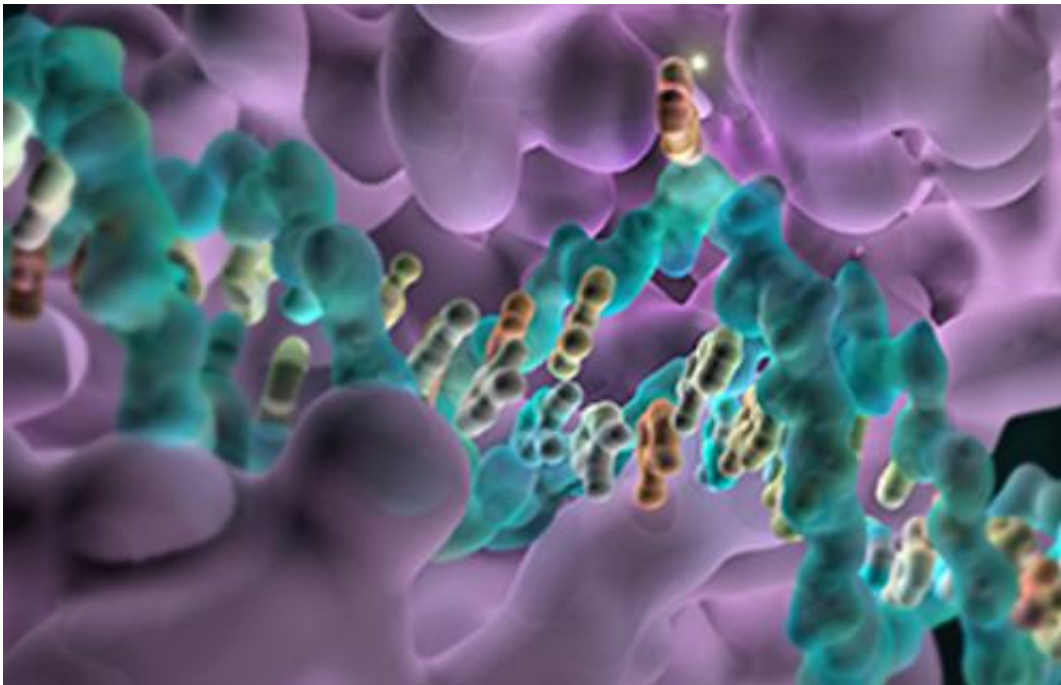


Epigenetic signatures that differentiate triple-negative breast cancers

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DNA in the process of being 'methylated'. Credit: Artwork by Dr Kate Patterson

Australian researchers have identified epigenetic 'signatures' that could help clinicians tell the difference between highly aggressive and more benign forms of triple-negative breast cancer.

The new study, published in *Nature Communications*, compares the breast cancer DNA 'methylome' with that of healthy individuals. The methylome provides a new picture of the genome and shows how it is

epigenetically 'decorated' with [methyl groups](#), a process known as DNA 'methylation'.

The study reveals "distinct methylation patterns" in the primary biopsy breast cancer cells indicating better or worse prognosis.

Triple-negative breast cancers, which make up 15-20% of all breast cancers, lack any of the three receptors (oestrogen, progesterone or HER2) that would make them responsive to targeted drugs. Overall, patients have a higher risk of disease recurrence and shorter survival than those with other breast cancers.

Triple-negative breast cancer patients tend to fall into two categories: those that succumb to their disease within 3-5 years, regardless of treatment; and those that remain disease free for longer than the average non-[triple-negative breast cancer](#) patient (at least 8 years post-diagnosis).

At present, there is no reliable way to 'stratify' triple-negative cancers into these two sub-groups. Clinicians use tumour size, degree of spread, and infiltration of lymph nodes to determine whether a patient falls into a high-risk or low-risk category. Ironically, the outcome of triple-negative breast cancers is far less associated with cancer stage than other breast cancers.

Professor Susan Clark, Dr Clare Stirzaker and Dr Elena Zotenko from Sydney's Garvan Institute of Medical Research, performed whole genome methylation capture sequencing on archival tissue samples from triple negative breast [cancer patients](#) and matched normal samples, followed by next generation sequencing to determine cancer-specific changes in DNA methylation.

"This is the first study to investigate the methylome of triple negative breast cancer - and its association with disease outcome," said project

leader Professor Susan Clark.

"There is a clear need for better informed disease management. In the absence of robust prognostic tools, too many women are being over-treated.

Pathologist Dr Glenn Francis, who analysed the tissue samples for the study, agreed. "The information we have at the moment is based on statistics and probability, and we are forced to treat [triple negative breast cancer](#) patients as a group, even though we know that they are not a uniform population," he said.

"By stratifying tumours epigenetically, this study should enable us to track selected groups of patients over time, monitoring how they respond to different treatments."

"From a purely practical standpoint, it's useful that reliable results were obtained from formalin-fixed, paraffin embedded tissue - as this is the material routinely used for diagnosis."

Dr Clare Stirzaker and Professor Susan Clark developed the methodology to sequence the methylome using DNA extracted from the archived tissue blocks.

"We were very pleased to find a way to interrogate this archival DNA - a valuable resource because methylation patterns can be correlated with patient outcomes," said Dr Stirzaker.

"Developing the methylation sequencing methodology allowed us to answer a new question."

Professor Clark acknowledges that the findings now warrant further investigation in much larger [breast cancer](#) cohorts. "We are very

encouraged to have found that epigenetics provides a promising new prognostic tool - and look forward to the results from the next phase of validation," she said.

Provided by Garvan Institute of Medical Research

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