Researchers reveal digital transcriptome of breast cancer

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GW Cancer Research Team in the Department of Biochemistry and Molecular Biology, in the School of Medicine and Health Sciences, published a study that is the first of its kind to use mRNA sequencing to look at the expression of genome, at a unprecedented resolution at the current time, in three types of breast cancer. The study titled, "Transcriptomic landscape of breast cancer through mRNA sequencing," is published in the Feb. 14 edition of the journal, *Scientific Reports*, a new open access *Nature* journal for large volume data.

Breast cancer is the leading cause of cancer death among women, accounting for about 23% of the total cancer cases and about 14% of the cancer deaths worldwide. One of current bottlenecks that hinder the translation of the current gene expression signatures for the benefits of patient is the highly heterogeneous nature of the disease. Therefore, one way to move forward is to identify and gain a deeper insight into the transcriptional regulatory machinery elements, which ultimately are responsible for phenotypic changes, for the next major leap in breast cancer genomic research and treatment. And this is exactly, what was done here, said the senior author and Team Leader Rakesh Kumar, Ph.D., of the project.

Using a sample set of 17 patients with three different types of breast cancer, the GW Research Team which also included collaborators from the John Hopkins College of Medicine and Baylor College of Medicine looked at similarities and differences in their gene expression patterns with a goal to identify biologically relevant, therapeutically important

sets of targets in breast cancer. The researchers undertook a high throughput study to define comprehensive digital transcriptome and performed extensive comparative analysis of three groups of breast cancer from the total 1.2 billion reads at various levels of the transcriptional process. The comparative transcriptomic analyses illuminated common as well as differentially expressing transcripts between the three breast cancer groups. Further, high numbers of novel and unannotated transcripts, revealing global breast cancer transcriptomic adaptations in all three breast cancers were also identified.

"We are excited to be a part of this new approach to understand breast cancer. For the first time mRNA sequencing of human breast cancer tissues provides knowledge on central transcriptional regulatory elements, demonstrating the unexplored niches that could change the way breast cancer is previously understood," said lead author Jeyanthy Eswaran, PhD, Director of the McCormick Genomic and Proteomic Center in the department.

While most research today is mainly focused on preselected genes, GW's approach used a completely unbiased approach in order to come up with original snapshot of the breast cancer transcriptome. The GW researchers are working to gain a better understanding of the fundamental occurrences orchestrating the events that lead to a patient suffering from breast cancer. While searching for the highly abundant primary transcript groups which, the team identified osteonectin, guanine nucleotide binding protein beta polypeptide 2-like 1, calnexin calreticulin, ferritin L subunit, and beta-2 microglobulin (B2M) as the top five highly abundant primary transcript group in all three breast cancers. The GW research group is now teaming up with other breast cancer researchers to expend and validate some of the key findings of this work.

"From the on-going, follow-up work in the laboratory, it is clear that the significance of this study has implications beyond the current digital transcriptome of breast cancer as team is actively characterizing novel mutations in protein-coding genes and other elements of human genome that might be relevant in breast cancer," said Dr. Kumar. In addition, the work is likely to influence breast cancer genomics, the transcriptional regulation of cancer, and help built new biologic pathways in breast cancer in the coming years.

More information: www.nature.com/srep/2012/12021 … /full/srep00264.html

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