Two members of the phosphoinositide 5-phosphatase family, SKIP and SHIP2, have been associated with cell migration in glioblastoma; however, the precise role these enzymes play in the process - and whether they work in concert - remains unclear.

Ramos et al., compared phosphoinositide 5-phosphatases expression in glioblastoma primary cells and cell lines and showed that SHIP2 and SKIP expression greatly varies between different cell types, while OCRL, another phosphoinositide 5-phosphatase, is constitutively expressed. Upon adhesion of U-251 MG cells to fibronectin, SHIP2, SKIP and PI(4,5)P2 co-localized in membrane ruffles. Upregulation of PI(4,5)P2 was observed in SKIP-depleted U-251 MG cells compared to control cells, but only when cells were adhered to fibronectin. Both PTEN-deficient (U-251) and PTEN-containing (LN229) glioblastoma cells showed a decrease in cell migration velocity in response to SKIP downregulation. Moreover, a SHIP2 catalytic inhibitor lowered cell migration velocity in the U-251 MG cell line. We conclude that integrin activation in U-251 cells leads to co-localization of both SKIP and SHIP2 in ruffles, where they act as potential drivers of cell migration. Depending on their expression levels in glioblastoma, phosphoinositide 5-phosphatases could cooperate and synergize in the regulation of cell migration and adhesion [1)].

1)
Ramos AR, Ghosh S, Dedobbeleer M, Robe PA, Rogister B, Erneux C. Lipid phosphatases SKIP and SHIP2 regulate fibronectin-dependent cell migration in glioblastoma. FEBS J. 2019 Jan 29. doi: 10.1111/febs.14769. [Epub ahead of print] PubMed PMID: 30695232.