

Public Abstract

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Title:Microenvironmental Regulation Of Ovarian Cancer Dissemination Via Activation Of The Wnt Signaling Pathway

Ovarian carcinomas arise from the surface of the ovary; tumor spread initiates by shedding of tumor cells from the ovary into the peritoneal cavity. Within this cavity, epithelial ovarian carcinoma cells exist as single cells and in small clusters known as multicellular aggregates (MCAs) and experience a unique microenvironment. This environment exposes disseminating tumor cells to a signaling molecule, lysophosphatidic acid (LPA), increased intraperitoneal fluid force exerted by accumulating ascites, a malignant fluid that develops as the cancer progresses, and an atypically adhesive mesothelium that lines the peritoneal cavity. These ovarian tumor microenvironmental factors (integrin engagement of mesothelium and submesothelial matrix, LPA, and mechanical force) facilitate uncharacteristic activation of Wnt signaling, which normally controls early development and is switched off in the adult human. Such a modification of ovarian carcinoma cells leads to uncontrolled cell growth and cell migration, protecting from programmed cell death. This work beings to clarify research and clinical observations of alterations in Wnt signaling, and may provide a basis for future studies of drug treatments, specifically engineered to target the Wnt pathway, in ovarian cancer.