UNC Lineberger scientists lead cancer genome analysis of breast cancer

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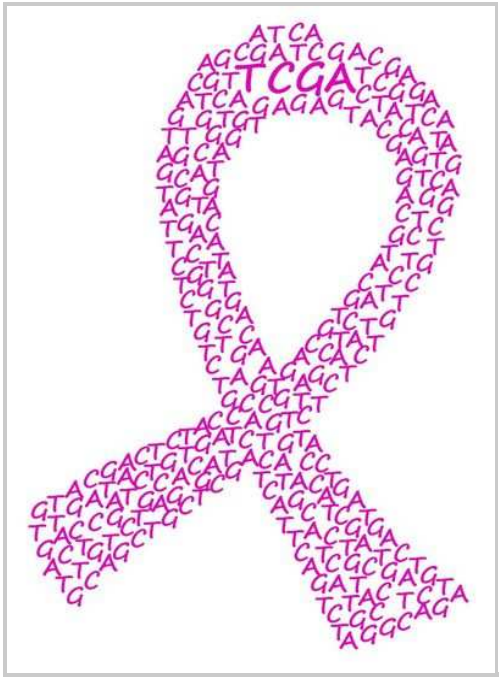
Team identifies genetic causes and similarity to ovarian cancer

Chapel Hill, **NC** - A team of scientists with The Cancer Genome Atlas program reports their genetic characterization of 800 breast tumors, including finding some of the genetic causes of the most common forms of breast cancer, providing clues for new therapeutic targets, and identifying a molecular similarity between one sub-type of breast cancer and ovarian cancer.



Graphic designed by Katherine Hoadley

Their findings, which offer a more comprehensive understanding of the mechanisms behind each sub-type of breast cancer, are reported in the September 23, 2012 online edition of the journal Nature.

The researchers, including a large group from the University of North Carolina at Chapel Hill, analyzed tumors using two basic approaches: first, using an unbiased and genome-wide approach, and second, within the context of four previously known molecular sub-types of breast cancer: HER2-enriched, Luminal A, Luminal B and Basal-like. Both approaches arrived at the same conclusions, which suggest that even when given the tremendous genetic diversity of breast cancers, four main subtypes were observed. This study is also the first to integrate information from six analytic technologies, thus providing new insights into these previously defined disease subtypes.

Charles Perou, PhD, corresponding author of the paper, says, “Through the use of multiple different technologies, we were able to collect the most complete picture of breast cancer diversity ever. These studies have important implications for all breast cancer patients and confirm a large number of our previous findings. In particular, we now have a much better picture of the genetic causes of the most common form of breast cancer, namely Estrogen-Receptor positive/Luminal A disease. We also found a stunning similarity between Basal-like breast cancers and ovarian cancers.”

“This study has now provided a near complete framework for the genetic causes of breast cancer, which will significantly impact clinical medicine in the coming years as these genetic markers are evaluated as possible markers of therapeutic responsiveness.”

Dr. Perou is the May Goldman Shaw Distinguished Professor of Molecular Oncology and a member of UNC Lineberger Comprehensive Cancer Center.

Among the many discoveries include findings of some of the likely genetic causes of the most common form of breast cancer,

which is the Estrogen-Receptor positive Luminal A subtype. Luminal A tumors are the number one cause of breast cancer deaths in the USA accounting for approximately 40 percent, and thus, finding the genetic drivers of this subtype is of paramount importance. The TCGA team found that the mutation diversity within this group was the greatest, and that even specific types of mutations within individual genes, were associated with the Luminal A subtype. Some of these mutations may be directly targetable by a drug(s) that is in clinical development, thus possibly offering new options for many patients.

In addition, the team compared basal-like breast tumors (also known as triple-negative breast cancers) with high-grade serous ovarian tumors and found many similarities at the molecular level, suggesting a related origin and similar therapeutic opportunities. These data also suggest that basal-like breast cancer should be considered a different disease than ER-positive/Luminal breast cancer, and in fact, both basal-like breast cancer and ovarian cancer were more similar to each other than either was to ER-positive/Luminal breast cancer.

Dr. Perou adds, “Cancer is, of course, a complex disease that includes many types of alterations, and thus, no one technology can identify all of these alteration; however, by using such a diverse and powerful set of technologies in a coordinated fashion, we were able to identify the vast majority of these alterations.”

Katherine Hoadley, PhD, study co-author, explains, “Our ability to compare and integrate data from RNA, microRNA, mutations, protein, DNA methylation, and DNA copy number gave us a multitude of insights about breast cancer. In particular, highlighting how distinct basal-like breast cancers are from all other breast cancers on all data types. These findings suggest that basal-like breast cancer, while arising in the same anatomical location, is potentially a completely different disease.”

Dr. Perou describes UNC’s role on the TCGA Breast cancer project as “extensive, including generating the RNA expression data, performing integrated data analyses, and playing a major role in the writing of the paper and crafting of the new hypotheses coming from this work.”

TCGA is a groundbreaking effort to genetically characterize the entire genome of 20 different cancer types, involving scientists from around the world. UNC Lineberger was one of the original consortium members and will receive over $20 million in grants to fund this research. TCGA is funded jointly by the National Cancer Institute and the National Human Genome Research Institute, both part of the National Institutes of Health.

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