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Better classification to improve treatments for breast cancer

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Breast cancer can be classified into ten different subtypes, and scientists have developed a tool to identify which is which. The research, published in the journal *Genome Biology*, could improve treatments and targeting of treatments for the disease.

Cancer arises due to genetic changes which cause normal cells to develop into tumors. As we learn more about breast cancer, we are seeing that it is not one single disease – the mutations in the genes that cause different cancers are not alike, and this is why tumors respond differently to treatment and grow at different rates. Currently, there are two key markers that clinicians use to predict response to treatments.

Spotting the trends in tumor genetics and creating a system to diagnose tumor types is a primary objective of cancer scientists. To this end, researchers at Cancer Research UK and the University of Cambridge have been developing the IntClust system, which uses genomic technology to create a classification system with enough detail to more accurately pinpoint which type of breast cancer a patient has, and therefore what treatment would be most appropriate.

To test the system, the scientists looked at the 997 tumor samples they had used to develop the system, and 7,544 samples from public databases, along with the genomic and clinical data including data from The Cancer Genome Atlas. They classified these using their IntClust system, and the two main systems in use today – PAM50, which groups cancers into five types, and SCMGENE, which classifies cancer into

four.

They found that IntClust was at least as good at predicting patients' prognosis and response to treatment as the existing system. But the system identified a previously unnoticed subgroup of tumors in just 3.1% of women with very poor survival rates, which appeared to be resistant to treatment. Identifying the genomic signatures for this group could flag up these high risk cancers early, and having the genomic data for these could aid in the investigation of new avenues for treatments for this type of cancer.

At present, using this system to classify tumors would be costly for most clinicians, and interpreting the results requires training that many clinical settings don't have access to. But the detail and accuracy of this system could be of great use to breast cancer researchers, who will be able to investigate the reasons that certain groups of cancer respond better to certain treatments, in order to find clinical markers, or to identify new targets for breast cancer treatments.

Raza Ali, lead author from Cancer Research UK Cambridge Institute, says: "We have developed an expression-based method for classification of breast tumours into the IntClust subtypes. Our findings highlight the potential of this approach in the era of targeted therapies, and lay the foundation for the generation of a clinical test to assign tumors to IntClust subtypes."

More information: Genome-driven integrated classification of breast cancer validated in over 7,500 samples, Hamid R Ali, Oscar M Rueda, Suet-Feung Chin, Christina Curtis, Mark J Dunning, Samuel AJR Aparicio and Carlos Caldas, *Genome Biology* 2014, 15:431.