FGFR substrate 2

fibroblast growth factor receptor substrate 2 gene.

Basic fibroblast growth factor (bFGF) promotes medulloblastoma (MB) tumor cell invasion through Fibroblast growth factor receptor (FGFR) in vitro and that blockade of FGFR represses brain tissue infiltration in vivo. Transforming growth factor Beta (TGF-β) regulates pro-migratory bFGF function in a context-dependent manner. Under low bFGF, the non-canonical TGF-β pathway causes ROCK activation and cortical translocation of ERK1/2, which antagonizes FGFR signaling by inactivating FGFR substrate 2 (FRS2), and promotes a contractile, non-motile phenotype. Under high bFGF, negative-feedback regulation of FRS2 by bFGF-induced ERK1/2 causes repression of the FGFR pathway. Under these conditions, TGF-β counters inactivation of FRS2 and restores pro-migratory signaling. These findings pinpoint coincidence detection of bFGF and TGF-β signaling by FRS2 as a mechanism that controls tumor cell invasion. Thus, targeting FRS2 represents an emerging strategy to abrogate aberrant FGFR signaling [1)].

1)
Santhana Kumar K, Neve A, Guerreiro Stucklin AS, Kuzan-Fischer CM, Rushing EJ, Taylor MD, Tripolitsioti D, Behrmann L, Kirschenbaum D, Grotzer MA, Baumgartner M. TGF-β Determines the Pro-migratory Potential of bFGF Signaling in Medulloblastoma. Cell Rep. 2018 Jun 26;23(13):3798-3812.e8. doi: 10.1016/j.celrep.2018.05.083. PubMed PMID: 29949765.