Ubiquitination

The addition of ubiquitin to a substrate protein is called ubiquitination or ubiquitylation. Ubiquitination can affect proteins in many ways: it can signal for their degradation via the proteasome, alter their cellular location, affect their activity, and promote or prevent protein interactions.

Ubiquitination is carried out in three main steps: activation, conjugation, and ligation, performed by ubiquitin-activating enzymes (E1s), ubiquitin-conjugating enzymes (E2s), and ubiquitin ligases (E3s), respectively. The result of this sequential cascade binds ubiquitin to lysine residues on the protein substrate via an isopeptide bond, cysteine residues through a thioester bond, serine and threonine residues through an ester bond, or the amino group of the protein's N-terminus via a peptide bond.

The ubiquitin-proteasome system is a well-orchestrated system that controls the fate of most proteins by striking a dynamic balance between ubiquitination and deubiquitination of substrates, having a profound influence on the modulation of oncoproteins, tumor suppressors, and cellular signaling pathways.

Deubiquitinating enzymes (DUBs) have emerged as potential anti-cancer targets due to their targeting several key proteins involved in the regulation of tumorigenesis, apoptosis, senescence, and autophagy.

A review attempts to summarize recent studies of Glioblastoma-associated DUBs, their roles in various cellular processes, and discuss the relation between DUBs deregulation and gliomagenesis, especially how DUBs regulate glioma stem cells pluripotency, microenvironment, and resistance of radiation and chemotherapy through core stem-cell transcriptional factors.

Jin et al., also review recent achievements and progress in the development of potent and selective reversible inhibitors of DUBs, and attempted to find a potential Glioblastoma treatment by DUBs intervention [1].

1)
Jin WL, Mao XY, Qiu GZ. Targeting Deubiquitinating Enzymes in Glioblastoma Multiforme: Expectations and Challenges. Med Res Rev. 2016 Oct 24. doi: 10.1002/med.21421. Review. PubMed PMID: 27775833.