IQGAP1 (IQ motif containing GTPase activating protein 1) is a scaffolding protein that is highly conserved across species and is widely expressed in various tissues. It has been shown to play a critical role in many cellular processes, including cell adhesion, migration, proliferation, and differentiation.

IQGAP1 contains multiple domains, including IQ motifs that can bind to calmodulin and Ras GTPases, a WW domain that binds to proline-rich motifs, and a C-terminal domain that interacts with actin filaments. Through these interactions, IQGAP1 can modulate the activity of various signaling pathways, such as the Rho GTPase and MAPK pathways, and regulate the organization and dynamics of the actin cytoskeleton.

Studies have suggested that IQGAP1 is involved in the development and progression of several human diseases, including cancer, cardiovascular disease, and neurological disorders. Dysregulation of IQGAP1 expression and activity has been implicated in tumor invasion and metastasis, as well as in the pathogenesis of Alzheimer's disease and stroke.

Given its multifaceted roles in cellular physiology and pathology, IQGAP1 is an important subject of research in the fields of cell biology, cancer biology, and neuroscience.

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Diffuse invasion is an important factor leading to treatment resistance and a poor prognosis in gliomas. Zhang et al. found that expression of the tripartite motif containing 56 (TRIM56), a RING-finger domain containing E3 ubiquitin ligase, was markedly higher in glioma than in normal brain tissue, and was significantly correlated with malignant phenotypes and a poor prognosis. In vitro and in vivo experimental studies revealed that TRIM56 promoted the migration and invasion of glioma cells. Mechanistically, TRIM56 was transcriptionally regulated by SP1 and promoted the K48-K63-linked poly-ubiquitination transition of IQGAP1 at Lys-1230 by interacting with it, which in turn promoted CDC42 activation. This mechanism was confirmed to mediate glioma migration and invasion.

The study provides insights into the mechanisms through which TRIM56 promotes glioma motility, i.e., by regulating IQGAP1 ubiquitination to promote CDC42 activation, which might be clinically targeted for the treatment of glioma [1].

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Zhang Q, Zheng J, Wu W, Lian H, Iranzad N, Wang E, Yang L, Wang X, Jiang X. TRIM56 acts through the IQGAP1-CDC42 signaling axis to promote glioma cell migration and invasion. Cell Death Dis. 2023 Mar 4;14(3):178. doi: 10.1038/s41419-023-05702-6. PMID: 36870986.