Differentiation therapy has been proposed as an alternative for glioblastoma treatment, with the aim of bringing cancer cells into a post-mitotic/differentiated state, ultimately limiting tumor growth. As an integral component of cancer development and regulation of differentiation processes, kinases are potential targets of differentiation therapies.

Lane et al. in a study describe how the screening of a panel of kinase inhibitors (KIs) identified PDGF-Rα/β inhibitor CP-673451 as a potential differentiation agent in glioblastoma. They show that targeting PDGF-Rα/β with CP-673451 in vitro triggers the outgrowth of neurite-like processes in glioblastoma cell lines and glioblastoma stem cells (GSCs), suggesting differentiation into neural-like cells while reducing proliferation and invasion in 3D hyaluronic acid hydrogels. In addition, they report that treatment with CP-673451 improves the anti-tumor effects of temozolomide in vivo using a subcutaneous xenograft mouse model. RNA sequencing and follow-up proteomic analysis revealed that upregulation of phosphatase DUSP1 and consecutive downregulation of phosphorylated-p38 mitogen-activated protein kinases can underlie the pro-differentiation effect of CP-673451 on Glioblastoma cells. Overall, the present study identifies a potential novel therapeutic option that could benefit Glioblastoma patients in the future, through differentiation of residual GSCs post-surgery, with the aim to limit glioblastoma recurrence and improve quality of life [1)].

1)
Lane R, Cilibrasi C, Chen J, Shah K, Messuti E, Mazarakis NK, Stebbing J, Critchley G, Song E, Simon T, Giamas G. PDGF-R inhibition induces glioblastoma cell differentiation via DUSP1/p38MAPK signaling. Oncogene. 2022 Apr 7. doi: 10.1038/s41388-022-02294-x. Epub ahead of print. PMID: 35393545.