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Synergic effect of Mifepristone on resistance to Temozolomide associated with DNA damage repair and apoptosis in glioblastoma

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lioblastoma multiforme is the most common primary central nervous system tumor. The standard treatment \mathbf{J} is surgery, followed by chemotherapy (Temozolamide) and radiotherapy. However, the response has not been sufficient with an average survival of patients 10-16 months. Therefore it is important to have new strategies that increase therapeutic efficacy. Recent studies have shown that Mifepristone (Mif) increases the cytotoxicity of various antineoplastic. The aim of the present study is to investigate whether Mifepristone can modulate the growth of glioma tumors treated with Temozolamide, as well as the study of the molecular mechanisms involved in the response to therapy. The effect of Mifepristone combined with Temozolamide was evaluated in an orthotopic model of glioblastoma. C6 cells were implanted in Wistar rats and the weight was followed throughout the study, after 2 weeks post-implantation the rats were arranged in four groups including: A) Sham, B) Vehicle, C) Tz, D) Mif and E) Tz-Mif. Cell proliferation was evaluated by PET/CT images using 18F-FLT and KI-67; hematoxylin and eosin was used to observe the morphology. For the evaluation of apoptosis and repair to DNA damage were performed western blot using the corresponding antibodies (Bcl-2, Bax and caspase 3 and the DNA repair enzyme O6-methylguanine DNA methyl transferase). Our results showed an accelerated decrease in the weight in vehicle, Tz and Mif groups, while in the rats with Tz-Mif the weight was maintained throughout the study and few Ki-67 positive cells were observed; these results were comparable with PET/CT images, showing a decrease of 18F-FLT uptake. In western blot we observed an increase in the levels of Bax and CL-caspase 3 and a decrease in Bcl-2 levels, as well as in MGMT in the group of Tz-Mif. Our results suggest that the combination of the mifepristone with temozolomide could improve the therapeutic efficacy in glioblastoma.



Recent Publication

1. Llaguno-Munive M, Medina L A, Jurado R, Romero-Pina M and Garcia-Lopez P (2013) Mifepristone improves chemo-radiation response in glioblastoma xenografts. Cancer Cell Int. 13:29.

Biography

Monserrat Llaguno-Munive has completed her PhD in Biomedical Sciences at the Universidad Nacional Autonoma de Mexico, Instituto Nacional de Cancerologia, Ciudad de Mexico, Mexico. She has a research track of over four years working in Instituto Nacional de Cancerologia on projects related to gliobastoma multiforme. She has published one papers in reputed journal and presented in international conferences. She is research interests are focused in the pharmacological repositioning for glioblastoma multiforme.

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