AB066. P038. HHLA2 is overexpressed in pancreatic ductal adenocarcinoma and precancerous lesions

Han Yan, Ji-Shu Wei, Wanglong Qiu, Helen E. Remotti, Min Tu, Chun-Hua Xi, Ye-Ran Yang, Yun-Peng Peng, Wei-Yann Tsai, Yi Miao, Gloria H. Su

Columbia University Medical Center, New York, NY, USA

Abstract: Although immune-based cancer therapies, such as immune checkpoint inhibitors, are showing promising potentials, current strategies remain unsatisfactory for treating pancreatic cancer. HHLA2 is a newly identified immune checkpoint as a member of the B7 protein family which contributes to regional tumor-related immune suppression by regulating T cells' proliferation and function. Approaches have been made in targeting HHLA2 alone or co-targeting with PD-1/PD-L1 for cancer immunotherapy. However, there are limited information about HHLA2 expression profile available in pancreatic cancer. In this study, we performed Immunohistochemistry (IHC) using tissue microarrays (TMAs, n=92) from surgical resection of pancreatic ductal adenocarcinoma (PDAC) with matched peritumoral tissues. Positive staining was seen in 77.17% (71/92) of PDAC tissues. Of the 20 cases of pancreatic intraepithelial neoplasia (PanIN) in variant stages captured from peritumoral tissues, 95% (19/20) were featured with HHLA2 positive staining, suggesting that HHLA2 expression and its induced immunosuppression has been induced from early PanIN lesions. We also examined HHLA2 expression in TMAs containing intraductal papillary mucinous neoplasm (IPMN) cohort (n=41). The overall HHLA2 positive staining rate of IPMNs is 70.73% (29/41), with low grade dysplasia at 67.65% (23/34) and high-grade dysplasia at 85.71% (6/7). Among the different morphological subtypes, HHLA2 positive staining rates of the intestinal type (92.86%, 13/14) and pancreaticobiliary type (83.33%, 5/6) are higher than the gastric type (52.38%, 11/21). In conclusion, HHLA2 is widely expressed from early pancreatic precancerous lesions (both PanINs and IPMNs) to the late stages of carcinoma in PDAC. HHLA2 is also highly overexpressed in all subtypes of IPMN. Our findings suggest that HHLA2 represents a novel immunosuppressive mechanism and an attractive target for checkpoint inhibitor therapies in pancreatic cancer.

doi: 10.21037/apc.2018.AB066

Cite this abstract as: Yan H, Wei JS, Qiu W, Remotti HE, Tu M, Xi CH, Yang YR, Peng YP, Tsai WY, Miao Y, Su GH. HHLA2 is overexpressed in pancreatic ductal adenocarcinoma and precancerous lesions. Ann Pancreat Cancer 2018;1:AB066. doi: 10.21037/apc.2018.AB066