New gene may provide breast cancer diagnostic marker

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In a research article published in this week's *PLoS Medicine*, Ann Killary (from the University of Texas M. D. Anderson Cancer Center) and colleagues describe a new gene called DEAR1 that is genetically altered by mutation and deletion in breast tumors, and that may provide a new breast cancer prognostic marker.

Each year, more than one million women discover that they have breast cancer. Although breast cancer is usually diagnosed in women in their 50s or 60s, some women develop breast cancer much earlier. Cancer in younger women tends to be more likely to recur or spread, and young women with breast cancer have a lower overall survival rate than older women with cancer. It would therefore be particularly useful to be able to identify those young women who are specifically at the greatest risk of cancer recurrence, so that they could be offered intensive surveillance.

In this study, the researchers used a genetic technique termed "suppression subtractive hybridization" to identify a new gene that is located on Chromosome 1 in a region where loss of heterozygosity (a specific type of genetic alteration) regularly occurs. They called the gene ductal epithelium-associated RING Chromosome 1, or DEAR1. Further analysis of a series of 14 samples showed that DEAR1 protein expression was reduced or lost in 71% of ductal carcinomas in situ (abnormalities that can develop into breast cancer). Sequence analysis of 55 primary breast tumors obtained from The University of Texas M. D. Anderson Cancer tumor bank also showed that 13% contained genetic

alterations in DEAR1.

In addition, Ann Killary and colleagues found that DEAR1 expression was frequently lost in women with early-onset breast cancer and the loss of DEAR1 expression correlated with a strong family history of breast cancer and with a breast cancer subtype that has a poor outcome. At 5-year follow-up of a cohort of 123 pre-menopausal women with onset of breast cancer between the ages of 25 and 49 years, DEAR1-positive expression correlated significantly with a 95% local recurrence-free survival.

Although laboratory experiments may not necessarily reflect what happens in people, the authors say that these findings "indicate that DEAR1 expression is an independent predictor of local recurrence in early-onset breast cancers and suggest that DEAR1-negative staining on immunohistochemistry could be an important marker to stratify early-onset breast cancer patients for increased vigilance in follow-up and adjuvant therapy."

In a related expert commentary on the new study, Senthil K. Muthuswamy from the Ontario Cancer Institute, Toronto, Canada, who was not involved with the original study, says "these observations identify DEAR1 as an excellent predictive biomarker for early onset breast cancers".

More information: Lott ST, Chen N, Chandler DS, Yang Q, Wang L, et al. (2009) DEAR1 Is a Dominant Regulator of Acinar Morphogenesis and an Independent Predictor of Local Recurrence-Free Survival in Early-Onset Breast Cancer. PLoS Med 6(5): e1000068. doi:10.1371/journal.pmed.1000068

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