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Role of Sulf1/Sulf2 in Cell Signaling and Drug Resistance in Glioblastoma

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Glioblastoma is a lethal brain cancer with very poor prognosis that activates a number of receptor tyrosine kinase (RTK) signaling pathways. RTK activities driving tumour growth and/or metastasis can be predicted to be inhibited by extracellular Sulf1 and Sulf2 enzymes due to their ability to desulfate heparan sulfate proteoglycans required for RTK ligand receptor interaction. The present study, however, demonstrates marked functional divergence in Sulf1, Sulf2 activities in U251 glioblastoma cells.

Our gain and loss of Sulf1/Sulf2 function in U251 cells in the presence and absence of some ligands and their inhibitors show marked diversification of Sulf1 and Sulf2 function in glioblastoma cells. For example, Sulf2 up regulates PDGF cell signaling while full length Sulf1 has little effect, yet shorter inactive variant of Sulf1 fails to exert such effect and thus shows some similarity to Sulf2. This Sulf1/Sulf2 functional distinction is also observed in EGF cell signaling promotion by Sulf2 but not by full length active Sulf1 while shorter inactive variant of Sulf1 promotes both PDGF and EGF cell signaling similar to promotion of both these pathways by Sulf2. This study will describe the role of Sulf1 and Sulf2 enzymes in cell signaling and hypoxia as well as their differential roles in TMZ drug resistance during in vitro growth of some cell lines.

Biography:

Professor Dhoot graduated from university of London and gained PhD and DSc qualifications from university of Birmingham UK before working on regulation of muscle development and regeneration in the context of muscle nerve interaction. Following the discovery of Sulf1 and Sulf2, her subsequent work has exploited the properties of these enzymes in their ability to regulate cell signaling in both a positive and a negative manner. The Sulf1/Sulf2 mediated cell signaling modulation thus offers the potential to not only improve tissue regeneration but also the potential to inhibit tumour growth in which cell signaling and Sulf1/Sulf2 activities are highly dysregulated.