RM-01. RADIATION INDUCED PRMT5 EXPRESSION IS REGULATED BY miRNA-96 IN GlioBlastoma

Yeshavanth Kumar Banasavadi-Siddegowda, Jaime Imitola, Robert Baiocchi, and Balveen Kaur; Ohio State University, Columbus, OH, USA

BACKGROUND: Glioblastoma (GB) represent the most common and aggressive histological subtype among malignant gliomas and are associated with poor outcomes. It is composed of multiple types of tumor cells displaying multiple genetic and epigenetic defects affecting tumor suppressor gene expression, regulation of growth and apoptosis. Recurrence is the major concern with the current standard therapy. Protein arginine methyltransferase enzyme 5 (PRMT5), that regulates many cellular processes through its methylation-dependent and independent activity is overexpressed in this disease. We hypothesize that PRMT5 contributes to radioresistance in GB. Using patient derived GB neurosphere models we are probing the role of PRMT5 in inducing radioresistance in GB. METHODS: GB neurospheres dispersed into single cell, were treated with radiation or transfected with specified siRNAs. At appropriate time, cells were collected and probed for mRNA expression by qPCR and protein level by immunoblotting. RESULTS: We found that PRMT5 associates with Hsp90 in GB neurospheres and that this binding is essential for PRMT5 stability. In addition to higher levels of baseline expression, radiation treatment increases PRMT5 mRNA level by 2 fold and protein expression by 60%. This increase is independent of its post-translational stability conferred by its association with Hsp90. However radiation treatment decreases miRNA-96 level significantly ($p \leq 0.01$). Overexpression of miRNA-96 down regulates the expression of PRMT5 protein. Additionally we found that PRMT5 is important for regulation of HIF1alpha, a transcription factor induced post radiation and known to be involved in radiation resistance. We are currently investigating the implications of PRMT5 inhibition in conjunction with radiation in vivo. CONCLUSIONS: Based on our findings we conclude that radiation treatment induced suppression of miRNA-96 causes increased expression of PRMT5. This suggests that increased expression of PRMT5 may contribute for HIF-mediated radioresistance in GB.