Novel strategies to overcome multiple drug resistance in Glioblastoma multiforme

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Abstract

Glioblastoma multiforme is an aggressive brain tumor representing 60% to 70% of all gliomas with a 5-year survival rate of 6%. The distinctive intra and inter-tumor heterogeneity within the same GBM tumor makes it hard to treat with the aid of surgery, radiation, or conventional chemotherapies, while multiple drug resistance has been the major obstacle for developing new therapies. Multiple drug resistance in GBM is a multifactorial process including the methylation status of O6 - methylguanine-DNA methyltransferase (MGMT), presence of cancer stem cells (SCs), upregulation and activating mutations in various oncogenes, such as epithelial growth factor receptor (EGFR), platelet-derived growth factor receptor A (PDGFRA), and isocitrate dehydrogenase 1 (IDH1) as well as uncontrolled expression of multidrug resistance proteins such as Pgp are believed to be main reasons for chemotherapy failure. The current chemotherapy options are more palliative than being curative and only help in delaying the time of relapse. The webinar aims to discuss recent advances to overcome GBM drug resistance in general including nano-codelivery system with more focus on my research findings of targeting the multiple drug resistance gene MDR1 and its P-glycoprotein through silencing the RNA binding protein HuR to boost glioma cells sensitivity to chemotherapy. The human antigen R (HuR) is a member of the Hu family of RNA-binding proteins and its role has been extensively investigated in glioblastoma being a target for various cancer-related transcripts with AU-rich elements (ARE's), such as VEGF-A and COX-2 promoting proliferation, angiogenesis, and chemoresistance. HuR knockdown using si-RNA technology resulted in a massive reduction in MDR1 gene expression as well as downregulation of P-gP demonstrated by western-blotting analysis leading to an increase in glioma cells sensitivity to cisplatin however there was no change in IC50 of doxorubicin between sicontrol and si-HuR group.

Biography:

Mona Elmokadem is a Master student in pharmacology and drug discovery United Kingdo.