Concomitant over-expression of vascular endothelial growth factor and its receptors in pancreatic cancer.

Itakura J, Ishiwata T, Shen B, Kornmann M, Korc M.
Division of Endocrinology, Diabetes and Metabolism, Departments of Medicine, Biological Chemistry and Pharmacology, University of California, Irvine, CA, USA.

Vascular endothelial growth factor (VEGF) is a potent angiogenic polypeptide that activates 2 distinct high-affinity tyrosine kinase receptors, flk-1/KDR and flt-1. In the present study, we characterized the expression of VEGF and its receptors flk-1/KDR and flt-1 in the normal human pancreas and in human pancreatic cancer tissues and cell lines. VEGF, flk-1/KDR and flt-1 mRNA levels were elevated in cancer tissues compared with normal pancreas. By immuno-histochemistry, VEGF, flk-1/KDR and flt-1 immunoreactivity co-localized in many of the cancer cells within the tumor mass. Three (AsPC-1, Capan-1 and MIAPaCa-2) of 6 pancreatic cancer cell lines expressed flk-1/KDR mRNA and protein, and 4 cell lines (AsPC-1, Capan-1, T3M4 and PANC-1) expressed flt-1 mRNA transcripts. Binding studies with (125)I-labeled VEGF165 indicated that only Capan-1 cells exhibited high levels of specific binding. Furthermore, VEGF enhanced the growth of Capan-1 cells but was without effect in the other cell lines. VEGF also enhanced mitogen-activated protein kinase (MAPK) phosphorylation and c-fos induction in Capan-1 cells, whereas the MAPK kinase inhibitor PD98059 abolished the growth-stimulatory effect of VEGF. These data indicate that human pancreatic cancers have the capacity to over-express VEGF and its receptors and suggest that in some instances VEGF may directly promote pancreatic cancer growth via the MAPK pathway. Copyright 2000 Wiley-Liss, Inc.

PMID: 10585578 [PubMed - indexed for MEDLINE]