CBMS-05
COMPREHENSIVE METABOLOMIC ANALYSIS OF IDH1R132H CLINICAL GLIOMA SAMPLES REVEALS SUPPRESSION OF β-OXIDATION DUE TO CARНИTINE DEFICIENCY
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BACKGROUND: Gliomas with isocitrate dehydrogenase 1 (IDH1) mutation have alterations in several enzyme activities, resulting in various metabolic changes. Thus, the objective of this study was to investigate the mechanisms for the better prognosis of gliomas with IDH mutation by performing metabolomic analysis. METHODS: To comprehensively understand the metabolic state of human gliomas, we analyzed clinical samples obtained from surgical resection of glioma patients (grades II-IV) with or without the IDH1 mutation, and compared them with U87 glioblastoma cells expressing IDH1 or IDH1R132H-dDNA. We used capillary electrophoresis and liquid chromatography time-of-flight mass spectrometry for these analyses. RESULTS: In clinical samples of gliomas with IDH1 mutation, levels of 2-hydroxyglutarate (2HG) were significantly increased compared with gliomas without IDH1 mutation. Gliomas with IDH1 mutation also showed decreased 2-oxoglutarate and downstream intermediates in the tricarboxylic acid cycle. Recent advances in production of energy, amino acid, and nucleic acids. The marked difference in the metabolic profile in IDH mutant clinical samples compared with that of mutant IDH expressing cells includes a decrease in β-oxidation due to acyl-carnitine and carnitine deficiency. CONCLUSIONS: These metabolic changes may explain the lower cell division observed in IDH mutant gliomas and may be one mechanism of the better prognosis in IDH1 mutant gliomas.

CBMS-07
SERINE SYNTHESIS AND ONE-CARBON METABOLISM IN GLIOMA CELLS TO SURVIVE GLUTAMINE STARVATION
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Cancer cells optimize nutrient utilization to supply energetic and biosynthetic pathways. These metabolic processes also include reactive oxygen species and epigenetic regulation through nucleic acid and protein methylation, enhancing tumorigenicity and cellular resistance. But less is known about how cancer cells exhibit metabolic flexibility to sustain cell growth and survival from nutrient starvation. Here, we identify a key role for serine availability and one-carbon metabolism in the survival of glioma cells from glutamine deprivation. To identify metabolic response to glutamine deprivation in glioma cells, we analyzed metabolites using gas chromatography and mass spectrometry (GC/MS) in glioma cells cultured in glutamine-deprived medium and examined gene expression of key enzymes for one-carbon units using RT-PCR and western blotting methods. These expressions were also confirmed by immunohistochemical staining in glioma clinical samples. Metabolism studies indicated serine, cysteine, and methionine as key differentiating amino acids between glioma cells from glutamine deprivation. To identify metabolic response to nutrient starvation, we identified upregulation of Methylenetetrahydrofolate dehydrogenase 2 (MTHFD2) to regulate serine synthesis and one-carbon metabolism. Importantly, suppression of this metabolite impaired glioma cell survival in glutamine deprivation. In human glioma samples, MTHFD2 expressions were highest in poorly nutrient regions around "pseudopalisading (MTHFD2) to regulate serine synthesis and one-carbon metabolism. Importantly, suppression of this metabolite impaired glioma cell survival in glutamine deprivation. In human glioma samples, MTHFD2 expressions were highest in poorly nutrient regions around "pseudopalisading (MTHFD2) to regulate serine synthesis and one-carbon metabolism. Importantly, suppression of this metabolite impaired glioma cell survival in glutamine deprivation. In human glioma samples, MTHFD2 expressions were highest in poorly nutrient regions around "pseudopalisading (MTHFD2) to regulate serine synthesis and one-carbon metabolism. Importantly, suppression of this metabolite impaired glioma cell survival in glutamine deprivation. In human glioma samples, MTHFD2 expressions were highest in poorly nutrient regions around "pseudopalisading (MTHFD2) to regulate serine synthesis and one-carbon metabolism. Importantly, suppression of this metabolite impaired glioma cell survival in glutamine deprivation. In human glioma samples, MTHFD2 expressions were highest in poorly nutrient regions around "pseudopalisading tumors. Serine availability and one-carbon metabolism in glioma cells may explain the better survival from glutamine starvation. Here, we identify a key role for serine availability and one-carbon metabolism in the survival of glioma cells from glutamine deprivation. To identify metabolic response to glutamine deprivation in glioma cells, we analyzed metabolites using gas chromatography and mass spectrometry (GC/MS) in glioma cells cultured in glutamine-deprived medium and examined gene expression of key enzymes for one-carbon units using RT-PCR and western blotting methods. These expressions were also confirmed by immunohistochemical staining in glioma clinical samples. Metabolism studies indicated serine, cysteine, and methionine as key differentiating amino acids between glioma cells from glutamine deprivation. To identify metabolic response to nutrient starvation, we identified upregulation of Methylenetetrahydrofolate dehydrogenase 2 (MTHFD2) to regulate serine synthesis and one-carbon metabolism. Importantly, suppression of this metabolite impaired glioma cell survival in glutamine deprivation. In human glioma samples, MTHFD2 expressions were highest in poorly nutrient regions around "pseudopalisading tumors. Serine availability and one-carbon metabolism in glioma cells may explain the better survival from glutamine starvation.