

Breast Density

Breast density refers to the amount of fat and tissue in the breast. A dense breast has more tissue than fat. Whether or not a woman has dense breasts is determined by looking at the breast tissue during a mammogram. Having dense breasts can affect both your risk for and survival of breast cancer. Women with dense breasts are 4 to 5 times more likely to develop breast cancer than women with average or low breast density. They are also more likely to be diagnosed with aggressive types of breast cancer, which can decrease survival. Even more, some women without dense breasts can have a breast tumor that is considered 'dense', which increases the chance that the cancer will spread. Despite these statistics, little is known about why or how breast density affects breast cancer risk and outcomes.



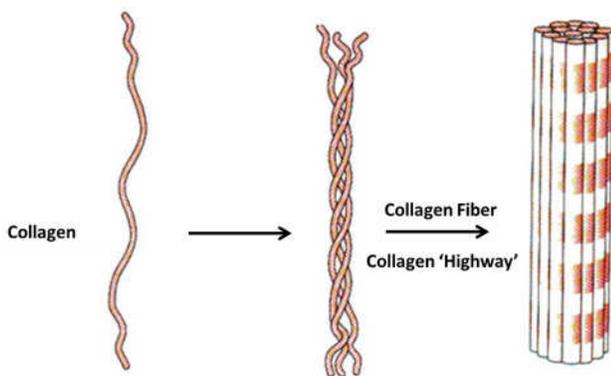
Dr. Gregory Longmore's laboratory at Washington University School of Medicine in St. Louis searches for answers on why breast density affects metastasis.

In a high-profile article published in *Nature Cell Biology*, Komen grantee Dr. Gregory Longmore, Professor of Medicine and Cell Biology and Physiology and the Director of the ICCE Institute (Integrating Communications within the Cancer Environment) at Washington University Medical School, St. Louis, reveals exciting findings that shed some light on why breast or tumor density is such an important factor for breast cancer survival.

Learn more about breast density

<http://sgk.mn/1BXcgkT>

Breast Tumor Cells and Collagen Highways

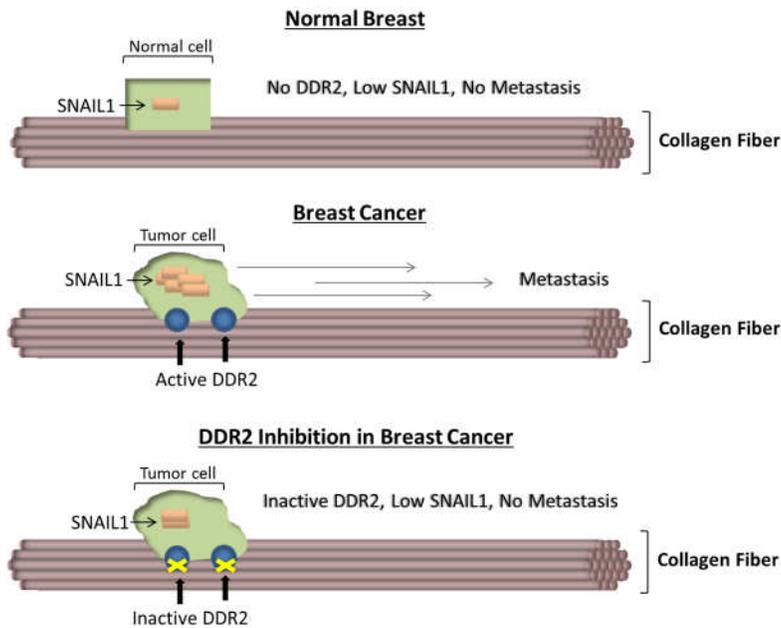


Collagen protein bundles together to make collagen fibers, also referred to as collagen 'highways'.

Some studies suggest that dense breasts may increase the ability of breast cancer to spread to other parts of the body (metastasize). Unfortunately, little is known about how breast density affects metastasis. Breast tissue is partially made up of a protein called collagen, which is bundled together to create collagen fibers. These fibers are often referred to as the 'highways' of the breast tissue because breast tumor cells use them to travel through the breast tissue and spread to other parts of the body. Because dense breasts have more tissue than fat, they also have higher levels of collagen and more collagen fiber 'highways' for breast tumor cells to travel along. Researchers believe that this allows the tumor cells to more easily move and metastasize. But how does this process work and can the tumor cells be prevented from spreading?

Understanding Collagen's Role in Metastasis

With Komen funding, Dr. Gregory Longmore and his colleagues have identified a protein that helps tumor cells use collagen fiber highways to travel, and metastasize to other parts of the body. The researchers found that a protein called discoidin domain receptor 2, or DDR2, promotes breast cancer metastasis, especially in the presence of high levels of collagen (as occurs in dense breasts). DDR2 is a protein only found in invasive cancer cells (tumor cells that have the ability to spread), not normal breast cells, and can interact with collagen in breast tissue. By interacting with collagen, the DDR2 protein helps the tumor cell use the collagen fiber highways to move away from the primary tumor and spread to other parts of the body.



Collagen fibers act as the 'highways' of the breast tissue – allowing breast cancer cells to travel or spread. DDR2 acts as the wheels on the tumor cell, and SNAIL1 as the gasoline that runs the engine to move the tumor cells. If you remove or block the wheels (DDR2) or the gasoline (SNAIL1), the cancer cells will be unable to travel or metastasize.

DDR2 is not the only protein helping tumor cells spread – Longmore also found that a protein called SNAIL1 is involved in the process. Some breast cancer cells have more SNAIL1 than normal cells. Dr. Longmore's research shows that when DDR2 and collagen interact, this turns on DDR2, or makes it active. When DDR2 is active, it increases the amount and activity of SNAIL1 within the cancer cell.

SNAIL1 helps the tumor cells move along the collagen fiber 'highways' by controlling the levels of other proteins involved in this process. If collagen fibers are considered the 'highways' – allowing breast cancer cells to travel or spread – DDR2 can be thought of as the wheels on the tumor cell, and SNAIL1 as the gasoline that runs the engine. Regardless of how dense the breast is (or how much collagen is present), if you can take away the wheels (DDR2) or the gas (SNAIL1), the cancer cells will be unable to travel or metastasize.

What's Next?

Dr. Longmore's studies show that DDR2 plays a critical role in promoting metastasis. He believes that therapies which target DDR2 may be effective at preventing metastasis and could improve outcomes for all breast cancer patients, not just those with dense breasts. Dr. Longmore and his colleagues have recently identified novel compounds that specifically target DDR2 and prevent DDR2 from interacting with collagen. Early experiments indicate these compounds can block the ability of tumor cells to invade the surrounding breast tissue and metastasize. The next steps will be to test the drug in preclinical models of breast cancer, and then in clinical trials designed for breast cancer patients with dense breasts and those at high risk for metastatic disease.

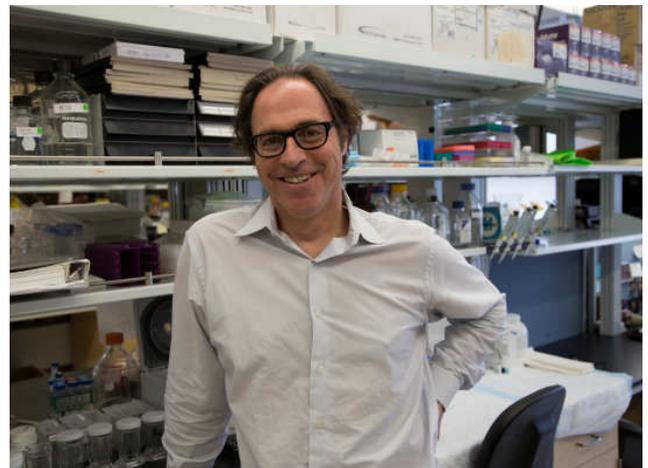
'With continued support from funding agencies like Komen and established partnerships with collaborating scientists and pharmaceutical companies, these studies will produce a new drug which can block the ability of [breast] tumor cells to invade, thus preventing metastasis,' says Longmore.

What it Means for Patients

Women with dense breasts are more likely to be diagnosed with breast cancer, and once diagnosed, may have an increased chance of developing aggressive or metastatic breast cancer. The metastatic spread of breast cancer to other parts of the body, such as the lung and brain, decreases a breast cancer patient's chance of survival. Therefore, the development of drugs which prevent metastasis is very important to improving patient prognosis. Thanks to the efforts of scientists like Dr. Longmore, we now know that dense breasts contain higher levels of collagen. When bundled together, these collagen fibers act as the 'highways' in the breast tissue environment, which breast cancer cells use to travel or spread to other parts of the body. We also know that breast cancer cells use other proteins such as DDR2 and SNAIL1 to help them move or metastasize. Dr. Longmore's continued studies to develop drugs targeting DDR2 and SNAIL1 could help reduce breast cancer metastasis and increase patients' chances of long term survival.

Creating His Own Path to the Cure

When asked to summarize his career, Dr. Longmore jokingly asked 'how much time do you have?' Like most scientists, Dr. Longmore's path to his current work is complex. However, he has pursued his passion at every step - to understand how cells behave. In doing this, he strives to create hope for those facing the fear of breast cancer. Dr. Longmore did not begin his career studying breast cancer, but by studying basic biochemistry. After his graduate training in biochemistry at the University of Toronto, he continued on to Medical School at McGill University in Montreal, Quebec. While he enjoyed medical training, he could not forget his love for basic research. So, upon completing medical school, he pursued additional clinical and research training at Harvard Medical School and the Massachusetts Institute of Technology (MIT) where, as a postdoctoral research fellow, he studied leukemia. During these studies, Dr. Longmore developed a keen interest in studying how normal blood cells move around the body in blood vessels. He expanded this work into understanding how *tumor cells* move around the body, causing metastasis. 'By understanding how a cancer cell can invade or move around the body, we can identify ways to prevent the cancer cell from metastasizing,' says Longmore.



Dr. Gregory Longmore, Professor of Medicine and Cell Biology and Physiology, Washington University School of Medicine, St. Louis

Now, as a professor and scientist, his research involves a variety of topics which include the study of breast cancer metastasis and tumor cell behavior. ***'Although my background has been diverse, the overarching goal of my career has been to understand how cells respond to their environment and how cells move around the body,'*** he adds. Having a passion for both basic research and clinically-impactful science, Dr. Longmore has shown a remarkable ability to translate what he learns from basic research to develop new tools aimed at improving patient outcomes.

Dr. Longmore's studies were published in Nature Cell Biology in June 2013 - <http://www.nature.com/ncb/journal/v15/n6/full/ncb2743.html>.



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