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### Novel Approach in Resolving the Mechanism Behind Brain Tumour Heterogeneity and Therapy Response

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UWill Discover – Oral Presentation  
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Novel Approach in Resolving the Mechanism Behind Brain Tumour Heterogeneity  
and Therapy Response

Glioblastoma multiforme (GBM) is the most aggressive form of brain tumour with 5-year survival rates of less than 10%. Data supports that select cell populations within the tumour mass, referred to as Brain Tumour Initiating Cells (BTICs), are the drivers of GBM growth. While the true origin of these cells is debatable, physiologically these cells possess immature properties of normal neural stem cells. They are highly resistant to drug treatment, radiation and form tumours at a high rate when transplanted into mice. Adding to GBM complexity is the fact that not all the tumours are the same; most patients can be grouped into at least 3 different ‘subtypes’ of GBM using modern genetic tools. This project builds on exciting data demonstrating that a unique cell cycle regulator, Spyl (or RINGO by other groups) is found in normal neural stem cells during brain development, yet, it controls expansion of BTICs. Understanding which specific BTIC populations within the GBM heterogeneous mass are driven by Spyl and whether this is subtype dependent, may represent novel and effective treatment strategies.

Utilizing brain tumour patient-derived cells of genetically determined GBM subtype and based on expression of well defined BTIC markers, I established a BTIC bank through application of different cell sorting techniques. This approach allows me to further dissect the role of Spyl in those dangerous cell populations, both *in vitro* and *in vivo*, to understand how specific BTICs grow, divide, and what role they play in each of the GBM subtypes, which is the aim of this project.

Primary results revealed a strong association of specific combinations of markers within distinct GBM subtypes and significant correlation of Spyl levels with specific BTIC populations, which sets a potential direction for assessment of new therapy targets and effective treatment strategies against GBM.

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