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Infiltrating Cancer's Recruitment Center: How Beneficial Cells Are Subverted to Support Cancer Growth

The most common connective tissue cell in animals is the fibroblast, which plays an important role in healing wounds. But Dr. Neta Erez of Tel Aviv University's Sackler Faculty of Medicine has now demonstrated that fibroblasts can also do a body great harm, helping to "recruit" immune cells for tumor growth.

At the onset of a tumor's creation when cancer cell proliferation is beginning, fibroblasts rush to the scene to aid in healing. However, Dr. Erez's research shows that these ordinarily helpful cells can actually be turned against the body, enhancing tumor growth by stimulating inflammation.

Her research was done in animal models using fresh mouse skin cancer as well as human tumors extracted in the operating room. It was originally carried out at the University of California, San Francisco in the lab of Prof. Douglas Hanahan. Published in *Cancer Cell*, her most recent findings demonstrate that a growing tumor can co-opt fibroblasts, turning them into cancer-associated fibroblasts (CAFs) making them do the dirty work of supporting tumors.

Cancer and Inflammation -- A Two-way Street

In recent years, scientists have begun to understand the link between inflammation and cancer. Their findings suggested why long-term aspirin therapy -- which reduces inflammation -- can help prevent or slow cancer growth.

Inflammation causes cancer, and researchers are now finding that the reverse is also true: cancer can also cause inflammation by attracting immune cells to sites of growing tumors. Inflammatory cells are implicated in all solid tumors, including liver cancer, which may start with chronic liver inflammation due to hepatitis, and intestinal or colon cancer, which can be triggered by chronic inflammation of the bowels from an ulcer, colitis or Crohn's disease.

"Cancer cells recruit CAFs at very early stages," Dr. Erez says. "Under normal circumstances fibroblasts are very

good for health and healing, but we've shown for the first time how they can be coerced into supporting inflammation that enhances the growth of tumors."

CAFs stimulate inflammation and angiogenesis -- the creation of new blood vessels -- which in turn enable cancer cell proliferation. Without the recruitment of new blood vessels, cancer couldn't grow bigger than a millimeter. Tumor growth requires the assistance of other tissues in our body, and Dr. Erez's research implicating fibroblasts breaks new ground in science.

New Avenues for Drug Research

CAFs appear to be able to recruit immune cells from the body that can enhance tumor growth, Dr. Erez explains. In addition, normal skin fibroblasts can be "educated" by cancer cells to express pro-inflammatory genes.

Armed with this information, Dr. Erez plans to study the molecular pathways that link tumor cells to their environments around the tumors, hoping to develop drug targets to disrupt any cellular processes that support tumor growth. Her research opens a new frontier, suggesting how inflammation in the body can be managed to reduce the growth and spread of cancer.

"My goal is to understand everything about the local environment where a tumor grows -- what feeds it, what cells play a role, and how they work together -- to improve existing therapeutics, or to create a new cancer drug," she says.

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