

Metabolomics of Glioblastoma: Discovery of differentially regulated metabolites encoding tumorigenicity and treatment resistance in cell culture models

Krishnan Thirumoorthy, Nicolaus Gordon, Disha Patel, Masa Okamoto, Arnab Chakravarti and Kamalakannan Palanichamy

Department of Radiation Oncology, The Ohio State University Medical Center, USA

Glioblastoma (GBM) is the most aggressive form of brain tumor. The average survival of patients with this condition is about 15 months regardless of treatment choice, which range from surgery, chemotherapy and radiotherapy. GBMs are often associated with molecular heterogeneity and it is becoming well understood that a small subpopulation of cells within the tumor referred to as glioma stem cells (GSC) mediate treatment resistance and enhanced tumorigenicity. Through this work, we have made an attempt to uncover whether these subtypes are maintained by differentially regulated metabolites using cell culture models comprising of normal human astrocytes, glioblastomas and GSCs. Metabolites in the extracellular and intracellular compartments of cells were analyzed both on the discovery mode using LC-MS Quadrupole Time of Flight (Q-TOF) and validation mode using LC-MS Triple Quad (QQQ). Our results disclosed an interesting list of differentially regulated metabolites when comparing extracellular / intracellular compartments. The differentially regulated metabolites were identified using multivariate analysis. The identified metabolites in endogenous and exogenous compartments correlate with the degree of tumorigenicity and treatment resistance. To avoid false positives, the differentially regulated metabolites were confirmed by chromatography retention time, isotopic and mass fragmentation patterns of synthetic compounds. Currently, we are conducting functional studies in cell lines by exogenous addition of metabolites. This study provides evidence of the differentially regulated metabolites which dictate the difference in the metabolism and pathways in GBM. The results of these studies will be presented.

Biography

Krishnan Thirumoorthy has completed his Ph.D from University of Kalyani, India and postdoctoral studies from California State University-East Bay, Hayward. He is currently working as a postdoctoral fellow at The Ohio State University, Medical Center. He was worked as a research fellow at Birla Institute of Technology and Science (BITS) - Pilani and National Chemical Laboratory (NCL) - Pune, India. His research interest focuses on Metabolomics and System Biology.