Glioblastoma multiforme in the Dock

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Glioblastoma multiforme (GBM) is the most common malignant brain cancer in humans. Patients with GBM have a poor prognosis because it is a highly aggressive form of cancer that is commonly resistant to current therapies.

A team of researchers -- led by Bo Hu and Shi-Yuan Cheng, at the University of Pittsburgh Cancer Institute, Pittsburgh -- has now identified a molecular pathway that drives the aggressive cancerous nature of a substantial proportion of glioblastomas; specifically, those that overexpress the protein PDGFR-alpha. This pathway could represent a new therapeutic target for treating individuals with glioblastomas that overexpress PDGFR-alpha.

PDGFR-alpha is overexpressed in a substantial proportion of GBMs, and overexpression of this protein is associated with a poor prognosis and shorter survival time. Hu, Cheng, and colleagues found that PDGFR-alpha signaling in human glioblastoma cells triggered a signaling cascade that involved phosphorylation of the protein Dock180 at tyrosine residue 1811 (Dock180Y1811) and downstream activation of the protein Rac1, which led to tumor cell growth and invasion. In human glioblastoma cells, if Dock180 was manipulated so that it could not be phosphorylated at tyrosine residue 1811 PDGFR-alpha failed to promote tumor growth, survival, and invasion. Thus, these data define a signaling pathway of importance in driving the aggressive cancerous nature of glioblastomas that overexpress PDGFR-alpha.

More information: Activation of Rac1 by Src-dependent

phosphorylation of Dock180Y1811 mediates PDGFR-alpha–stimulated glioma tumorigenesis in mice and humans, *Journal of Clinical Investigation.*