Genomic signature in post-menopausal women may explain why pregnancy reduces breast cancer risk

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Women who have children, particularly early in life, have a lower lifetime risk of breast cancer compared with women who do not. Now, Fox Chase Cancer Center researchers have identified a gene expression pattern in breast tissue that differs between post-menopausal women who had children and post-menopausal women who did not. The results will help scientists understand why pregnancy reduces breast cancer risk and may help them develop chemopreventive strategies that can provide similar protection for women who did not have children.

Pregnancy triggers differentiation and growth of breast tissue; however breast tissue in post-menopausal women looks similar regardless of childbearing history. That similarity has left researchers wondering why pregnancy is protective throughout a woman's life. This study starts to explain that effect, says Ricardo López de Cicco, PhD, a senior research associate at Fox Chase, who will present the work at the AACR 102nd Annual Meeting 2011 on Tuesday, April 5.

"When a woman has multiple pregnancies beginning at a relatively young age, we see a protective effect against breast cancer," Lopez says. "In this study, we identified a post-pregnancy genomic signature that can still be seen even after menopause. That is very important because it could begin to help us understand why women who have children early benefit from a reduced risk of breast cancer throughout their lives."

By comparing gene expression in breast tissue from 44 post-menopausal women who had children and 21 post-menopausal women who did not, the team identified 208 genes that are differentially expressed. The signature was subsequently validated in an independent cohort of 61 post-menopausal women, 38 who had children and 23 who did not.

"We are now quite sure that these 208 genes – 305 transcripts – represent the genomic signature of the effects of pregnancy," says Jose Russo, MD, director of the Breast Cancer Research Laboratory at Fox Chase, who led the new study.

"Finding that signature was our end goal," Russo emphasizes. "If we want to develop chemopreventive strategies, then we need a standard or test to see if they are working. This genomic signature may be that standard."

Among the differentially expressed genes, the team detected several that are involved in processing RNA transcripts. Russo hypothesizes that the increased RNA processing proteins help ensure that no abnormal proteins are made, thereby reducing the likelihood of abnormal growth and cancer.

The team also saw reduced expression of cancer-associated genes in breast tissue from women who had children. For example, the insulin-like growth factor receptor, which is associated with increased cell proliferation, was expressed at a lower level in the samples from women who had children (parous) compared to samples from women who did not (nulliparous). Similarly, genes involved in stem cell maintenance were down-regulated, which may be because the mammary stem cells have already undergone proliferation and differentiation in the women who had children. By contrast, the stem cells are still poised to grow and produce new mammary tissue in the women who did not have children. Some theories of oncogenesis suggest that cancers arise from stem cells

that go awry.

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