team (Collège de France, INSERM, CIRB, Paris), funded by a 5 years European Research Council (ERC) condolidator grant (2020-2025). This translational work aims at studying glutamatergic mechanisms in glioma growth and epilepsy , mostly on human material and on a rodent model of glioblastoma. The post-holder will have the opportunity to explore electrophysiologically, both in vitro and in vivo, tumor growth and epilepsy processes. Duration: 2 years renewable up to 5 years.

GliomaSignals.
Oncometabolitic control of tumor growth and epileptogenesis in IDH mutated gliomas: D2HG signaling mechanism.

Objectives
Dysregulated growth processes of gliomas interact with pro-epileptic plasticity of brain circuits in such a way that the excitatory transmitter glutamate promotes autocrine tumor invasion as well as epileptic synchrony in surrounding cortical regions. Most low-grade gliomas are associated with mutations of Isocitrate DesHydrogenase (IDH) genes which lead to an excess of the oncometabolite D-2-Hydroxyglutarate (D2HG). With a structure mimicking glutamate, D2HG is thought to participate in both epileptogenic and oncologic processes. Importantly, while epileptic activity is accentuated, tumor prognosis is improved in affected people. Preliminary data now suggest a dual function for D2HG, acting as a glutamatergic agonist at high levels, but as an antagonist in the presence of glutamate. Solving this paradox will be a step forward in glioma science.
The GliomasSignals project will examine the role of D2HG in the neurobiology of gliomas bringing electrophysiology concepts and tools to neuro-oncology, seeking to transform our understanding. It seeks to better understand how D2HG modulates glutamatergic signaling, affects neuronal excitability and tumor growth, and to detect the extent to which tumor infiltration colocalizes with epileptic remodeling.

Proposed approach
The post-holder will explore in vitro on human postoperative tissues and on cultured human cortical slices (and on rodent tissues) the effects of combined D2HG and glutamate on glutamate and GABA ionotropic receptors and on epileptic activities. This in vitro electrophysiological approach will be associated with an in vivo investigation on a rodent model of glioblastoma. Human glioblastoma cell lines will be grafted in mice together with an osmotic pump delivering D2HG locally to explore the effects of D2HG and IDH mutation on tumor growth and epilepsy.

Host institution and lab.
The College de France is an old institute settled in the center of Paris. Our team belongs to a biology institute (Center for Interdisciplinary Research in Biology) and studies neuroglial interactions in pathophysiology with a special focus on human tissues. We collaborate with several hospitals and neurosurgery teams in Paris, which allows work on human tissues. Our skills: in vivo (rodents and human), in vitro (cultured tissues, including human cortex) and ex vivo (acute tissue slices) electrophysiology (MEA, patch-clamp, Ca imaging …), 2photons and STEAD microscope imaging.
The post-doc (and the whole project) is funded by the ERC (consolidator grant / Gilles Huberfeld)

Expected profile
- Experience in both in vivo (rodents) and in vitro electrophysiology (extracellular recordings and patch-clamp)
- Skills in organotypic cultures and fluorescence imaging are welcomed
- Capacity to work on human tissues

Interested?
Please send the following documents to gilles.huberfeld@college-de-france.fr.
- Cover letter (please include contacts of references).
- CV including major achievements.