Master's thesis project at the Institute of Complex Systems – Zelluläre Biophysik, Forschungszentrum Jülich

Role of EAAT1 chloride channel on glioma pathogenicity

Gliomas are aggressive tumors that derive from glial cells and make up about 80% of all malignant brain tumors. Gliosarcoma arise from mesenchymal tissue and represent a rare form of glioma with a patients median survival of around 9 months. The invasive behavior of glioma cells requires shape-volume changes for movement through narrow migratory pathways. Glioma cells accumulate $[Cl^-]_{int}$ to around 100.5 ± 11.1 mM and use the chloride gradient as osmotically driving force for rapid volume changes (Habela et al., 2008 *J Neurophysiol* **101** 750-757). Glioma cells downregulate EAAT (excitatory amino acid transporter) expression and function to alter glutamate homeostasis in the brain which supports their own growth, invasion and survival (Robert et al., 2014 *Cell. Mol. Life Sci.* **71** 1839-1854). However, EAATs are not only glutamate transporter, but also function as anion selective-channels. We recently showed that EAAT1 and EAAT2 directly affect glial $[Cl^-]_{int}$ during development and synaptic activity (Untiet et al., 2017 *Glia* **65** 388-400). The alteration of EAAT expression in glioma cells might change $[Cl^-]_{int}$ as well and facilitate chloride accumulation that allows for rapid volume adjustments.

The master thesis project aims at understanding the effects of glutamate transporters and intracellular chloride concentrations in gliosarcoma cells. Using fluorescence lifetime imaging microscopy (FLIM) and the chloride sensitive fluorescent dye MQAE the $[Cl^-]_{int}$ in EAAT1 transfected gliosarcoma cells will be investigated. Moreover, cell proliferation and migration will be studied in order to understand the correlation of $[Cl^-]_{int}$ and malignant growth in this type of cells.

During the master thesis, the prospective student will get experiences with cell culture, heterologous expression, immunocytochemistry, two-photon microscopy, fluorescence lifetime imaging microscopy, cell proliferation and migration assays

For further information please contact:

Dr. Verena Untiet

Institute of Complex Systems 4 (ICS-4)

Cellular Biophysics
Forschungszentrum Jülich GmbH
52425 Jülich

v.untiet@fz-juelich.de

Telefon: +49 2461 61-8067
Telefax: +49 2461 61-4216