Estrogen byproducts linked to survival in breast cancer patients

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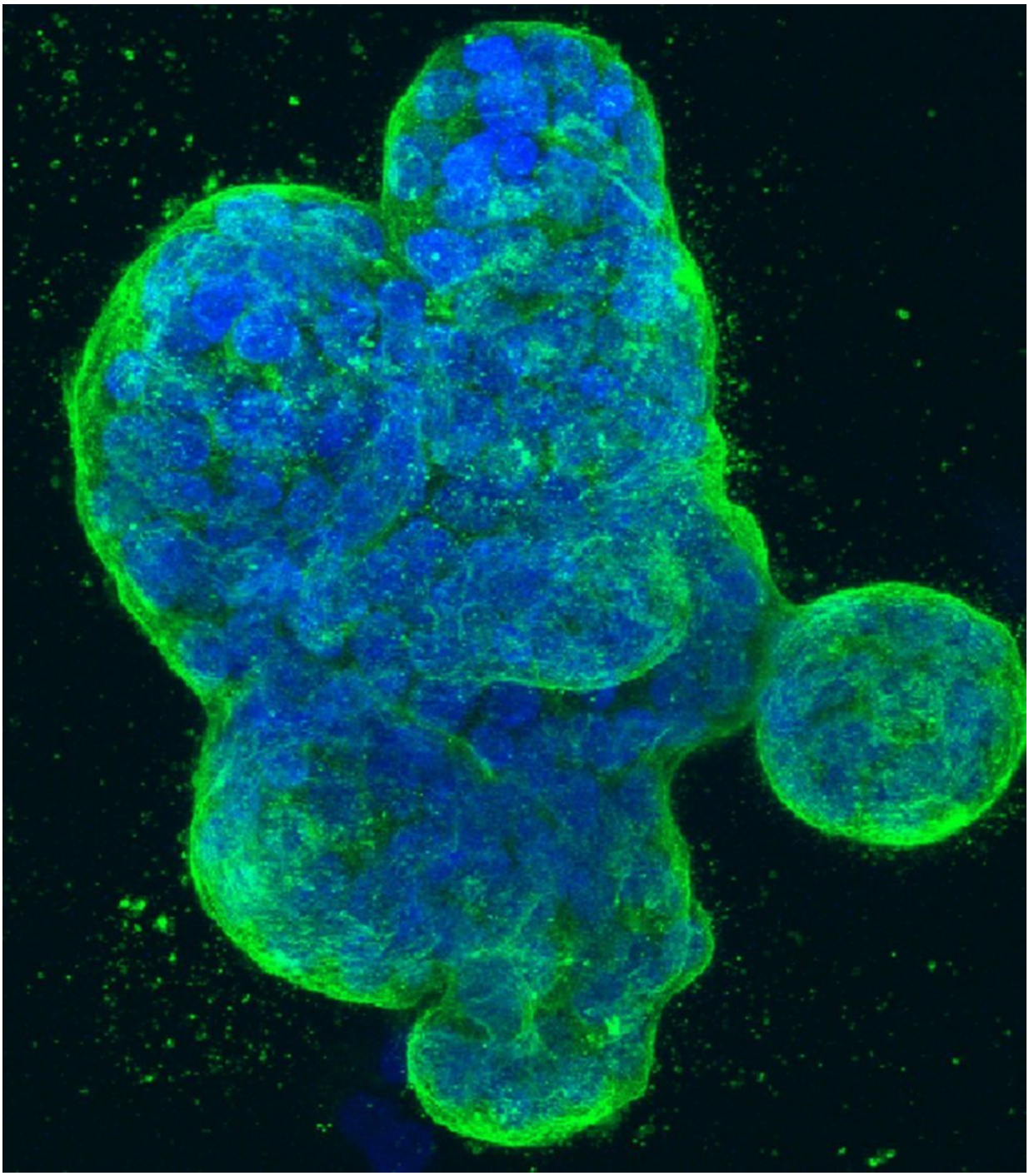

Three-dimensional culture of human breast cancer cells, with DNA stained blue and a protein in the cell surface membrane stained green. Image created in 2014 by Tom Misteli, Ph.D., and Karen Meaburn, Ph.D. at the NIH IRP.

Researchers from the University of North Carolina Lineberger Comprehensive Cancer Center found preliminary evidence that measuring byproducts of the hormone estrogen can help them predict survival for women with breast cancer.

In an abstract presented at the American Association for Cancer Research Annual Meeting, researchers report findings from a study in which they measured levels of estrogen byproducts in urine from a group of women with breast cancer. Relative levels of "good" versus "bad" estrogen byproducts were linked to survival, they reported.

"A lot of research has been done to link these two metabolites with the probability of developing breast cancer," said the study's first author Tengteng Wang, a doctoral candidate in the UNC Gillings School of Global Public Health. "So far, we believe we are the first to look at the association of metabolites in relation to mortality after 18 years of breast cancer diagnosis."

Estrogen is a hormone in the body that drives development of female sex characteristics. Free estrogen in the body is broken down into several byproducts, one of which is 2-hydroxyestrone, or 2-OHE, which is known is a "good" type of byproduct. Researchers report that it is known to interfere with the cancer-linked effects of estrogen. Another metabolite, which is called 16-alpha-hydroxyestrone, is known as a "bad" metabolites because of its pro-cancer effects that lead to abnormal growth and DNA damage.

"Researchers are most interested in examining the ratio of the two metabolites 2-OHE and 16-alpha-OHE, which reflects the relative balance of the 'good' metabolite versus the 'bad,'" said UNC Lineberger's Marilie Gammon, Ph.D., professor in the UNC Gillings School of Global Public Health. "This ratio may therefore represent an individual's inherent estrogen metabolism profile. Our study reported here is the first

to focus on the association between urinary estrogen metabolites and survival after breast cancer."

In their study, researchers examined the balance of these two metabolites in relation to mortality. Specifically, they found that if the level of 2-OHE was more than, or equal to, 1.8 times the level of 16-alpha-OHE in urine, there was an associated 26 percent reduction in any cause of death in women with breast cancer. They also saw that there was a lower risk of breast cancer death, or cardiovascular death, for women who had higher levels of the "good" metabolite.

They studied these associations in group of 687 women who were diagnosed with breast cancer between 1996 and 1997, and who participated in the Long Island Breast Study Project. Levels of estrogen byproducts were measured in urine within three months after diagnosis.

"We found that a higher urinary concentration of the 'good' versus the 'bad' metabolite was associated with a 24 to 27 percent reduced risk of dying from breast cancer, cardiovascular diseases, and any cause of death among breast cancer survivors," Gammon said.

One of the major surprises, Gammon added, was that the association continued in different scenarios that took into account other factors, such as lifestyle, diet, medical history, and whether a woman was pre-or-postmenopausal at diagnosis.

"Our findings appear to indicate that, regardless of the assumed levels of estrogen in a woman's body, the relative balance of the estrogen metabolites appear to predict prognosis after breast cancer," she said.

Researchers say they have additional questions remaining after the study, such as whether the subtype of breast cancer a woman has is important for the pattern they saw, and whether treatments that women may or may

not have received could be playing a role as well. In addition, they want to know if estrogen metabolism can help inform higher risk of death from cardiovascular disease from women with breast cancer, and how the risk might change long-term, or with different timing for when estrogen measurements are taken.

Researchers say one next step would be the study associations after measurements of estrogen metabolites over time, using samples collected at important time windows at diagnosis, and after it. Also, they want to use more advanced tests that have become available, and measure more types of estrogen byproducts.

"We've taken the first step with this study, but additional work is needed to elucidate the predictive value of estrogen metabolites on mortality for women with breast cancer," Wang said.

Provided by UNC Lineberger Comprehensive Cancer Center

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