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Review

New insights into perineural invasion of pancreatic cancer: More than pain

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ABSTRACT

Pancreatic cancer is one of the most malignant human tumors. Perineural invasion, whereby a cancer cell invades the perineural spaces surrounding nerves, is acknowledged as a gradual contributor to cancer aggressiveness. Furthermore, perineural invasion is considered one of the root causes of the recurrence and metastasis observed after pancreatic resection, and it is also an independent predictor of prognosis. Advanced research has demonstrated that the neural microenvironment is closely associated with perineural invasion in pancreatic cancer. Therapy targeting the molecular mechanism of perineural invasion may enable the durable clinical treatment of this formidable disease. This review provides an overview of the present status of perineural invasion, the relevant molecular mechanisms of perineural invasion, pain and hyperglycemia associated with perineural invasion in pancreatic cancer, and the targeted therapeutics based on these studies.

Contents

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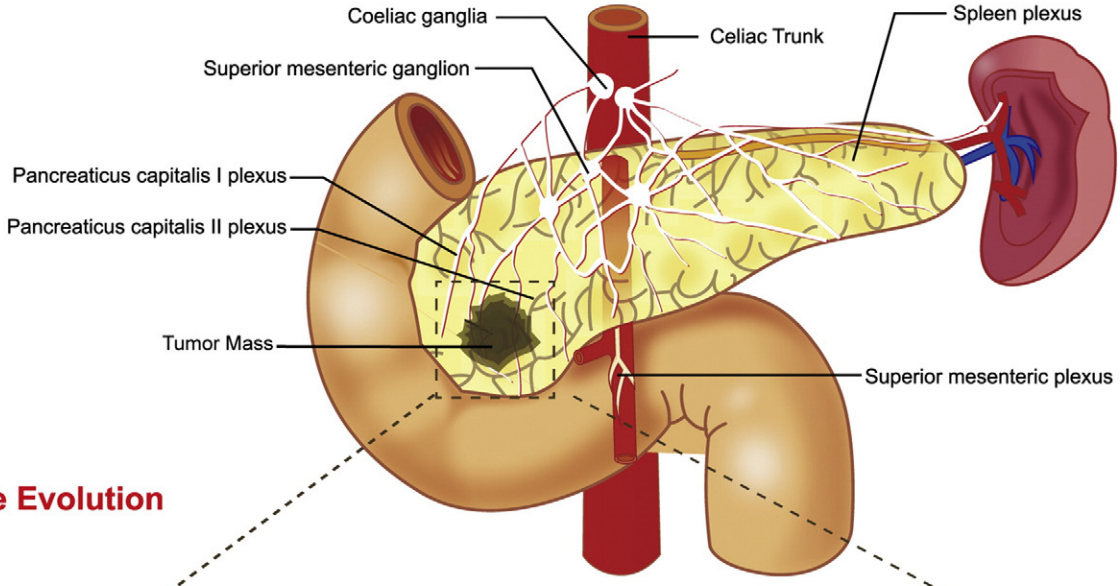
PNI of Pancreatic Cancer

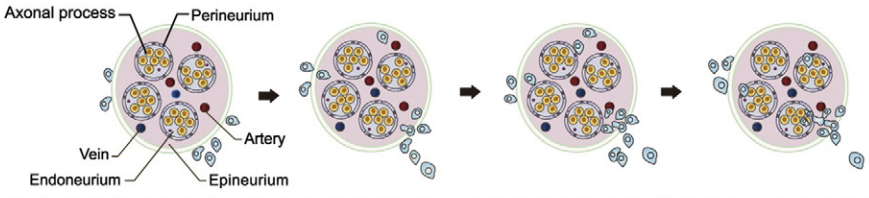
A Clinical Symptoms

- ◇ Abdominal pain
- ◇ Tumor metastasis and invasion in the early phase
- ◇ Local postoperative recurrence
- ◇ Poor prognosis and decreased survival

B Pathological Anatomy



C Microstructure Evolution



D Nerve Microenvironment

- ◇ Neurotrophins: NGF family, GDNF family
- ◇ Chemokines: CXCL12/CXCR4 axis, CX3CR1/CX3CL1 axis
- ◇ Matrix metalloproteinases: MMP-2, MMP-9
- ◇ PNI related cell: Tumor-associated macrophages, Schwann cells, Pancreatic stellate cells
- ◇ Related genes and proteins