PTS-1.4 Pancreatic cancer cells enrich phospho-paxillin in their filopodia during neural invasion (W)

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Introduction: Neural invasion (NI) is a leading cause of local recurrence, neuropathic pain sensation in pancreatic ductal adenocarcinoma (PDAC) and is encountered in up to 100% of PDAC cases. The changes that occur in the cytoskeleton of neuro-invasive PDAC cells has, however, never been analyzed.

Methods: Human PDAC cells and dorsal root ganglia (DRG) neurons isolated from newborn C57BL/6 mouse were suspended in a 3D migration assay and monitored via Apotome-supported digital time-lapse microscopy. The density and length of cancer cell filopodia were quantified with the FiloQuant® software, and the expression of phospho-paxillin was measured and compared between the neuron-facing migration front and control front. Cancer cells were treated with DRG supernatants, and the expression of phospho-paxillin was determined by Western Blotting. Tumor specimens obtained from 18 PDAC patients were immunostained against phospho-paxillin, and the phospho-paxillin content of cancer cells around nerves was compared to cancer cells that were in no contact with nerves.

Results: In the 3D-migration assays, the neuron-facing tumor cells acquired a typical morphological change of their cytoskeleton. In particular, phalloidin stainings shows that cancer cells migrating towards DRG exhibited a more “polygonal shape” with a consequent increase of their cell volume. The density and length of filopodia were increased, and the filopodia exhibited a specific enrichment of phospho-paxillin in the migration front, when compared to the back front. Accordingly, phospho-paxillin expression was increased in tumor cells around nerves when compared to tumor cells away from nerves in human PDAC tissues. After treatment of PDAC cell with DRG supernatants, the phospho-paxillin expression was prominently enhanced in PDAC cells.

Conclusion: Neuro-invasive PDAC cells exhibit highly characteristic alterations in their cytoskeletal conformation and specifically enrich phospho-paxillin in their filopodia.