The Role of the Microenvironmental Landscape in Brain Cancer Progression and Therapy Resistance

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Glioblastoma multiforme (GBM) is a type of brain tumour that is categorized as having the highest degree of aggressiveness, invasiveness, and metastatic potential. GBM accounts for 60% of brain tumours in adults, and patient prognosis is very poor - ranging from only 14 to 15 months following diagnosis. Despite extensive chemo- and radio-therapy treatments, patients relapse. Thus, better understanding of GBM biology is crucial to the advent of novel and effective therapeutic interventions. The tumour niche, also known as the cancer stroma, is composed of the extracellular matrix and several types of recruited cells including astrocytes, fibroblasts and immune cells. Astrocytes, as well as fibroblasts, secrete diverse molecules of structural nature which were found, in other types of cancer, to contribute to the maintenance of malignant characteristics of the tumour mass. Therefore, we hypothesize that the brain tumour niche, as well as the activation of its fibroblasts and astrocytic components plays a crucial role in the aggressiveness of GBM. My project is the first to study the role and activation of normal fibroblasts and astrocytes in the progression of GBM. We will first study the content and characteristics of the fibroblast populations in sections obtained from GL261 glioma cell line-derived brain tumours, in comparison to normal brain tissue, using immunohistochemistry. We will further establish mouse normal primary astrocyte cell lines and employ commercially available mouse embryonic fibroblasts to establish cocultures with GL261 cells *in-vitro*. Both monolayer and 3D culture models will be utilized to study the activation and the role of the astrocyte/fibroblast component in the control of GBM progression and therapy resistance. In summary, my project will not only contribute to a better understanding of the mechanisms regulating GBM microenvironment, but it will also identify potential novel treatment approaches.