World Academy of Science, Engineering and Technology
International Journal of Medical and Health Sciences
Vol:11, No:07, 2017

Evaluation of Mito-Uncoupler Induced Hyper Metabolic and Aggressive Phenotype in Glioma Cells

Authors : Yogesh Rai, Saurabh Singh, Sanjay Pandey, Dhananjay K. Sah, B. G. Roy, B. S. Dwarakanath, Anant N. Bhatt

Abstract : One of the most common signatures of highly malignant gliomas is their capacity to metabolize more glucose to lactic acid than normal brain tissues, even under normoxic conditions (Warburg effect), indicating that aerobic glycolysis is constitutively upregulated through stable genetic or epigenetic changes. However, oxidative phosphorylation (OxPhos) is also required to maintain the mitochondrial membrane potential for tumor cell survival. In the process of tumorigenesis, tumor cells during fastest growth rate exhibit both high glycolytic and high OxPhos. Therefore, metabolically reprogrammed cancer cells with combination of both aerobic glycolysis and altered OxPhos develop a robust metabolic phenotype, which confers a selective growth advantage. In our study, we grew the high glycolytic BMG-1 (glioma) cells with continuous exposure of mitochondrial uncoupler 2, 4, dinitro phenol (DNP) for 10 passages to obtain a phenotype of high glycolysis with enhanced altered OxPhos. We found that OxPhos modified BMG (OPMBMG) cells has similar growth rate and cell cycle distribution but high mitochondrial mass and functional enzymatic activity than parental cells. In in-vitro studies, OPMBMG cells showed enhanced invasion, proliferation and migration properties. Moreover, it also showed enhanced angiogenesis in matrigel plug assay. Xenografted tumors from OPMBMG cells showed reduced latent period, faster growth rate and nearly five folds reduction in the tumor take in nude mice compared to BMG-1 cells, suggesting that robust metabolic phenotype facilitates tumor formation and growth. OPMBMG cells which were found radio-resistant, showed enhanced radio-sensitization by 2-DG as compared to the parental BMG-1 cells. This study suggests that metabolic reprogramming in cancer cells enhances the potential of migration, invasion and proliferation. It also strengthens the cancer cells to escape the death processes, conferring resistance to therapeutic modalities. Our data also suggest that combining metabolic inhibitors like 2-DG with conventional therapeutic modalities can sensitize such metabolically aggressive cancer cells more than the therapies alone.

Keywords : 2-DG, BMG, DNP, OPM-BMG
Conference Title : ICNMB 2017 : International Conference on Nuclear Medicine and Biology
Conference Location : Zurich, Switzerland
Conference Dates : July 27-28, 2017