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Effects of a new potential anti-cancer beta-carboline on Hs683 glioma cells

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Statement of the Problem: Gliomas represent the most common primary brain tumors, accounting for 81% of malignant brain tumor. The poor prognosis is partially due to the therapeutic resistance developed by the cells, while the development of new drugs for these tumors faces challenges, such as effective drug delivery (crossing the blood-brain-barrier, BBB). Evidence indicates that protein synthesis plays an important role in cancer onset and progression. In this project, we have investigated the effects of a potential anti-cancer agent, CM16: a new harmine-derivative acting on protein synthesis of Hs683 glioma cells *in vitro*.

Methodology: Two major approaches, molecular biology and proteomics, were used in this work to investigate CM16 effects on the glioma cell line Hs683. Transcription and translation phases were investigated through metabolic labeling assays and further evaluated by sucrose gradients and protein expression level analysis. The study also includes evaluation conducted by the National Cancer Institute (NCI). To study the effects of CM16 on the glioma cells proteome, shotgun proteomics and 2-D electrophoresis were employed.

Findings: CM16 is cytostatic at its IC50 concentration and is more selective towards cancerous than non-cancerous cell lines. The growth inhibition profile of the NCI 60-cell-line to CM16 correlates with those of other protein synthesis inhibitors. CM16 induces inhibition of protein synthesis and these effects likely occur at the initiation phase of translation. Proteome investigation showed significantly different patterns of Hs683 cells treated with CM16 for 15 h and 24 h. Several proteins involved in the global effects of CM16 on the glioma cells were evidenced with the proteomics evaluation.

Conclusion & Significance: CM16 is a potential new anti-cancer agent with the ability to cross the BBB (demonstrated previously in a theoretical model acting on the protein synthesis (initiation phase)) of Hs683 cells. Proteomics evaluation revealed that CM16 does not lead to unspecific down regulation of proteins, it rather affects specific proteins.

Biography

Annelise Carvalho obtained her Master's degree in Pharmacy in 2012 at the Federal University of Santa Catarina (Brazil). She is now pursuing a PhD at the Université Libre de Bruxelles (Belgium) with a scholarship granted by CAPES/Brazil. Her research interest encompasses the broad field of Drug Discovery and Development. More specifically, her current project aims at deciphering the mechanism of action of a novel beta-carboline derivative as a protein synthesis inhibitor of cancer cells.

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