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Researchers identify key gene in deadly inflammatory breast cancer

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Aggressive, deadly and often misdiagnosed, inflammatory breast cancer (IBC) is the most lethal form of primary breast cancer, often striking women in their prime and causing death within 18 to 24 months. Now, scientists from The Cancer Institute at NYU Langone Medical Center have identified a key gene—eIF4G1—that is overexpressed in the majority of cases of IBC, allowing cells to form highly mobile clusters that are responsible for the rapid metastasis that makes IBC such an effective killer.

The new findings, Essential Role for eIF4G1 Overexpression in Inflammatory Breast Cancer Pathogenesis, scheduled for publication on *Nature Cell Biology*'s website could lead to the identification of new approaches, therapies and a new class of drugs to target and treat IBC. This would be a critical development in the fight against IBC, which respond poorly to chemotherapy, radiation or any other current treatments for breast cancer, according to the study's lead authors Dr. Robert Schneider, associate director for translational research at The Cancer Institute, co-director of breast cancer research, and the Albert B. Sabin Professor of Molecular Pathogenesis at NYU School of Medicine, and Dr. Deborah Silvera, a postdoctoral research fellow.

"The tragedy of IBC is that it is often misdiagnosed and misclassified. Rather than presenting as a 'typical' lump, IBC looks like an inflammation of the breast and is frequently mistaken for an infection. Physicians often prescribe antibiotics, losing valuable time for treating this fast-moving killer," says Dr. Schneider, noting that IBC accounts for

several percent of all breast cancer cases but takes a high toll on mortality, with an incidence that is 50 percent higher in African American women. He adds that there has been little progress in treating IBC over the past two decades, and there are no drugs specifically for this form of cancer. "In fact, IBC has only recently been recognized as a unique, genetically distinct form of breast cancer."

Dr. Schneider and his colleagues found that the overexpression of the gene eIF4G1 reprograms how the IBC tumor cells make proteins. Other researchers have identified genes associated with IBC, but this is the first gene shown to orchestrate how IBC tumor cells form special structures—unique to this disease—known as "tumor emboli." These small clusters of highly mobile tumor cells are responsible for the rapid metastasis of IBC. Because these cell clumps are not stationary or fixed, they can quickly travel to other areas of the body.

"The good news is that we're beginning to understand IBC at both a molecular and genetic level," says Dr. Schneider. "We believe this gene is a target for new drug discovery, and we also believe it is possible to silence the gene without hurting normal cells. Our next step will be to focus on the genetic basis of this disease and look at the genetic changes underlying IBC to reveal more targets at the genetic level."

Source: NYU Langone Medical Center / New York University School of Medicine

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