proceedings

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Abstract

Differential Expression Analysis in Genes Associated with the Mitochondrial Metabolism Reveals a Potential Influence on the Progression of Glioblastoma from Astrocytoma †

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† Presented at the 4th International Electronic Conference on Cancers, 6–8 March 2024; Available online: https://sciforum.net/event/IECC2024.

Abstract: The most common forms of primary brain tumors are low-grade astrocytoma (ACT) tumors and their progression to the glioblastoma multiforme (GBM), in a high-aggressiveness form. Understanding mechanisms of progression is necessary, and mitochondrial mechanisms are not yet as well elucidated and may be a factor in this disease. Therefore, in this study, we analyzed differential gene expression (DGE) between GBM and ACT, using the MitoXplorer 2.0 to screen nuclear genes involved in mitochondrial metabolism, totaling 1193 genes. The analysis used ACT (n = 195) and GBM (n = 157) samples made available by The Cancer Genome Atlas (TCGA) database. As a complement, we checked the expression of differentially expressed genes (DEGs) in normal tissues using the GTEx Portal, as well as checking disease-free survival (DFS) using GEPIA2. DGE showed five potential DEGs, three of which were downregulated (ACSM2A, ACSM2B, and PRODH2) and two were upregulated (TERT and FBP2). In non-cancerous tissues, upregulated DEGs are normally expressed basally in brain tissue and TERT is normally expressed in tissues such as testis and small intestine, while FBP2 is expressed in the stomach, skeletal muscle, testis, pancreas, and adrenal glands. Alternatively, downregulated DEGs normally show basal or zero expression in brain tissues and are normally expressed in the liver and kidneys. DFS analysis showed that the high expression of the TERT is associated with poor survival, and is the only gene found to be significant among the five DEGs (p-value 0.05). Briefly, our analyses showed five mitochondrial DEGs as potential markers of GBM progression in relation to ACT. Four of the five DEGs have not been reported as factors that can influence the GBM cascade until this work, while the TERT gene has already been indicated as a potential biomarker of brain cancer, having an essential function in the protection of the mitochondrial genome.

Keywords: brain cancer; astrocytoma; glioblastoma; mitochondrial function; metabolism

Citation: de Oliveira, R.C.; Cavalcante, G.C. Differential Expression Analysis in Genes Associated with the Mitochondrial Metabolism Reveals a Potential Influence on the Progression of Glioblastoma from Astrocytoma. *Proceedings* **2024**, *100*, 11. https://doi.org/10.3390/proceedings2024100011

Academic Editor: Stephen Geoffrey Ward

Published: 27 March 2024

Author Contributions: Conceptualization, R.C.d.O. and G.C.C.; methodology, R.C.d.O.; biostatistical analysis, R.C.d.O.; investigation, R.C.d.O.; writing—review and editing, R.C.d.O. and G.C.C. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq).

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: The data presented in this study are available on The Cancer Genome Atlas database (https://portal.gdc.cancer.gov/projects/TCGA-LGG and https://portal.gdc.cancer.gov/projects/TCGA-GBM), accessed on 20 August 2023. In this research we only used the open access data available by TCGA.

Conflicts of Interest: The authors declare no conflict of interest.