

Project 1.5 Targeting tumour-host interactions in paediatric malignant gliomas to reinvigorate immunity and improve radio- and immunotherapy efficacy

Supervisor: Katarzyna Leszczyńska, PhD / Prof. Bożena Kamińska-Kaczmarek Ph.D., D.Sc.

Laboratory: Molecular Neurobiology

www: : <https://kaminska-lab.nencki.edu.pl/>

Background:

Paediatric high-grade gliomas (pHGGs) are malignant, deadly tumours developing in infants and children. Mutations in histone coding genes disturb epigenetic regulation and in cooperation with other oncogenes promote tumour initiation and progression. pHGGs are fast-growing and diffusive which makes them hard to remove or treat. Surgery (unattainable in midline brain regions) and radiotherapy (RT) remain the only option with transient benefits as median survival is 9-15 months. Those tumours are immunosuppressed, thus immunotherapy is ineffective. Knowledge of tumour-immune cell interactions in the tumour microenvironment (TME) would reveal novel targets allowing to find new ways to eradicate mutated tumour cells, improve efficacy of RT, and reinvigorate anti-tumour immunity. The project is part of larger proposal carried out by the international, multidisciplinary consortium HIT-GLIO, which the Ph.D candidate will join. In the project we will create cellular and animal models of increasing complexity: human glioma-microglia co-cultures, xenografts and syngeneic pHGG mouse models which would be platforms for mechanistic studies and drug screening. We will evaluate hypoxia-inducible epigenetic inhibitors and blockers of tumour-host interactions to improve RT and immunotherapy responses. Functionalised nanocarriers will be used to target immune cells and deliver drugs to the brain. The expected outcomes of HIT-GLIO would ultimately pave ways to new clinical trials to improve the way pHGGs are treated.

The candidate will focus on studying the interactions of glioma cells with immune cells in vitro and in in vivo mouse models. The candidate will investigate the impact of hypoxia (hypoxia) on tumor-host interactions in the context of improving response to RT.

Aim:

The aim of the project is to analyze the poorly understood tumor microenvironment and immune system interactions in pediatric malignant gliomas (pHGG). We will use the unique new research tools of single-cell transcriptomics and multimodal imaging to understand these interactions and develop strategies to enhance the immune system's response and to radiotherapy (RT).

Requirements:

- Very good knowledge of English, high motivation and readiness to master new laboratory techniques are required,
- completing internships/apprenticeships and experience in laboratory work with cancer cells, as well as having a certificate to work with animals will be a huge advantage.

For further information, please contact Dr. Katarzyna Leszczyńska (k.leszczynska@nencki.edu.pl) or Prof. dr hab. Bożena Kamińska-Kaczmarek (b.kaminska@nencki.edu.pl).