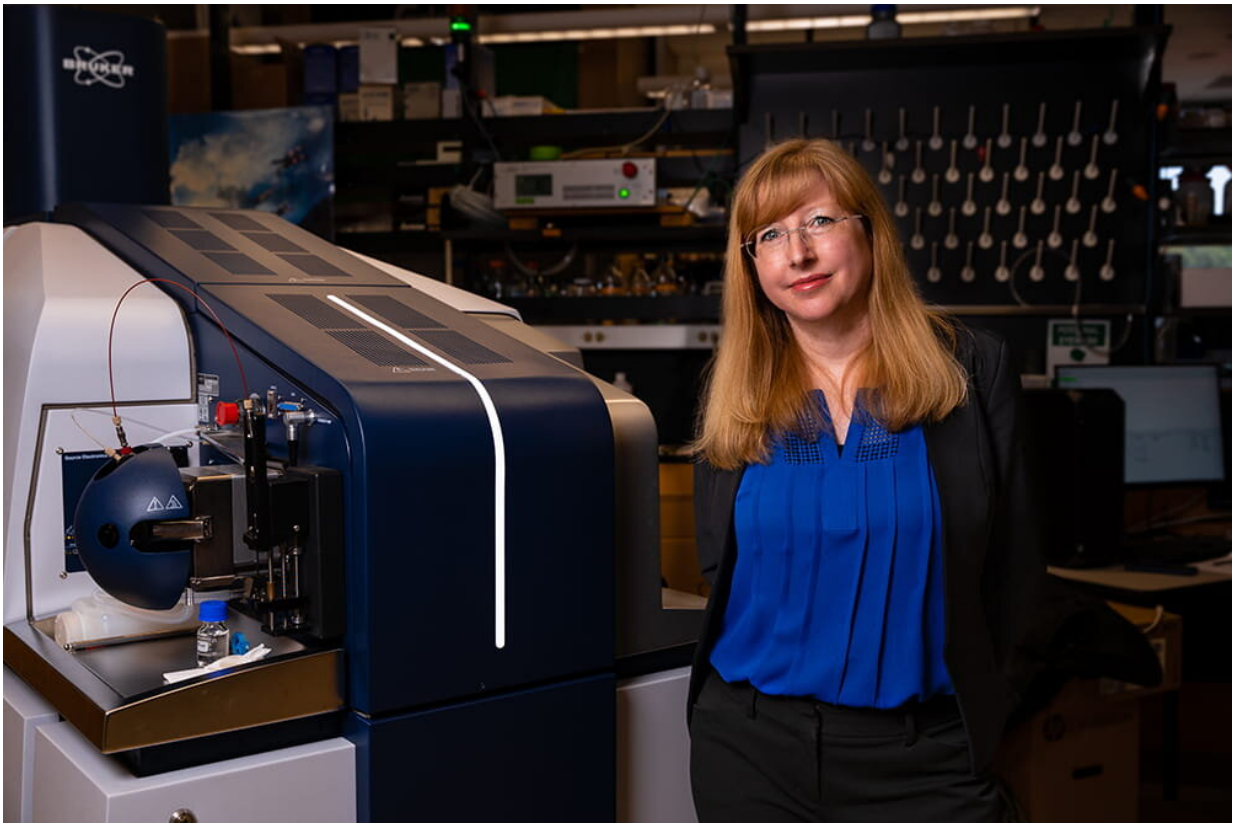
Researcher looks at molecular changes for clues to disparities in breast cancer outcomes

August 24 2022



Peggi Angel, Ph.D., is in looking at how socioeconomic stressors may influence metabolic processes that could in turn create a "tumor permissive" environment. Credit: Clif Rhodes

It's a figure that stands out. Black women have a 36% higher breast

cancer mortality rate than other races in spite of having a similar incidence to White women. Black women also are both more likely to be diagnosed with breast cancer at a younger age than White women and have double the rate of the aggressive, harder-to-treat triple negative breast cancer.

There's ongoing debate about how much of these disparities is due to social determinants of health, such as access to health care, and how much is caused by biology, notes MUSC Hollings Cancer Center researcher Peggi Angel, Ph.D. One hypothesis is that chronic social and economic stressors result in ancestry-dependent molecular changes that create a tumor permissive tissue microenvironment in normal breast tissue, she said, citing findings of her team's recent study published in *Frontiers in Oncology*.

Angel, an analytical chemist by training, is interested in what's happening at the molecular level. Her recent study with her graduate student Denys Rujchanarong looked at normal breast tissue tagged as at-risk for breast cancer, according to the Gail Model, which assigns an estimated risk of breast cancer based on personal factors, such as age, the age at start of menstruation and age at birth of first child, and saw associations between socioeconomic stressors and specific N-glycosylation patterns in Black and White women.

N-glycosylation is a metabolic process of creating a sugar modification on a protein structure. The research was an initial step toward linking molecular markers to socioeconomic stress, Angel said.

"We tried to look at differences in social status among Black women and White women and compare that to molecular factors that might be predictive," she said. "I think this is such a needed area of research because it is really complicated, and there's clearly some molecular changes that could be linked to geographical origin."

She noted that it's important to start looking at differences in breast tissue before cancer arises.

"Differences in baseline glycosylation in normal breast tissue may be contributing to specific differences in breast stromal biology disproportionally affecting Black women," the paper reported.

Angel's team obtained donated normal breast tissue samples from both Black and White women from the Susan G. Komen for the Cure Tissue Bank. The two groups were compared by age, body mass index, education level, Gail score, household income and marital status. Using mass spectrometry, the distribution of N-glycans in the tissues were then assessed, leading to the identification of 53 N-glycans. From there, the N-glycans were associated with specific socioeconomic factors.

The results from these samples, which included tissue from 30 White women and 30 Black women, pointed toward metabolic patterns linked to socioeconomic stressors as a potential factor in the breast cancer disparities between Black and White women.

This study might also be the first to look at the spatial distribution of fucosylation structures in normal breast tissue, Angel said. Fucosylation is a glycosylation modification that has been observed at increased levels in malignant transformations in breast, liver, pancreatic, prostate and colorectal cancers.

The study cited that based on current literature and the team's findings, it is possible that in normal tissue, changes in fucose patterns may be contributing to a tumor-permissive microenvironment associated with more severe breast cancers influenced by genetic ancestry and BMI (body mass index).

Angel said they have found that post-translational modifications called

glycosylation (sugar residues added to proteins) varies by BMI in ancestry-defined normal breast. Body weight is an important measure to track, as current statistics show that Black women in the U.S. have higher rates of BMIs that fall in the overweight or obese categories as compared with White women.

BMI and weight gain have been recognized as an important risk factor for breast cancer, said Angel, referencing a study that found that an 11-pound increase in BMI corresponded to a 2% increase in breast cancer risk. Studies have linked obesity to an increased incidence of a specific and more aggressive type of breast cancer, triple negative breast cancer, in Black women. So not only do Black women experience an unequal burden of obesity, but they are diagnosed with breast cancer at younger ages and at higher rates of aggressive breast cancer types relative to their White counterparts, she noted.

Angel said it's critically important to continue to investigate spatial distribution of collagen protein types and post-translational modifications to understand more fully the impact socioeconomic status has on specific biological factors, processes and modifications contributing to development of disease such as breast cancer.

BMI is only a part of the picture. Her team's study results suggest that from a subset of N-glycans significantly altered by ancestry, certain N-glycans were strongly associated with household income for White women, while the same N-glycans were strongly associated with marital status for Black women.

This may imply that immune responses triggered by specific lifestyle stressors are different for White and Black women and that future studies should look at glycosylation changes associated with immune components, a promising area of research that links molecular markers to socioeconomic stress. However, more research needs to be done to

identify specific N-glycan biomarkers associated with socioeconomic stresses, like household income and marriage, in order to determine which glycan signatures are associated with increased breast cancer risk, she said in the study.

"This broadens our understanding of glycosylation regulation and the possibility that such regulation may be influenced by socioeconomic stressors. To our knowledge, this is the first study to investigate N-glycan patterns associated with socioeconomic stresses that may differ by ancestry. This is important because it contributes to the understanding of the complexities linking socioeconomic stresses and molecular factors to breast cancer risk and aggressiveness in Black women. Additional factors to consider include disposable income, family size, childhood socioeconomic status and educational quality, as these are factors that can also play a role in the ongoing health disparities that Black women face."

Angel said the research is at an important juncture, as she has developed an approach that allows her team to define the collagen protein structure spatially within the tissue microenvironment. This allows them to investigate not only where the collagen structure is post-translationally modified but the location and cell types and the expression associated with that change.

The goal is for researchers to use the molecular signatures to develop more specific diagnoses of breast cancer, including, perhaps, subtypes of breast cancer. Also, being more specific in defining the collagen structure may help them to determine biomarkers and develop more targeted therapies.

"The disparities gap in Black women's mortality in breast cancer is an urgent problem that needs to be solved," she said. "I hope we can discover the molecular signatures that form tumor-permissive breast

density and develop therapeutic approaches that can reverse this change."

More information: Denys Rujchanarong et al, Metabolic Links to Socioeconomic Stresses Uniquely Affecting Ancestry in Normal Breast Tissue at Risk for Breast Cancer, *Frontiers in Oncology* (2022). DOI: 10.3389/fonc.2022.876651

Provided by Medical University of South Carolina