CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP120390

Project Title:
Control of cross-talk between ovarian cancer cells and the tumor microenvironment

Award Mechanism:
Individual Investigator

Principal Investigator:
Naora, Honami

Entity:
The University of Texas M.D. Anderson Cancer Center

Lay Summary:

Ovarian cancer is called the “silent killer” because this disease progresses throughout the peritoneal cavity in an aggressive, often asymptomatic, manner. Most women who are diagnosed with ovarian cancer have extensive intraperitoneal disease and are rarely cured by conventional chemotherapy. Ovarian cancer cells typically spread by shedding into the peritoneal fluid and attach to surfaces in the peritoneal cavity, particularly the omentum. The omentum is composed of mesothelial cells that line connective (fibroblastic) and fatty (adipose) tissues, and suspends over the intestines. Growth of tumors on the omentum often results in fatal bowel obstruction. Our proposal investigates the mechanisms that control interactions of ovarian cancer cells with three different types of normal cells: mesothelial cells, omental fibroblasts and adipose-derived mesenchymal stem cells. We have identified a transcription factor called HOXA9 that is frequently expressed in ovarian cancers, is strongly associated with reduced survival in patients, and promotes growth of ovarian tumors in the peritoneal cavity of mice. We hypothesize that HOXA9 promotes the aggressive behavior of ovarian cancer by enabling tumor cells to dynamically adapt to and exploit the peritoneal microenvironment. Using a combination of molecular, cellular and animal studies, we will determine the mechanisms by which HOXA9 promotes attachment of ovarian cancer cells to mesothelial cells and “educates” normal omental fibroblasts and adipose-derived mesenchymal stem cells to support tumor growth. Our goal is to identify effector molecules of HOXA9 that are realistically “druggable”. These studies will provide critical insights into how interactions between ovarian cancer cells and normal cells in the tumor microenvironment stimulate disease progression, and how preventing these cellular interactions can serve as promising therapeutic approaches.