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Are basal microvilli on the microvasculature of pancreatic ductal adenocarcinoma a tumor specific target for therapies?

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Pancreatic ductal adenocarcinoma (PDAC) is a uniformly lethal malignancy with near 6 months median survival. It is a stromarich, vascular-poor and hypo-perfused tumor, which was considered to prevents efficient drug or nutrient delivery in tumor microenvironment. Paradoxically, the tumor cells have robust glucose uptake and rare necrosis, suggesting that the microvasculature has might adopted an alternative way for nutrient uptake and cellular trafficking. Using adapted thick tumor section immunostaining and three-dimensional (3D) construction imaging in human fresh tissue samples, we identified an undiscovered feature of the mature microvasculature in advanced PDAC tumors; long, hair-like projections on the basal surface of micro vessels that we refer to as 'basal microvilli'. Basal microvilli were also observed in intrahepatic cholangiocarcinoma (ICC) and metastatic pancreatic neuroendocrine tumor (panNET), but not in hepatocellular carcinoma, glioblastoma and renal clear cell carcinoma. Basal microvilli in PDAC are richer and denser than ICC and panNET. Functionally, these basal microvilli have an actin-rich cytoskeleton and endocytic and exocytic properties and contain glucose transporter-1 (GLUT-1)-positive vesicles. Clinically, as demonstrated by PET-CT, the tumor microvasculature with the longest and most abundant basal microvilli correlated with high glucose uptake of the PDAC tumor itself. In addition, these basal microvilli were found in regions of the tumor with low GLUT-1 expression, suggesting that their presence could be dependent upon the glucose concentration in the tumor milieu. Similar microvasculature features which contain glucose were also observed in a K-Ras-driven model of murine PDAC. Altogether, these basal microvilli mark a novel pathological feature of PDAC microvasculature and ICC and panNET. Because basal microvilli are pathological features with endo and exocytic properties, they may provide a non-conventional method for cellular trafficking in PDAC tumors.

Biography

Hexige Saiyin has completed his MD from Shanghai Medical University and worked as a Lecture in Fudan University. He has completed his PhD study in the School of Life Science, Fudan University. He has also worked as a Visiting Assistant Professor in MD Anderson Cancer Center in Houston. He has discovered the "hairy" micro vessels which contain many basal cellular projections in PDAC, named the projection as "basal microvilli". He is an Assistant Professor in the School of life Sciences, Fudan University. He has published more than 50 papers in reputed journals.

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