Joya Chandra, Brain Disord Ther 2016, 5:3(Suppl)
http://dx.doi.org/10.4172/2168-975X.C1.007

International Conference on

Neuro Oncology and Rehabilitation

July 21-22, 2016 Brisbane, Australia

Joya Chandra

University of Texas MD Anderson Cancer Center, USA

Epigenetically targeted strategies for brain tumor therapy

Glioblastoma multiforme (GBM) is the most common and most aggressive malignant brain tumor, with a five year survival rate of less than 10%. Large scale profiling studies in glioblastoma have afforded insight into the genes that are aberrantly expressed in patients, however, translating this knowledge into improved clincial outcomes remains challenging. Epigenetic enzymes control gene expression and have become popular targets for cancer therapy. In particular, inhibitors of histone deacetylases (HDACi) have been developed for clinical use but have limited activity as single agents. We designed a novel epigenetically targeted strategy based on our finding that high levels of expression of LSD1 (lysine specific demethylase 1) or KDM1A is seen in glioblastoma cells compared to normal human astrocyes, and in pateint derived GBM stem cells compared to normal neural stem cells. LSD1 cooperates with HDAC1/2 and is implicated in several cancers, and we found that histone methylation was modulated by HDACi. Inhibition of LSD1, by knockdown using short hairpin RNA, or with pharmacological inhibitors, induced apoptosis in GBM lines but not normal counterparts, indicating selectivity of this approach for malignant cells. Using FDA approved drugs that target HDACs and LSD1, vorinostat and tranylcypromine, we tested *in vivo* efficacy of this combination in orthotopic mouse models of GBM and found enhanced survival. RNA-Seq conducted in cell lines suggested that *TP53* and *TP73* may be viable biomarkers to predict response to these agents, and was validated *in vivo*. Taken together, our results delineate a novel therapeutic strategy for the treatment of glioblastoma.

Biography

Joya Chandra, PhD, is an Associate Professor at the University of Texas MD Anderson Cancer Center. Research in her lab is directed towards understanding the basis for sensitivity and resistance to cancer therapeutics and optimizing their use. She has published on this topic for the past 15 years. Several of her recent publications have described the mechanism of action of epigenetically targeted agents such as histone deacetylase inhibitors, either as single agents or in combination with other therapies. She has authored over 50 original research papers, invited reviews and book chapters.

jchandra@mdanderson.org

Notes: