frontiers in Oncology

ORIGINAL RESEARCH
published: 30 March 2022
doi: 10.3389/fonc.2022.827051

Up-Regulated MISP Is Associated With Poor Prognosis and Immune Infiltration in Pancreatic Ductal Adenocarcinoma

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Specialty section:
This article was submitted to Gastrointestinal Cancers: Hepato Pancreatic Biliary Cancers, a section of the journal Frontiers in Oncology

Received: 05 January 2022
Accepted: 07 March 2022
Published: 30 March 2022

Citation:
Huang X, Zhao L, Jin Y, Wang Z, Li T, Xu H, Wang Q and Wang L (2022) Up-Regulated MISP Is Associated With Poor Prognosis and Immune Infiltration in Pancreatic Ductal Adenocarcinoma. Front. Oncol. 12:827051. doi: 10.3389/fonc.2022.827051

Background: Pancreatic ductal adenocarcinoma (PDAC) is a highly malignant disease with a poor prognosis. More effective biomarkers and treatment options remain to be discovered. Mitotic Spindle Positioning (MISP), also called C19orf21, has been reported to be upregulated in several malignancies. However, the effects of MISP on PDAC have yet to be investigated.

Materials and Methods: The differential expression of MISP at the mRNA and protein levels were evaluated using Gene Expression Profiling Interactive Analysis 2 (GEPIA 2), Gene Expression Omnibus (GEO), and the Human Protein Atlas (HPA) databases, and was further verified by quantitative real-time PCR and western blotting in PDAC cell lines. Correlations between MISP expression and clinical characteristics were explored using Kaplan-Meier Plotter Database and clinical data from The Cancer Genome Atlas (TCGA). CCK-8 assays, Transwell assays, and immunoblotting were used to determine the role of MISP in PDAC proliferation, migration, invasion, and epithelial-mesenchymal transition (EMT) *in vitro*. Gene Ontology (GO), Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis were executed by the R package 'clusterProfiler'. Correlations between MISP expression and immune cell infiltration, immune checkpoints, immunophenoscore (IPS) and the tumor mutational burden (TMB) in PDAC were explored using the R package 'CIBERSORT', the Tumor Immune Estimation Resource 2.0 (TIMER2.0), and The Cancer Immunome Atlas (TCIA) database based on TCGA data.

Result: MISP expression was significantly higher in pancreatic cancer tissues compared to normal pancreas tissues, which was associated with a poor prognosis. Increased expression of MISP was related to the proliferation, migration and invasion of PDAC cell lines. GO and KEGG pathway analyses determined that MISP is involved in the Ras signaling pathway and immune regulation. Higher expression of MISP was associated with decreased infiltration levels of activated CD4+ memory T cells, CD8+ T cells, M2 macrophages and neutrophils. Furthermore, increased MISP was associated with lower expression of immune checkpoint molecules, higher gene mutation burden and IPS.