Platelet-derived growth factor in human glioma.

Westermark B, Heldin CH, Nistér M.

Department of Pathology, University Hospital, Uppsala, Sweden.

Platelet-derived growth factor (PDGF) is a 30 kDa protein consisting of disulfide-bonded dimers of A- and B-chains. PDGF receptors are of two types, alpha- and beta-receptors, which are members of the protein-tyrosine kinase family of receptors. The receptors are activated by ligand-induced dimerization, whereby the receptors become phosphorylated on tyrosine residues. These form attachment sites for signalling molecules, which inter alia activate the Ras-Raf pathway. PDGF has important functions in development and is required for a proper timing of oligodendrocyte differentiation. The v-sis oncogene of simian sarcoma virus (SSV) is a retroviral homolog of the B-chain gene, and induces transformation by an autocrine activation of PDGF receptors at the cell surface. SSV induces malignant glioma in experimental animals, suggesting a role for autocrine PDGF in glioma development. PDGF and PDGF receptors are frequently coexpressed in human glioma cell lines. Specific and nonspecific PDGF antagonists block the growth of some glioma cell lines in vitro and in vivo, suggesting that autocrine PDGF is involved in transformation and tumorigenesis. In situ studies of human gliomas show overexpression of alpha-receptors in glioma cells of high-grade tumors. In a few cases, overexpression is caused by receptor amplification. Since high-grade glioma cells also express the PDGF A-chain, an autocrine activation of the alpha-receptor may drive the proliferation of glioma cells in vivo.

Publication Types:
- Review

PMID: 8586462 [PubMed - indexed for MEDLINE]