

# Epigenetic study reveals new insights into breast cancer

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The most comprehensive analysis yet of the epigenetic modifications present in breast cancer has revealed potentially important new ways to detect and treat the disease, Belgian researchers have reported.

Epigenetics is a term used to describe modifications to the [DNA molecule](#) that affect way its code is translated into proteins. These changes include methylation, a form of chemical modification.

Although researchers knew epigenetics was important in cancer, information about its exact contribution to breast [carcinogenesis](#) was scant, Dr Sarah Dedeurwaerder, from Université Libre de Bruxelles, in Brussels, explained at the IMPAKT [Breast Cancer](#) Conference.

"Our goal was to assess the epigenetic differences between normal tissue and primary tumor samples on a genome-wide scale, similarly to what has been done for gene expression patterns," Dr Dedeurwaerder said. "Here, we provide a glimpse to what DNA methylation profiling of primary breast tumors might bring to our understanding of their biology and diversity... that should contribute to better management of breast cancer patients."

The researchers performed a comprehensive DNA methylation profile on two independent sets of frozen breast tissue samples: a 'main set' of 123 samples, and a 'validation set' of 125 samples.

Their first finding was two major sub-types of breast cancer, defined

according to whether the cancer expresses receptors for estrogen, are widely epigenetically controlled. "When we performed a clustering analysis of our samples based on their DNA methylation profiles, tumors segregated naturally into two distinct groups," Dr Dedeurwaerder said.

The first group was mainly composed of estrogen receptor-negative tumors, and the second one of estrogen receptor-positive tumors. "This indicates that ER-negative and ER-positive tumors have very different methylation profiles," she said.

"Furthermore, when we looked at more than 400 genes whose expression is positively or negatively correlated to the expression of the ER gene, we showed a reverse correlation between methylation and expression status of the majority of these genes. This suggests that epigenetics is probably involved in the regulation of expression of genes playing an important role in the establishment of the two major phenotypes of breast cancer determined by ER status."

The analysis also revealed new information about new sub-types of breast cancer. The researchers showed that DNA methylation profiles enabled breast tumors to be classified in more groups than those currently defined.

"This is really the most interesting part of these data," Dr Dedeurwaerder said. "Indeed, several patients displaying the same known sub-type of breast cancer can respond differently to a given drug. An epigenetic difference between the tumors of these patients might explain the difference observed in terms of treatment response. Therefore, DNA methylation profiling could help to refine the current breast cancer classification and thus might help to stratify patients within a particular sub-type both in terms of prognosis and prediction to treatment response."

"I think we can harness epigenetic information to improve cancer care in several ways," Dr Dedeurwaerder said. "Firstly, several lines of evidence suggest that epigenetic dysregulation occurs early during carcinogenesis and can be detected in bodily fluids. Therefore, DNA methylation markers could help to provide an earlier detection of the disease."

"Secondly, it has already been shown that DNA methylation markers might help to better stratify patients in terms of prognosis. Thirdly, such markers could also help to predict response to a given drug."

"Lastly, an epigenetic therapy of cancer, alone or in combination with conventional therapies, is conceivable," Dr Dedeurwaerder said. "Indeed, several drugs have been developed and several clinical trials have already shown promising results, in particular for leukemia."

"In this study, we have generated the largest and most comprehensive DNA methylation dataset for human breast tumor tissues," the researchers conclude. "By laying the ground for better understanding of breast cancer heterogeneity and improved tumor taxonomy, the precise epigenetic portraits drawn in our work should contribute to better management of breast cancer patients."

Commenting the study, which he was not involved in, Prof Fortunato Ciardiello, from Seconda Università di Napoli, Naples, Italy, noted that gene expression profiles by microRNA analysis have allowed to identify sub-groups of human breast cancers with different biological behaviors and eventually different prognosis.

"Now, for the first time, whole genome epigenetic analysis reveals, in a large number of human breast cancers, a series of sub-types which could help better define more homogeneous groups, which could be useful to select appropriate and more personalized therapeutic approaches."

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