A Novel Dynamic Proteomic Strategy to Analyze the Effects of Perillyl Alcohol on Glioblastoma Cells (A172)

Fischer, J.S.G.[1,2], Liau, L.[2], Carvalho, P.C.[2,3], Carneiro V.C[3]. Carvalho , M.G.C.[4], Domont, G.B.[1], Yates III, J.R.[2]

[1]Department of Biochemistry, Institute of Chemistry, Federal University of the Rio de Janeiro and The Proteomic Network of Rio de Janeiro, RJ, Brazil [2]Department of Chemical Physiology, The Scripps Research Institute, La Jolla, California, USA. [3]Systems Engineering and Computer Science Program, COPPE, Federal University of Rio de Janeiro, RJ, Brazil.[4] Institute of Biophysics Carlos Chagas Filho, Federal University of Rio de Janeiro, RJ, Brazil.

Glioblastoma multiform (GBM) is by far the most malignant glioma and is associated with a dismal prognosis. During the last 25 years, no significant advances in GBM treatments were accomplished, making the quest for new chemotherapeutic agents a must. Perillyl alcohol (POH), a naturally occurring terpene, is a new and promising chemotherapeutic agent; however, little is known about its effects at a molecular level. Here, we studied early protein alterations of A172 cells when exposed to POH by introducing a high-throughput dynamic shotgun proteomics strategy. The later uses two-dimensional liquid chromatography coupled on-line with tandem mass spectrometry to analyze membrane enriched protein fractions of A172 exposed to POH at different time points (0, 1min, 10min, 30min, 60min). We then developed a computational strategy to statistically group proteins according to similar temporal expression profiles and automatically infer the biological functions of these groups through annotation databases (ex. Gene Ontology). We identified more than 4000 proteins, many of which play a critical role in cancer signaling pathways, and groups of proteins related to the Ras pathway, tissue homeostasis, induction of apoptosis, metallopeptidase activity, and ubiquitin-protein ligase activity to name a few. When necessary, results were confirmed with western blot.

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