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Letter to Editor **Open Access**

Ganglioside GM3-growth Factor Receptor Interaction and Cellular Regulation: VEGFR-2 and TGFβR

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Angiogenesis is closely associated with the growth and metastasis of human solid tumor, and is regulated by the balance between angiogenic stimulators and inhibitors released from tumor cells and stromal cells in the tumor microenvironment. Of the angiogenic factors, vascular endothelial growth factor (VEGF) is the most potent endothelial-specific mitogen which activates endothelial cells in tumor neovascularization. GM3 is an anti-angiogenic factor in tumor microenvironment and negatively regulates VEGF-mediated tumor angiogenesis by suppressing the activation of the VEGF receptor-2 (VEGFR-2). GM3 blocked VEGF-stimulated neovascularization in matrigel plugs and chorioallantoic membrane (CAM) assays. VEGF-mediated VEGFR-2 activation was inhibited by GM3. GM3-specific interactions with the extracellular domain (ExD) of VEGFR-2 were clearly demonstrated, and GM3 blocks VEGFR-2 dimerization and the binding between VEGF and VEGFR-2. In C57BL/6 mice inoculated with Lewis lung carcinoma cells, the intraperitoneal injection of GM3 reduced the volume of primary tumors,and an immunohistochemical study indicated that GM3 inhibits the angiogenesis and proliferation of primary tumor cells. Inanother case, TGF-β-induced epithelial-mesenchymal transition (EMT) induces the proliferation and migration of the humanlens epithelial (HLE) cells caused by the posterior capsular opacification (PCO) after cataract surgery.

The relation between GM3 and TGF-β-induced EMT in the HLE B-3 cells is poorly understood. GM3 is involved with TGF-β1-induced EMT in HLE B-3 cells. GM3 and GM3 synthase are significantly increased in TGF-β1-induced HLE B-3 cells. Transcriptional activation of GM3 synthase gene is regulated by Sp1 in HLE B-3 cells upon TGF-β1 stimulation. On the GM3-depleted experiment using by d-PDMP and shGM3, the reduced expression of ganglioside GM3 significantly suppresses the TGF-β-induced migration and EMT-related signaling in HLE B-3 cells. By exogenous treatment of GM3, the suppressed EMT-molecules and cell migration are recovered during TGF-β1-induced EMT. Finally, GM3 is interacted with TGFβRs in TGF-β1-induced HLE B-3 cells. Taken together, the results indicate that GM3 is a blocker of VEGR-VEGFR2 interaction in tumor regression and regulates the EMT by interaction with TGFβRs.

The Gangliosidabbau place in the lysosomes instead. It is carried out by highly specific glycosylhydrolases which sequentially cleave the terminal sugar residues. The GM1 ganglioside is the Stammgangliosid as intermediates generated during the degradation GM2 and GM3 ganglioside. Disorders of Gangliosidabbaus can cause serious disorders (lysosomal storage diseases), the Sphingolipidoses lead. The by the β-galactosidase-related -Defizienz accumulation of GM1 ganglioside in the central nervous system explains the progressive cerebral symptoms in patients with GM1 gangliosidosis. For the degradation of GM2 ganglioside hexosaminidases A and B have jurisdiction. Thus ends the defect of hexosaminidase A in autosomal - recessive inherited Tay-Sachs disease, which is accompanied by an increase in the concentration of the ganglioside GM2, untreated before reaching the third year fatal. Through amniocentesis, however, and examination of amniotic fluid on beta-N-Acetylhexosaminidaseaktivität the Tay-Sachs disease may already be diagnosed during fetal development phase. A deficiency of α-galactosidase A causes an accumulation of globotriaosylceramide, whereby the Fabry disease is caused.

Gangliosides are on their fat-soluble anchored share in the outer cell membrane. Your structural backbone is from Aminodialkoholsphingosine formed. Grob represented contain gangliosides a complex oligosaccharide, a long-chain fatty acid and the sphingosine backbone.