Increased expression of Nodal correlates with reduced patient survival in pancreatic cancer.

Nodal (nodal growth differentiation factor) and its inhibitor Lefty (left right determination factor), which are ligands of the TGF (transforming growth factor) ? superfamily, are responsible for the determination of left-right asymmetry in vertebrates. Nodal/Lefty signaling has been suggested to play a role in the development of metastatic melanoma and breast cancer. However, it remains unclear whether this pathway is also involved in human pancreatic ductal adenocarcinoma (PDAC). Pancreatic cancer patient specimens with clinical data (n = 54) were used to investigate the clinical significance of Nodal-Lefty signaling. A set of in vitro assays were carried out in a human pancreatic cancer cell line (Colo-357) to assess the functional relevance of Nodal-Lefty signaling. Nodal was absent in the human normal pancreas, while Lefty was present in islet cells. Though Nodal and Lefty expression were found in cancer cells at various expression levels, the cancer-associated tubular complexes were particularly positive for Lefty. Survival analysis revealed that high expression of Nodal correlated with reduced patient survival (median survival 17.8 vs 33.0 months, p = 0.013). Cultured pancreatic cancer cell lines expressed Nodal and Lefty at different levels. In vitro functional assays revealed that treatment with human recombinant Nodal inhibited cell growth and increased invasion of...
Colo-357 pancreatic cancer cells whereas no effect was found upon treatment with recombinant Lefty. Nodal-Lefty signaling might be involved in the pathogenesis of PDAC as Nodal expression marks a subtype of PDAC with unfavorable prognosis.