Researchers identify new genes that determine breast cancer prognosis

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Researchers at Wake Forest Baptist Medical Center have made a discovery that brings them one step closer to being able to better predict which patients have the best chance of surviving breast cancer.

The group has identified 16 genes, or proteins, all involved in iron metabolism, that provide better prognostic information than conventional, standard markers of prognosis.

Last summer, some of the same investigators published a study showing that women who had high levels of a protein called ferroportin – the only known protein to eliminate iron from cells – and low levels of another protein, called hepcidin, had the best prognosis, or chance of survival without recurrence. Low levels of ferroportin and high levels of hepcidin were found to be associated with the most aggressive and recurring cancers. Both proteins are involved in the body's metabolism of iron, a key food source for cancerous cells.

The finding suggested that testing for ferroportin levels in women with breast cancer may one day help doctors to more accurately predict whether their patients' cancers will return. It may also help some women with high levels of the protein to avoid invasive or toxic treatments such as chemotherapy.

Building upon that information, the researchers set out to evaluate other proteins involved in iron metabolism and determine if they provide any prognostic value for breast cancer patients, as well.

As it turns out, they do.

The study, supported by the National Institutes of Health, is now available online in Cancer Research.

"We're really interested in trying to understand, at a deeper functional level, what these genes are doing," said Frank Torti, M.D., MPH, director of the Comprehensive Cancer Center at Wake Forest Baptist and senior investigator on the paper. "Many of these genes have been discovered because they have something to do with body iron management, but they haven't really been studied in tumor development, and we know that tumors are iron consumers. There's a lot still left to understand about the function of these genes in breast tissue, but we're finding out that iron, and how it's metabolized, has a whole lot to do with cancer."

The researchers looked at 61 genes involved in iron regulation to see how many of them were related to breast cancer prognosis and found that almost half were. They next narrowed those genes down even further to a subset of 16 that are most closely associated with prognosis.

"Ferroportin and hepcidin aren't the only iron-regulating genes playing a role in breast cancer," Torti said. "As it turns out, many iron genes are associated with breast cancer outcomes. These 16, we've discovered, convey the most valuable information."

Within this group of 16 genes, called the Iron Regulatory Gene Signature, Torti and colleagues found that there are several pairings, called dyads, that work together to regulate iron in a cell. Ferroportin and hepcidin, the original gene dyad they found, control iron export. Now, they have found that an additional pair of genes that control iron import, called transferrin receptor and HFE, is also important. Understanding how changes in those relationships affect breast cancer

prognosis is the focus of the team's future research.

"There's a growing understanding that tumor cells have an altered metabolism," Torti said. "We know that they consume sugar and fats in different ways. These findings now show that tumor cells also handle iron in different ways from non-cancer cells, and that this has important consequences for patient prognosis. There are more genes in the Iron Regulatory Gene Signature whose function in breast cancer we don't fully understand, so there's certainly more discovery to be done. All of this work and new information will help us be able to better predict prognosis for breast cancer patients and hopefully, one day, will help guide our treatment recommendations."

Provided by Wake Forest Baptist Medical Center