HG-100
THE ROLE OF HYPOXIA ON LIPID DROPLET PRODUCTION IN GLIOBLASTOMA

Robert Murren, Daniel Tennant, Andrew Peet
HG-100. THE ROLE OF HYPOXIA ON LIPID DROPLET PRODUCTION IN GliOBLASTOMA

Robert Murren1,2, Daniel Tennant2, and Andrew Peet1,3; 1Institute of Cancer and Genomic Sciences, University of Birmingham, Birmingham, UK; 2Institute of Metabolism and Systems Research, University of Birmingham, Birmingham, UK; 3Birmingham Children’s Hospital NHS Foundations Trust, Birmingham, UK

Glioblastoma is a highly malignant disease with limited therapeutic options and a poor prognosis which affects both children and adults. An area of recent interest in glioblastoma is lipid droplets which are quickly emerging as an influential facet of cancer cell biology. Considered dynamic organelles composed of a neutral lipid core and single-layer phospholipid membrane they are associated with higher grade and poorer prognosis in astrocytomas. Furthermore, highly hypoxic areas in glioblastomas are known to alter lipid metabolism as well as being resistant to treatments such as radiotherapy. However the impact of hypoxia on lipid droplets and the mechanisms for lipid droplet formation in glioblastoma is yet to be elucidated. Changes in lipid droplet number between normoxia and hypoxia (0.3% O2) were investigated using confocal fluorescence microscopy. Pharmacological targeting of autophagy and lipid synthesis and degradation was employed to investigate the cellular role of lipid droplets in both adult (T98G and U87) and paediatric (HGG01 and HGG03, Hulleman VUMC, NL) immortalised glioblastoma cell lines. Acute and chronic hypoxic incubation significantly increased lipid droplet expression whilst pharmacological inhibition of lipid synthesis failed to abrogate lipid droplet formation. Instead lipid droplet formation was reliant upon autophagy and lipase function in the U87 and HGG03 cell lines and exogenous uptake from serum in the T98G and HGG01 cell lines. Taken together our data suggests that hypoxia induces an increased level of lipid droplet expression through either autophagy or exogenous uptake from serum and raises the possibility of pharmacological targeting.