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Bone Marrow Stroma Roles in Breast Cancer Dormancy

[We are studying how the cells that line the bone marrow cavity keep metastatic breast cancer cells from growing]

Some women who develop breast cancer that appears to be localized only in the breast, some of the cancer cells have already left the breast tumor through the blood stream and have deposited in the bone marrow. These cells are known as micrometastases and are not usually obvious unless a physician looks for them by doing a bone marrow aspiration. Often, these micrometastatic breast cancer cells sit in the bone marrow for years without dividing. This is called dormancy. Sometimes, these cells begin to divide and form tumors in the bone marrow that signify relapse of the disease. This can happen many years later. It is not known what causes the micrometastatic cells to remain dormant in the bone marrow and what causes them to begin dividing. This proposal plans to carry out experiments to determine one possible reason for dormancy. The bone marrow contains many proteins that control the growth of cells. One such protein is called basic fibroblast growth factor or FGF-2. We and others have shown that FGF-2 can prevent breast cancer cells from dividing. We propose to mimic the bone marrow setting in the lab by culturing normal bone marrow from volunteers under an institutional Review Board-approved protocol. The cultured bone marrow forms a layer of cells, proteins and other factors on the bottom of laboratory dishes, known as stroma, that can be used to support that growth of breast cancer cells. We will block FGF-2 made by these stroma from acting on the breast cancer cells that are cultured on top of the stroma and determine if their dormant state is also blocked. We will isolate cells that are dormant on the stroma and ones that are not and will study the molecular differences between them. This project is a collaboration between UMDNJ-New Jersey Medical School where these studies will take place, and Rider University, where a technology will be developed in collaboration with Sarnoff Corporation in Princeton, NJ, to design devices called microfluidic chips that can measure molecular changes in single cells. This technology must be developed in order to determine what is happening on the molecular level in a single cell that is dormant on bone marrow stroma. These studies will give us a first glimpse at some of the controls that keep a breast cancer cells dormant in the bone marrow and may help in the future understanding of what causes these patients to relapse.