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# GPR120 promotes metastasis but inhibits tumor growth in pancreatic ductal adenocarcinoma

Xiaoyuan Sun [a], Huijun Chu [b], Ke Lei [c], Yandong Ci [d], Haijun Lu [e], Jia Wang [c], Meng Zhou [a], He Ren [c, **], Tongsen Zheng [a, *]

[a] Department of Gastrointestinal Medical Oncology, Harbin Medical University Cancer Hospital, Harbin, 150081, China
[b] Department of Gynecology, Affiliated Hospital of Qingdao University, Qingdao, 266003, China
[c] Department of Gastroenterology, Center of Tumor Immunology and Cytotherapy, Medical Research Center, Affiliated Hospital of Qingdao University, Qingdao, 266003, China
[d] Department of Orthopedics, Qingdao Eighth People's Hospital, Qingdao, 266003, China
[e] Department of Radiation Oncology, Affiliated Hospital of Qingdao University, Qingdao, 266003, China

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ABSTRACT

*Objectives:* G-protein-coupled receptor 120 (GPR120) is a long-chain unsaturated fatty acid receptor, which regulates glucose metabolism and lipid. To date, there are disputes on the roles of GPR120 in the pathogenesis of cancer. Besides, little is known about its roles in the pathogenesis of pancreatic ductal adenocarcinoma (PDAC). This study was designed to investigate the roles of GPR120 in the pathogenesis of PDAC.

*Methods:* Immunohistochemical staining (IHC) was used for detecting the level of GPR120, epithelial-mesenchymal transformation (EMT) markers, Ki-67 and CD31 in ninety-one PDAC patients. Western blot, CCK8, flow cytometry and transwell assays were performed to determine proliferation, apoptosis, and motility *in vitro*. Subcutaneous tumor model was established to validate the roles of GPR120 *in vivo*.

*Results:* GPR120 was highly expressed in PDAC tissues, which was associated with free fatty acids (FFAs), lymph node metastasis (LNM), and poor prognosis. Moreover, GPR120 activation led to down-regulation of E-cadherin and up-regulation of Snail, Vimentin, N-cadherin, MMP2, MMP9, and CD31. Additionally, GPR120 decreased the expression of P-PI3K, P-AKT and CMYC and increased the level of P-JAK2, P-STAT3, Wnt5a, total β-catenin and β-catenin in nucleus.

*Conclusions:* GPR120 promoted proliferation inhibition and apoptosis of PDAC, and contributed to PDAC metastasis via inducing EMT and angiogenesis. GPR120 served as a double-edged sword in the pathogenesis of PDAC.



## 1. Introduction

Pancreatic ductal adenocarcinoma (PDAC), constituting approximately 90% of pancreatic malignancies, is the fourth leading cause of cancer-related death worldwide [1]. To date, the treatment of PDAC is mainly relied on surgery, chemotherapy and radiotherapy [2,3]. Unfortunately, most patients showed a poor prognosis with a five-year survival rate of 9% [4,5]. Early diagnosis of PDAC is still a challenge as there are no pancreatic cancer-specific symptoms [6]. Upon diagnosis, merely 20% of them are eligible for surgery [7,8]. Therefore, early diagnosis based on biomarkers is urgently required to improve their survival.

G protein-coupled receptor 120 (GPR120), functionally activated by long- and medium-chain free fatty acids (FFAs), is reported to play important roles in the regulation of blood lipid and glucose metabolism, together with inflammatory regulation and insulin sensitization [9]. In recent years, some researchers have suggested the roles of GPR120 in tumor progression. For instance, overexpression of GPR120 has been associated with angiogenic switching and cell motility in colorectal carcinomas [10]. Similarly, in 2015, Fukushima et al. reported that GPR120 stimulated the motility and tumorigenicity of pancreatic cancer cells (i.e. HPD1NR, HPD2NR and Panc-1), demonstrating the roles of GPR120 in the

* Corresponding author.
** Corresponding author.
*E-mail addresses:* herenrh@163.com (H. Ren), zhengtongsen@hrbmu.edu.cn (T. Zheng).

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