TITLE
Metabolic heterogeneity in malignant glioma

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RESEARCH PROJECT DESCRIPTION:
The notion of altered tumor cell metabolism was originally introduced in the 1920's when Otto Warburg made the observation that, even in the presence of sufficient oxygen, cancer cells take up an excess of the sugar glucose and utilize it via fermentation as opposed to respiration. Even though this process generates less energy compared to glucose utilization via respiration, it is significantly faster, providing a growth advantage when glucose is present. Dysregulated cellular energetics is now a well-accepted hallmark of cancer, and glucose has been central to the study of cancer metabolism. However, the recent focus on metabolism in the field of oncology has led to fundamental discoveries that demonstrated the importance of multiple metabolic processes in cancers that appear to be more metabolically heterogeneous and plastic than originally described and not exclusively addicted to sugar.

Our goal is to characterize the metabolic heterogeneity and plasticity present in brain cancer and identify cellular compartments and specific mechanisms responsible for the metabolic adaptation of brain tumors.

Medical students will participate in assessing functionally the effect of different experimental metabolic treatments on a particular cell population that we recently identified [1] and that we demonstrated to drive glioma initiation and recurrence. Students will quantify and compare cell death, expansion rates and frequencies determined via flow cytometry, sphere forming frequency assay and *in vivo* limiting dilution transplantation assay, respectively [1-3].

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REFERENCES
1 Deleyrolle, L. P. *et al.* Evidence for label-retaining tumour-initiating cells in human glioblastoma. *Brain : a journal of neurology* **134**, 1331-1343, doi:10.1093/brain/awr081 (2011).

2 Deleyrolle, L. P. *et al.* Determination of somatic and cancer stem cell self-renewing symmetric division rate using sphere assays. *PLoS One* **6**, e15844, doi:10.1371/journal.pone.0015844 (2011).

3 Hu, Y. & Smyth, G. K. ELDA: extreme limiting dilution analysis for comparing depleted and enriched populations in stem cell and other assays. *Journal of immunological methods* **347**, 70-78, doi:10.1016/j.jim.2009.06.008 (2009).