

A Review on the Research Progress of Inducible Nitric Oxide Synthase in the Pathogenesis of Pancreatic Malignancy

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Abstract: Pancreatic cancer is a common tumor of the digestive system, at present, the pathogenesis is still unclear, but in the current research on the pathogenesis of pancreatic malignant tumors, the research on inducible nitric oxide synthase is particularly extensive. Therefore, this article focuses on the research progress of inducible nitric oxide synthase in the pathogenesis of pancreatic cancer. This is a review.

Keywords: Inducible nitric oxide synthase; Pancreatic cancer; Research progress

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1. Introduction

Pancreatic cancer is a highly malignant tumor of the digestive system. In recent years, the incidence and mortality of pancreatic cancer have continued to rise. Epidemiological data show that pancreatic cancer is expected to become the second leading cause of cancer and related deaths by 2030 ^[1]. Pancreatic ductal adenocarcinoma (PDAC) is the most common type of pancreatic cancer, accounting for more than 90% of pancreatic cancer. PDAC has a highly inflammatory tumor microenvironment. Recent studies have shown that inflammatory mediators produced by tumors and mesenchymal cells are involved in the occurrence and development of PDAC ^[2]. Nitric oxide (NO) is a free radical and an important mediator of immune and inflammatory response. In addition to playing a role in key biological processes such as vasodilation and neurotransmission, it is also an important immune and inflammatory response mediator. However, there is a large amount of evidence that NO plays an important role in the occurrence and development of cancer ^[3-8].

NO is produced by the family of nitric oxide synthase, including endothelial nitric oxide synthase (eNOS) and neuronal nitric oxide synthase (nNOS) and induced expression after injury type nitric oxide synthase (iNOS). eNOS and nNOS belong to the constitutive isomer NOS and only produce a small amount of NO, while iNOS is the inducible isomer NOS, which will produce a large amount of NO under the action of external factors ^[3]. A large number of clinical studies of PDAC ^[9-14] show that the massive production of NO and the expression of iNOS in the course of PDAC are closely related to PDAC, which can promote the occurrence of cancer and angiogenesis ^[15-17].

Jiangwei Liu ^[18] tested the expression level of iNOS in patients with pancreatic ductal carcinoma and found that the protein expression rate of iNOS was 62.7%, which was related to lymph node metastasis. In

addition, their group also found that the expression of iNOS was closely related to the expression of COX 2. iNOS and COX 2 may play a synergistic role in the occurrence and development of pancreatic cancer, and promote tumor angiogenesis and metastasis.

In order to study the role of iNOS in PDAC in depth, Wang ^[19] established a PDAC genetically engineered mouse model (KPC mouse) and an iNOS knock-out (iNOS^{-/-}) KPC mouse model (NKPC mouse), and found that the expression of iNOS in KPC mice was significantly increased and the survival cycle was significantly shortened, while the progression of PDAC in NKPC mice was slowed down and the survival cycle was significantly prolonged. Their research group further separated KPC and NKPC mouse primary tumor cells, and used the Xcelligence system to monitor the proliferation of tumor cells in real time and dynamically. It was found that the proliferation of primary tumor cells in NKPC mice was reduced, and the apoptosis index Caspase-3 was detected. Compared with KPC mice, the apoptosis of pancreatic tumor cells in NKPC mice was significantly increased. In addition, qRT-PCR found that the expression of E-cadherin, a phenotypic marker of EMT, was significantly higher in primary tumor cells of NKPC mice than in KPC mice. Tip: iNOS is involved in the progression of PDAC, and iNOS gene knockout may delay the progression of PDAC ^[20-21].

In summary, iNOS is involved in the occurrence of PDAC, and the in-depth study of the role of iNOS in PDAC will provide new ideas for the clinical treatment of PDAC.

Disclosure statement

The author declares no conflict of interest.

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