Could therapeutic vaccines treat hard to beat breast cancers?

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A comprehensive analysis of nearly 1,600 tumor samples has found that CT-X genes are expressed in nearly half the breast cancers that lack the estrogen receptor (ER). CT-X gene products are the targets of therapeutic cancer vaccines already in phase III clinical trials for lung cancer and melanoma. The study—to be published in the Early Edition of the *Proceedings of the National Academy of Sciences* this week—was led by the international Ludwig Institute for Cancer Research (LICR).

ER negative breast cancers, which account for a third of all breast cancer cases, are a group of tumors that has a generally poor prognosis and few therapy options. A subgroup of the ER negative group is triple-negative breast cancer (TNBC), which lacks the estrogen, progesterone and HER2 receptors. TNBC is responsible for most of the breast cancers that strike down African American and young women.

In the current study, gene and protein expression studies showed that nearly half of primary ER negative and triple-negative breast cancers express members of either or both the MAGEA and NY-ESO-1/CTAG1B families of CT-X genes. Approximately half of the primary tumor samples from patients with the basal-like form of breast cancer, which is usually ER negative, also expressed either or both of these gene families, and nearly two-thirds of metastases from basal-like tumors also expressed these genes.

These findings suggest that a therapeutic vaccine combining members of the two CT-X families could be a new therapy approach to filling a

critical unmet need.

Dr. Andrew Simpson, LICR scientific director and an author of the study, said that clinical trials based on the findings of the PNAS study could theoretically be initiated in the near future. "Vaccines targeting MAGEA3 are already in phase III trials, and the Cancer Vaccine Collaborative, a partnership between the Ludwig Institute and the Cancer Research Institute, has demonstrated the safety of different forms of the NY-ESO-1 antigen in phase I and II trials in a variety of tumor types."

According to LICR's Dr. A. Munro Neville, the senior author of the study, obtaining clinic-grade material for more members of the CT-X families and funding for a clinical trial will be the next steps in determining if therapeutic cancer vaccines can meet a critical need in breast cancer therapy.

CT genes—the X denotes chromosome localization—encode CT antigens, proteins that are recognized by the immune system. Spontaneous immune responses against CT antigens are thought to be a natural form of cancer control and might be the mechanism behind spontaneous remission.

Therapeutic cancer vaccines are being developed to induce, strengthen and/or sustain immune responses against cancer. GlaxoSmithKline (GSK), which licensed MAGEA3 and NY-ESO-1 from LICR, is currently conducting phase III clinical trials of a MAGEA3-based cancer vaccine, or "antigen-specific cancer immunotherapy" (ASCI) in non-small cell lung cancer and melanoma.

Source: Ludwig Institute for Cancer Research