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P0373 - METABOLIC TARGETING OF GLIOBLASTOMA CELLS

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Resumen

Objectives: To target glucose addiction of tumour cells.

Methods: Lab based study.

Results: In this study, we initially investigated the effect of glucose deprivation on adult glioma cell viability. We have shown that glucose deprivation induced glioma cell death *in vitro*. We have also shown that free radical scavenger N-acetylcysteine and methyl pyruvate suppressed glucose deprivation induced cell death. We have shown that glucose deprivation induced cell death is not mediated by apoptosis, autophagy or necrosis. Glucose deprivation led to energetic and endoplasmic reticulum (ER) stress in glioma cells. We have also shown that hypoxia rescued glucose deprivation induced cell death whereas glutamine withdrawal had no effect on glucose deprivation induced cell death. We then showed that metformin significantly enhanced glucose deprivation induced cell death which was not mediated by apoptosis, autophagy, necrosis or oxidative stress. We have also shown that AMPK mimic AICAR also promoted glucose deprivation induced cell death whereas 2-deoxyglucose (2DG) suppressed glucose deprivation induced cell death. We have also shown that metformin potentiated glucose deprivation induced energetic stress whereas it suppressed ER chaperone protein GRP78. We have shown that metformin and 2DG combination led to significant cell death in glioma cells which was caspase independent and not mediated by oxidative stress. Finally we have also showed that metformin potentiated 2DG mediated pAMPK upregulation whereas it down-regulated 2DG mediated autophagy and ER chaperone protein GRP78 to induce cell death.

Conclusions: Our experiments to see the effect of complete withdrawal of glucose on glioma cell viability provides a proof of concept that deranged tumour metabolism can be successfully targeted.

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