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Palladin is a Reliable Marker of Liver Metastasis in Primary Pancreatic Endocrine Neoplasms

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Background: Palladin is a proto-oncogene, intimately involved in cell structure and motility. Recently, palladin has been associated with tumor invasion and metastasis. In our microarray analysis palladin was one of the most differentially expressed genes in metastatic relative to clinically-localized primary pancreatic endocrine neoplasms. The purpose of this study was to validate the over-expression of palladin at the protein level in well-differentiated pancreatic endocrine carcinomas and to determine its association with liver metastases.

Methods: A tissue microarray (TMA) comprising well-differentiated pancreatic endocrine tumors/carcinomas (N=38) and matched non-neoplastic pancreatic islets was immunostained with rabbit anti-human Palladin antibody. The immunohistochemical expression of palladin was quantified using the Allred scoring scheme (Intensity score 0-3; stained cells (%) score 0-5; Total Allred score 0-8). Palladin expression and conventional pathologic criteria of malignancy were correlated with the presence of liver metastases.

Results: Patients: 19 males and 19 females. Age range: 27-79 (mean age 54). Tumor size: 0.9-11.5 cm (mean 3.8). Palladin was expressed by all 14 pancreatic endocrine carcinomas with hepatic metastases whereas 14 of 24 (58%) clinically-localized primary pancreatic endocrine tumors expressed palladin ($p < 0.01$) with median Allred scores of 5 (range 3-7) and 2 (range 0-6) respectively ($p < 0.0001$). High tumor expression of palladin showed strong association with liver metastasis ($p < 0.0001$) compared to other pathologic criteria of malignancy (tumor size, mitotic count, Ki-67, T-stage and N-stage). Mean Allred score for normal-neoplastic pancreatic-islets in metastatic (N=6) was higher (4.2) as compared to 2.5 for clinically-localized primaries (N=11) ($p = 0.23$).

Conclusion: Palladin appears to be a reliable marker of liver metastases in primary pancreatic endocrine tumors. Large-scale clinical validation studies are needed to further test palladin as a prognostic marker. The over-expression of palladin in metastatic primary PECAs and matched normal islets points toward its role both in the initiation and progression of these neoplasms.