2nd International Congress on

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mRNA expression of the glutathione related genes in cultured HeLa cells treated with valproic acid

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Statement of the Problem: The greatest challenge for anticancer therapy is the tendency of malignant cells to develop multidrug resistance (MDR). This phenomenon is manifested as a decrease in drug uptake, an increase in drug efflux by ABC transporters, and the activation of detoxification systems (phase II metabolism, the glutathione system), among other mechanisms of the MDR phenotype. Recently, a new group of anticancer drugs known as epigenetic agents, histone deacetylase inhibitors (HDACIs), has shown better clinical results. They are more specific and less toxic, and are capable of sensitizing malignant cells to conventional anticancer drugs. However, HDACIs have also proven to induce the MDR phenotype. Since glutathione (GSH) is the main detoxification system present in all tissues, the present study focuses on the relation between treatment with valproic acid (an epigenetic drug) and the expression of GSH-related genes in HeLa cell cultures.

Methodology & Theoretical Orientation: Firstly, the molecular analysis of mRNA expression was made by standard PCR, using the total RNA obtained from Hela cells. Then reverse transcription to cDNA was performed and a viability assay was made by using the MTT protocol to evaluate the effects of VPA and BSO (Buthionine sulfoximine), alone or in combination. The second step was to measure the level of intracellular GSH, previously exposing the cells to treatment with VPA and BSO.

Findings: A significant increase was found in the mRNA expression of the glutamate-cysteine ligase modifier subunit (GCLM) and glutathione synthase (GSS). The MTT assay showed a decrease in cell viability with the use of VPA and even more so with the combination of VPA+BSO. The measurement and analysis of variation in the level of GSH is still in progress.

Conclusion & Significance: The induction of MDR by VPA can be considered as mild. This agent may be useful in the treatment of tumors because it can induce death in cancer cells, alone or in combination with BSO or other anticancer drugs. Further studies are necessary to analyze the level of proteins participating in glutathione biosynthesis and recycling after VPA treatment.

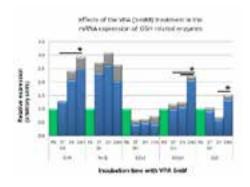


Figure 1: Effects of the VPA (5 mM) treatment in the mRNA expression of GSH related enzymes along time. Relative expression is shown in the y axis. Ribosomal RNA was used as positive control (green), comparisons were made between time zero, 2 and 24 hours of VPA exposition.

Recent Publication

- 1. Papanikolopoulou A, Syrigos KN and Nikolaos Drakoulis (2015) The role of glutamine supplementation in thoracic and upper aerodigestive malignancies. Nutrition and Cancer. 67(2):231-237.
- 2. Gul K, Muge A, Taner A, et al (2015) Oral glutamine supplementation reduces radiotherapy- induced esophagitis in lung cancer patients. Asian Pac J Cancer Prev. 16(1):53-58.

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- 3. Tsujimoto T, Yamamoto Y, Wasa M, et al (2015) L-glutamine decreases the severity of mucositis induced by chemoradiotherapy in patients with locally advanced head and neck cancer: a double-blind, randomized, placebo-controlled trial. Oncol Rep. 33(1):33-39.
- 4. Chattopadhyay S, Saha A, Azam M, et al (2014) Role of oral glutamine in alleviation and prevention of radiation-induced oral mucositis South Asian Journal of Cancer 3(1):8-12
- 5. Tutanc OD, Aydogan A, Akkucuk S, et al (2013) The efficacy of oral glutamine in prevention of acute radiotherapy-induced esophagitis in patients with lung cancer. Contemporary Oncology (Poznan) 17(6):520-524.

Biography

Benjamin Gonzalez Lopez has his expertise and passion in development of morphologic techniques, cell culture and molecular biology. He is a medic graduated in 2014 from Instituto Politecnico Nacional, Mexico City, now studying his 2nd year of master's degree in morphology at the same institution, interested in improving health and wellbeing of people in general, responsible and committed as a student, motivated for the acquisition of new knowledge and skills.

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