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GYNECOLOGICAL CANCER

Home is where the fat is

Home is where the fat is, or at least that is what some cancer cells seem to think. Such is the case for ovarian cancer cells, which tend to metastasize in the omentum, a large fatty structure that covers the abdomen and is rich in adipocytes. To find out more about the predilection of ovarian tumor cells for this site, Ernst Lengyel and collaborators used a mouse model in which they injected fluorescently labeled human ovarian cancer cells intraperitoneally; these cells migrated to the omentum in just 20 minutes. Further experiments proved how this migration was initiated in response to adipokines released from the adipocytes in the omentum. Because it had been previously described in samples of omental metastasis that ovarian cancer cells contained abundant lipids, the researchers wondered whether cancer cells were taking lipids from the adipocytes in the omentum rather than making their own. A series of experiments showed that ovarian cancer cells induce lipolysis in the adipocytes and then use the lipids to produce energy through β-oxidation, which allows them to grow faster. But how does this transfer of lipids from the adipocytes to the cancer cells occur? An analysis comparing protein expression in ovarian tumor samples and omental metastases from 22 patients revealed an increased expression of FABP4 in metastases. This protein is a regulator of metabolism that binds long-chain fatty acids and is, very likely, the mediator in the lipid tranfer occurring between adipocytes and cancer cells, making

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FABP4 a therapeutic target to stop intra-abdominal metastasis in ovarian cancer.

Along similar lines, Francesco Bertolini and collaborators have described how white adipose tissue is a rich reservoir of endothelial progenitor cells (EPC) expressing $CD34^+$, which have been widely implicated in angiogenesis. The researchers isolated $CD34^+$ EPCs from white adipose tissue samples from 38 women who had undergone a lipotransfer procedure (generally from the abdomen) for breast reconstruction after breast cancer surgery. Co-injection of these $CD34^+$ EPCs with breast cancer cell lines in immunodeficient mice resulted in increased tumor growth and metastasis in the lung compared with co-injection with $CD34^-$ EPCs or breast cancer cells alone.

These studies add to the growing evidence for a major role of adipocytes-enriched microenvironment in promoting tumor growth and metastases.

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Original articles Nieman, K. M. *et al.* Adipocytes promote ovarian cancer metastasis and provide energy for rapid tumor growth. *Nat. Med.* **17**, 1498–1503 (2011) | Martin-Padura, I. *et al.* The white adipose tissue used in lipotransfer procedures is a rich reservoir of $CD34^+$ progenitors able to promote cancer progression. *Cancer Res.* doi:10.1158/0008-5472