Invadopodia

Invadopodia are actin-rich, finger-like protrusions that are formed by invasive cancer cells. They are used by cancer cells to penetrate and invade surrounding tissues, which is a critical step in cancer metastasis. Invadopodia are thought to play a key role in the process of cancer cell migration and invasion by allowing cancer cells to degrade the extracellular matrix and invade adjacent tissues. Invadopodia are composed of a variety of proteins, including actin, cortactin, and several matrix metalloproteinases, which help to break down the extracellular matrix. Understanding the molecular mechanisms underlying the formation and function of invadopodia is an active area of research, with the ultimate goal of developing new treatments for cancer metastasis.

Invadopodia assays and zymography gels were used to examine the invadopodia activity capacity of GBM cells. Differential ultracentrifugation was utilized to isolate sEVs from conditioned medium and proteomic analyses were conducted on both GBM cell lines and their sEVs to determine the cargo present within the sEVs. In addition, the impact of radiotherapy and temozolomide treatment of GBM cells was studied.

Results: We found that GBM cells form active invadopodia and secrete sEVs containing the matrix metalloproteinase MMP-2. Subsequent proteomic studies revealed the presence of an invadopodia-related protein sEV cargo and that sEVs from highly invadopodia active GBM cells (LN229) increase invadopodia activity in sEV recipient GBM cells. We also found that GBM cells displayed increases in invadopodia activity and sEV secretion post radiation/temozolomide treatment. Together, these data reveal a relationship between invadopodia and sEV composition/secretion/uptake in promoting the invasiveness of GBM cells.

Data indicate that sEVs secreted by GBM cells can facilitate tumour invasion by promoting invadopodia activity in recipient cells, which may be enhanced by treatment with radio-chemotherapy. The transfer of pro-invasive cargos may yield important insights into the functional capacity of sEVs in invadopodia.¹⁾

1)

Whitehead CA, Fang H, Su H, Morokoff AP, Kaye AH, Hanssen E, Nowell CJ, Drummond KJ, Greening DW, Vella LJ, Mantamadiotis T, Stylli SS. Small extracellular vesicles promote invadopodia activity in glioblastoma cells in a therapy-dependent manner. Cell Oncol (Dordr). 2023 Apr 4. doi: 10.1007/s13402-023-00786-w. Epub ahead of print. PMID: 37014551.

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