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Metabolic reprogramming after inhibiting glycolysis and TCA cycle in human glioblastoma cells

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As a hallmark of cancer, metabolic reprogramming is recognized as new diagnostic tools and therapeutic targets of cancer. Enhanced glycolysis and mitochondrial dysfunction is the main character for cancer metabolism. Recently, agents that inhibited cancer glycolytic process and improved mitochondria were greatly developed and revealed good prospect for cancer therapy. However, current drugs targeting cancer energy metabolism showed relatively low selectivity and sensitivity and some side effects. Therefore, to clarify the metabolic changes after interrupting metabolic processes could provide comprehensive interpretation for metabolic adaption and clues for improving these therapeutic agents. Here, with normal brain cells HEB as control, we observed the metabolomic changes in U87-MG glioma cells after treatment with glycolysis inhibitor, 2-deoxy-D-glucose (2-DG) and ATPase inhibitor, oligomycin, to analyze the effects of both drugs. Firstly, the results showed that U87-MG cells showed distinguished metabolic characters, with highly increased glycolysis, amino acid and lipid metabolism. Upon 2-DG treatment, U87-MG cells showed metabolic tendency to tyrosine and valine metabolism. However, TCA cycle, glutamate and nucleic acid metabolism were obviously increased in HEB cells. This result suggested that apart from the glycolysis process, amino acid metabolism also played important roles for glioblastoma (GBM) development. After oligomycin treatment, with no significant observed in U87-MG cells, HEB cells exhibited enhanced lipid metabolism and glucose and amino acid metabolism inhibition. This implied that mitochondrial aerobic oxidation showed minor role in U87-MG cells than that in HEB cells. Our study proved that glycolysis played more important function in GBM cells than TCA cycle. However, the appropriate clinical therapeutic strategy and the specific target at metabolism for GBM therapy remain to be studied.

Biography

Erlong Zhang has completed his PhD from Third Military Medical University, China. He is mainly studying the relationship between hypoxia and metabolism and has published three papers in reputed journals.

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