Breast cancer risk can be seen years before it develops

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A person's risk of breast cancer could be decided many years before it develops, according to a new study.

Dr James Flanagan, a Breast Cancer Campaign scientific fellow in the Department of Surgery and Cancer at Imperial College London, has uncovered the first strong evidence that molecular or 'epigenetic' changes in a gene can be associated with breast cancer risk and can be detected many years before breast cancer develops.

The research, which is published in *Cancer Research*, involved 640 women with breast cancer and 741 controls who enrolled in three previous studies, the earliest of which began in 1992. The researchers analysed blood samples that the women donated on average three years before being diagnosed with breast cancer to find out whether the alteration of single genes by a process called methylation can predict whether women have an increased breast cancer risk.

Dr Flanagan found that the women with the highest level of methylation on one area of a gene called ATM were twice as likely to get breast cancer as women with the lowest level. This result was particularly clear in blood samples taken from women under the age of 60.

Importantly, because this is the first study using blood taken on average three years before diagnosis and in some cases up to eleven years, it shows that the genes were not altered because of active cancer in the body or by treatments for cancer, which has been a problem with

previous studies that took blood after diagnosis.

These findings provide strong evidence that looking at this type of epigenetic alteration (methylation) on individual genes could be used as a blood test to help assess breast cancer risk. When used in combination with other risk assessment tools such as genetic testing and risk factor profiling, this simple blood test could identify those at higher risk, helping doctors to monitor and one day maybe even prevent breast cancer ever developing.

The findings now need rigorous testing in many more individuals and many more genes that contribute to a person's risk profile need to be identified, as this is just one gene that makes up a small component.

Epigenetics research is changing the way scientists think about genes and their development and so could play an important role in helping to prevent cancer. It was previously thought that only errors in the fundamental genetic information from our DNA - whether inherited or caused by environmental factors - determined whether our cells become cancerous. However, new research is showing how chemical modifications to DNA, that control our genes, could be even more important than our DNA alone in determining how our cells grow.

Dr Flanagan said, "We know that genetic variation contributes to a person's risk of disease. With this new study we can now also say that epigenetic variation, or differences in how genes are modified, also has a role.

"We hope that this research is just the beginning of our understanding about the epigenetic component of breast cancer risk and in the coming years we hope to find many more examples of genes that contribute to a person's risk. The challenge will be how to incorporate all of this new information into the computer models that are currently used for

individual risk prediction.

“So far we have found alterations in one small region of a gene that appear to associate with risk of disease and so the next step with this epigenetic research is a genome wide approach to try and find all the associated genes.”

Baroness Delyth Morgan, Chief Executive of Breast Cancer Campaign said, “Dr Flanagan’s research into epigenetics is so exciting because it suggests that there is every possibility that the risk of developing breast cancer could be decided many decades in advance. By piecing together how this happens, we can look at ways of preventing the disease and detecting it earlier to give people the best possible chance of survival.”

More information: *Cancer Res* May 1, 2012 72; 2304 doi: 10.1158/0008-5472.CAN-11-3157

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