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Caveolin-1-containing extracellular vesicles transport adhesion proteins and promote malignancy in breast cancer cell lines.

America Campos, Carlos Salomon, Rocio Bustos, Jorge Díaz, Samuel Martínez, Veronica Silva, Constanza Reyes, Natalia Díaz-Valdivia, Manuel Varas-Godoy, Lorena Lobos-González & Andrew FG Quest.

Abstract

Breast cancer is one of the most frequently diagnosed cancers and the leading cause of cancer-related deaths in women worldwide, whereby mortality is largely attributable to the development of distant metastasis. Caveolin-1 (CAV1) is a multifunctional membrane protein that is typically upregulated in the final stages of cancer and promotes migration and invasion of tumor cells. Elevated levels of CAV1 have been detected in extracellular vesicles (EVs) from advanced cancer patients. EVs are lipid enclosed vesicular structures that contain bioactive proteins, DNA and RNAs, which can be transferred to other cells and promote metastasis. Therefore, we hypothesized that CAV1 containing EVs released from breast cancer cells may enhance migration and invasion of recipient cells. EVs were purified from conditioned media of MDA-MB-231 wild-type (WT), MDA-MB-231 (shCAV1; possessing the plasmid pLKO.1 encoding a 'small hairpin' directed against CAV1) and MDA-MB-231 (shC) short hairpin control cells. Nanoparticle tracking analysis revealed an average particle size of 40-350 nm for all preparations. As anticipated, CAV1 was detected in MDA-MB-231 WT and shC EVs, but not in MDA-MB-231 (shCAV1) EVs. Mass spectrometry analysis revealed the presence of specific cell adhesion-related proteins, such as Cyr61, tenascin (TNC) and S100A9 only in WT and shC, but not in shCAV1 EVs. Importantly, EVs containing CAV1 promoted migration and invasion of cells lacking CAV1. We conclude that the presence of CAV1 in EVs from metastatic breast cancer cells is associated with enhanced migration and invasiveness of recipient cells in vitro, suggesting that intercellular communication promoted by EVs containing CAV1 will likely favor metastasis in vivo.