Interlocking Relationship between PTK2B and MAPK Signaling Pathway in Glioma Development with *BRAF^{V600E}* Mutation

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Abstract

BRAF^{V600E} is a common oncogenic mutation found in various cancers. In the central nervous system, *BRAF^{V600E}* is predominantly seen in pediatric low-grade gliomas (20% of pLGGs). MAPK signaling pathway is activated in tumors with *BRAF^{V600E}* mutation, promoting rapid proliferation and metastasis of tumor cells. Here we identify Protein Tyrosine Kinase 2 Beta (PTK2B) or its ortholog in *Drosophila*, Focal adhesion kinase (Fak), as critical factor involved in human *BRAF^{V600E}*-mutated glioma and *dRaf^{GOF}*-induced glioma in fly brains, forming a dual regulatory axis with MAPK signaling to sustain glioma proliferation. We demonstrate a balanced relationship between PTK2B/Fak and MAPK signaling pathway in glioma cells, and inhibition of each of these two pathways suppresses tumor growth through distinct cellular processes. Currently we are investigating the specific interlocking regulatory mechanisms of these two pathways in glioma development with *BRAF^{V600E}* mutation.

Keywords

Glioma, *BRAF^{V600E}*, PTK2B, Fak, MAPK signaling pathway.