

Ovarian cancer metastases influenced by factors in target tissues

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Cancer researchers have wondered why ovarian cancer cells are so attracted to the abdominal cavity, especially the omentum, with the hope that such an understanding could lead to better disease management or even prevention. Results from a series of experiments suggest a two-step model of omental colonization in which i) cancer cells are attracted to and lodge within immune cell-containing structures known as milky spots, and ii) fat storage cells (adipocytes) fuel cancer cell growth and spread. This study is scheduled for publication in the August 2013 issue of *The American Journal of Pathology*.

The [omentum](#) is a large fatty structure that drapes off the stomach and blankets the peritoneal organs. Omental fat is composed of adipocytes, blood vessels, [immune cells](#), and other connective tissue and contains unusual immune cell-containing structures known as milky spots, which play a key role in many of its protective functions. In previous research, investigators focused either on the milky spots or the adipocytes as key to attracting metastatic [ovarian cancer](#) cells. The results of the current experiments show that "although there are clear strengths to both of these models, neither address the intimate and dynamic interaction among milky spots, surrounding adipocytes, and other components of omental tissues. We propose an alternative, more fully integrated model," says Carrie Rinker-Schaeffer, PhD, a professor in the Departments of Surgery (Section of Urology) and Obstetrics and Gynecology at The University of Chicago.

In the first experiment, researchers investigated whether abdominal fat

tissue that contains milky spots is a more attractive target for [cancer cells](#) than abdominal fat that does not contain milky spots. This study took advantage of the fact that mice have a second source of milky spot-containing abdominal fat (splenoportal fat) as well as fat that is devoid of milky spots (the gonadal, uterine, and mesenteric fat). They found that different ovarian cancer cell lines (mouse derived ID8, and human derived SKOV3ip.1, HeyA8, and CaOV3) specifically colonize omental and splenoportal fat, forming large lesions of cancer cells within milky spots. In contrast, ovarian cancer cells were rarely detected in abdominal fat that lacks milky spots.

The rapid localization of [ovarian cancer cells](#) to milky spots indicated that omental tissue secretes a factor, or factors that attract the cancer cells to these structures. Experiments showed that milky-spot-containing tissues in particular can condition cell growth medium to stimulate the migration of cancer cells. This study found that cell medium conditioned by omenta and splenoportal fat caused a 95-fold increase in cell migration, compared to controls. This study also examined mice with specific immunodeficiencies to show that ovarian cancer cell colonization of milky spots is not affected by deficiency or absence of T cells, B cells, and/or NK cells.

The authors also found an inverse relationship between ovarian [cancer cell growth](#) and depletion of adipocytes. "These data are consistent with previous reports from other investigators that indicate cancer cells use lipids stored in adipocytes as an energy source for their continued growth," says Dr. Rinker-Schaeffer. "Certain tumor cells (the 'seed') have a proclivity for specific organ microenvironments (the 'soil')," adds Dr. Rinker-Schaeffer. "Pioneers of metastasis research appreciated that the unique tissue architecture, physiology, and function of the target organ are essential to understanding metastatic organ specificity. With this in mind, we hope that our findings and discussion of how they fit into the big picture of omental colonization will facilitate studies that

continue to improve our understanding of this process."

In 2012, ovarian cancer was diagnosed in almost 23,000 American women and 16,000 died from the disease. It is estimated that 22,240 women will be diagnosed with and 14,030 women will die of cancer of the ovary in 2013.

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