

address web : [M2 nanoBiotechnologies](#)

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Host laboratory : Grenoble Institut Neurosciences (GIN)

Host group/team: Translational SNOOPER

Title of the M2 research internship: In vitro preclinical tests in electrophysiology recording and stimulation via an innovative medical device

Project summary: Glioblastoma (GBM) is the most common and malignant form of primary brain tumor with a median survival time of 14–16 months in GBM patients. Despite all the advances of modern medicine, it remains incurable, with an extremely poor prognosis. The current medical option for GBM patients is surgery to remove the macroscopic brain tumour, followed by a combination of radiotherapy and temozolomide treatment in order to gain a few more months of survival. Indeed, complete surgical resection to eliminate GBM is almost impossible due to its high invasiveness. Invasion and migration mechanisms have been extensively described at the molecular and cellular levels. However, most innovative targeted therapies such as anti-angiogenic or anti-invasive to latest-generation immunotherapies have failed. This therapeutic failure is explained by a high tumour heterogeneity resulting in molecular and cellular adaptations that favour relapse and therapy resistance. Besides well-characterized tumour genomic abnormalities, more recent research also demonstrated the driving impact of non/peri-tumoral microenvironment partners, including neurons, macrophages, and astrocytes. The implant device Neuro Snooper, a flexible micro-electrode array, originally developed for Brain Computer interface application, is a unique opportunity for GBM electrophysiological characterisation. It provides a unique solution to monitor the peritumoral GBM microenvironment to detect early relapse, monitor therapies and also stimulate in multi-focal points in the cavity in the case of GBM relapse. In vitro studies are of interest in parallel to the design of clinical trials.

The objectives of this research work are: to study the electrophysiological signals from an in vitro model of human GBM cell culture by performing recording and stimulation trials in vitro using the implant; to adapt specifically the design of the device for the stimulation; to check the implant/tissue interface by performing tissue sections, immuno-histochemistry and fluorescence microscopy characterisation.

F. Darlot, "Glial scarring around intra-cortical MEA implants with flexible and free microwires inserted using biodegradable PLGA needles", *Biomaterials*, Front. Bioeng. Biotechnol (2024), Volume 12

Allen NJ. Brain tumours manipulate neighbouring synapses. *Nature*. 2020 Feb;578(7793):46-47. doi: 10.1038/d41586-020-00137-x. PMID: 32020106.

Venkatesh HS, et al. Electrical and synaptic integration of glioma into neural circuits. *Nature*. 2019 Sep;573(7775):539-545. doi: 10.1038/s41586-019-1563-y. Epub 2019 Sep 18. PMID: 31534222; PMCID: PMC7038898.

Venkataramani V, et al. Glioblastoma hijacks neuronal mechanisms for brain invasion. *Cell*. 2022 Aug 4;185(16):2899-2917.e31. doi: 10.1016/j.cell.2022.06.054. Epub 2022 Jul 31. PMID: 35914528.

Requested domains of expertise (up to 5 keywords): electrophysiology, in vitro cell culture, signal analysis, micro electrode array implant