Studies reveal more clues on how pregnancy protects against breast cancer

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Scientists at Fox Chase Cancer Center have unearthed new clues about how pregnancy reduces women's risk of developing breast cancer. The research will be presented at the AACR Annual Meeting 2014.

Taking a detailed look at the genetic material of women who had and had not given birth, the researchers noted differences in elements related to key processes that, when they go awry, can increase the risk of developing cancer.

Ideally, researchers will one day be able to mimic these changes in women who have not been pregnant in order to reduce their risk of developing cancer, says study author Julia Santucci-Pereira, PhD,

Research Associate in the Breast Cancer Research Laboratory at Fox Chase.

"We are trying to understand how the natural process of giving birth helps prevent cancer," she says. "If we understand it, we can try to mimic this process somehow, especially in women who are at high risk of developing the disease."

In one study, that will be presented on the afternoon of Monday, April 7, Santucci-Pereira and her colleagues used sophisticated sequencing technology to compare the genetic activity of cancer-free breast tissue samples from more than 100 premenopausal women—30 of whom had never given birth. They spotted differences in the expression of genes that were associated with the process cells undergo to become specialized types, known as differentiation. This isn't a surprise, says Santucci-Pereira, since problems in differentiation can cause cells to become cancerous.

In addition, she and her colleagues noticed clear differences between mothers and non-mothers in the expression of genes related to the development of breast anatomy. This, too, makes sense, says Santucci-Pereira, as this process must be well regulated in order to avoid cancer.

In another study presented during the same session, Santucci-Pereira and her team identify additional genetic changes that may help explain how pregnancy protects against breast cancer. Looking at 10 women who had undergone menopause, they found that mothers and non-mothers displayed differences in how their genes were modified— specifically, by being tagged with chemical groups, which influences how those genes are used by the body. Here, again, they found differences in processes associated with the development of breast anatomy.

"Although this research brings scientists closer to understanding why

pregnancy protects the body from cancer, how that happens remains a puzzle," says Santucci-Pereira. One possibility, she says, is that the hormone produced during pregnancy—human chorionic gonadotropin (HCG)—induces these changes. Indeed, previous research in animals and human cells has found that adding HCG can produce other genetic changes tied to differentiation and development; study author Jose Russo, MD, who heads the Breast Cancer Research Laboratory at Fox Chase, is continuing to study HCG's effects on cancer. "We're trying to mimic pregnancy without making women get pregnant," says Santucci-Pereira.

Finally, in another study that will be presented on the morning of Monday, April 7, Santucci-Pereira and other scientists at Fox Chase looked deeply at differences in stretches of genetic material dubbed "non-coding," meaning they do not contain instructions for making protein. These are regions scientists once thought were "useless," says Santucci-Pereira, but now realize they interact with other parts of the genome and enhance their function. The next step is to try to understand what these non-coding regions actually do, including their role in cancer. "This is a very new field."

In the latest study, Santucci-Pereira and her colleagues identified 42 differences in non-coding regions between 8 mothers and 8 non-mothers. It's possible, she says, that these non-coding regions work with the genes identified in the other two studies to induce changes in the differentiation and development processes, thereby protecting women who have given birth.

Like with the other research, the goal is to find ways that mimic these effects in non-mothers—perhaps by administering compounds that target non-coding regions—they experience the same protection against breast cancer, says Santucci-Pereira. "There are ways, molecularly, to target non-coding regions," she says. "We are just trying to figure out

how that would work."

Provided by Fox Chase Cancer Center