Neural invasion in pancreatic cancer: a mutual tropism between neurons and cancer cells.

Abstract:
Neural invasion by pancreatic cancer cells (PCC) worsens the prognosis and frequently limits curative resection. We established a novel in-vitro model in which T3M4-PCCs were co-cultured with either isolated myenteric plexus cells (MP) or dorsal root ganglia (DRG) of newborn rats within a three-dimensional extracellular matrix gel. The close vicinity of MP or DRG to T3M4-PCCs induced early morphologic changes on T3M4-PCCs at the migration front prior to the migration process with elongated and neurite-targeting PCCs, compared to round and non-grouping at the non-migrating front. T3M4-PCCs built cancer-cell clusters around the DRG or MP, a process which was accelerated by increasing number of T3M4-PCCs or neurons. These findings indicate that neuro-cancer interactions start prior to PCC migration and induce evident changes in cancer and nerve biology. These findings can be reproduced within the introduced 3D in-vitro migration assay which allows investigation in the early pathogenesis of neural PCC invasion.