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Discovery suggests new combination therapy strategy for basal-like breast cancers

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Multiple research projects – including a 2006 study conducted at the University of North Carolina at Chapel Hill – have used DNA microarray analysis to identify several breast cancer subtypes, including luminal A, luminal B, basal-like and HER2-enriched. Simple tests are being developed to help doctors identify these subtypes and to treat their patients in a more biologically-based way. In turn, these tests have made several studies possible that indicate that basal-like, or triple negative breast cancer, is more prevalent in African Americans than their Caucasian counterparts.

A new study led by UNC Lineberger scientist Charles Perou, PhD, and Sean Egan, PhD, from The Hospital for Sick Children in Toronto, Ontario, demonstrates that deletion of a sugar transferase called LFNG (nicknamed "lunatic fringe"), promotes cell proliferation and tumor formation of basal-like breast cancers. The study was published last week in the journal Cancer *Cell*.

In a laboratory model, the deletion of LFNG not only caused tumors to form but also activated two cellular signaling pathways thought to be important in tumor formation. The team found increased activation of both notch signaling (a receptor found on the surface of cells that is involved in stem cell differentiation and development) and increased expression of the Met oncogene.

Taking the laboratory model a step further, the team examined these same genes and signaling pathways in basal-like tumors and found the

same genetic signature.

"This is exciting because there are drugs in development that target each of these pathways. While targeting each pathway alone might work, our findings suggest that combination therapy could be a promising strategy for treating these basal-like tumors," says Dr. Perou, who is the May Goldman Shaw Distinguished Professor of Molecular Oncology and professor of genetics, and pathology and laboratory medicine at the UNC School of Medicine.

Basal-like breast cancer tends to be more aggressive and have a poorer prognosis than other types, making up about 15 percent of all breast cancers. In young African-American women who develop breast cancer, the subtype makes up about 39 percent of all diagnoses. It is primarily treated with chemotherapy, although newer targeted drugs are being tested in clinical trials.

Provided by University of North Carolina Health Care

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