In vitro expansion of U87-MG human glioblastoma cells under hypoxic conditions affects glucose metabolism and subsequent in vivo growth

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Résumé en anglais	Hypoxia is a characteristic feature of solid tumors leading to the over expression of hypoxia-inducible factor (HIF)-1α protein and therefore to a specific cellular behavior. However, even though the oxygen tension in tumors is low (<5 %), most of the cell lines used in cancer studies are grown under 21 % oxygen tension. This work focuses on the impact of oxygen conditions during in vitro cell culture on glucose metabolism using 1-13C-glucose. Growing U87-MG glioma cells under hypoxic conditions leads to a two- to threefold reduction of labeled glutamine and an accumulation of fructose. However, under both hypoxic and normoxic conditions, glucose is used for de novo synthesis of pyrimidine since the 13C label is found both in the uracil and ribose moieties. Labeling of the ribose ring demonstrates that U87-MG glioma cells use the reversible branch of the non-oxidative pentose phosphate pathway. Interestingly, stereotactic implantation of U87-MG cells grown under normoxia or mild hypoxia within the striatum of nude mice led to differential growth; the cells grown under hypoxia retaining an imprint of the oxygen adaptation as their development is then slowed down.
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