Expression of the IIIc Variant of FGF Receptor-1 Confers Mitogenic Responsiveness to Heparin and FGF-5 in TAKA-1 Pancreatic Ductal Cells.

Kornmann M, Lopez M, Beger H, Korc M.

Department of General Surgery, University of Ulm, 89070 Ulm, Germany.

Human pancreatic cancer is a devastating disease with a poor prognosis (1). Although the exact reasons for the aggressive nature of this disorder are unknown, certain observations have pointed to the important role of growth factors in its pathobiology (2). Many of these cancers frequently overexpress fibroblast growth factors (FGFs) (3). FGF signaling is mediated through four high-affinity tyrosine kinase receptors, termed fibroblast growth-factor receptors (FGFRs) (3,4). The extracellular domain of FGFRs is usually composed of three immunoglobulin (Ig)-like domains (I-III), a transmembrane region followed by a juxtamembrane domain, and a split tyrosine kinase catalytic domain. Several isoforms of FGFR-1, -2, and -3 have been identified, some of which exhibit different ligand-binding properties (3,5). Alternative splicing of the second half of Ig domain III of FGFR-1 results in three receptor variants, termed IIIa, IIIb, and IIIc. The IIIa splice variant yields a secreted receptor that is devoid of any signaling capacity (5). The expression of the IIIb variant is generally restricted to epithelial cell types, whereas the expression of the IIIc variant is restricted to mesenchymal cell types (6-11).