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Vital clues to future cancer development in normal breast tissue DNA

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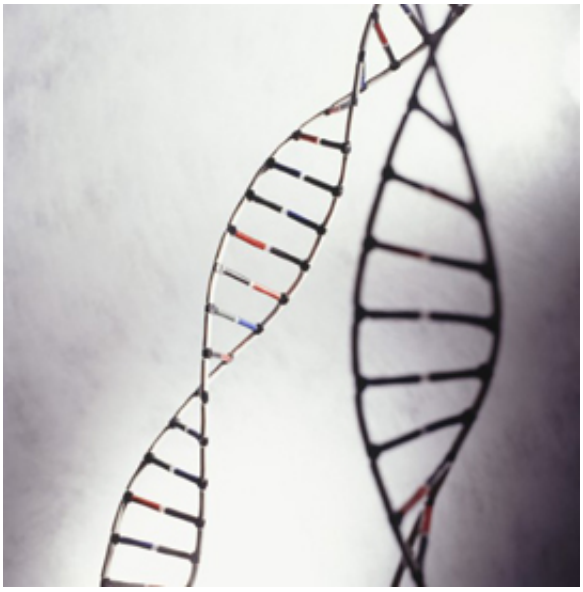

Credit: NIH

Detecting molecular alterations in early breast cancer development is key in the development of more effective cancer prevention and early detection strategies. New research funded by The Eve Appeal and the European Union's Seventh Framework Programme, published today in science journal *Nature Communications* shows clear evidence that DNA changes are already present in the healthy tissue from women with breast cancer.

The research, undertaken by the Department of Women's Cancer at

UCL and led by Professors Martin Widschwendter and Andrew Teschendorff, aims to decode how the most common women's cancer - breast cancer - develops. Previous research has shown that there are key risk factors associated with an increased risk of cancer development. These include, a family history of breast cancer, starting periods early or entering menopause late.

These risk-mediating factors slightly alter the genetic program inherent in breast cells at the time of exposure to the risk; and these alterations are memorised by the cells over several decades. The system in our cells that is responsible for this is called the 'epigenome'. The epigenome refers to the cells' software which gives all the different cells in our body their identity, and are vital to an individual's normal health and development. They consist of a series of processes which control the accessibility of our DNA sequence and as such influence the interpretation of the genome and fate of the affected cell.

These new findings significantly move our understanding forward and is consistent with the view that an altered epigenetic program, which limits the ability of cells to differentiate predisposes them to the development of breast cancer.

Researchers analysed a total of 668 breast tissue samples, including samples from women without cancer, normal breast and cancer tissue from women with a cancer, as well as an independent set of non-invasive and invasive breast cancer samples. They did so using a unique statistical approach which was developed by Prof Andrew Teschendorff. They found that normal tissue adjacent to breast cancer is characterized by tens to thousands of epigenetic alterations.

Importantly a large component of the detected variable epigenetic signature was enriched in the corresponding breast cancer tissue, supporting the view of the researchers that this variable epigenetic

signature marks susceptible precursor cells crucially involved in breast cancer development. Furthermore, those cases of breast cancer which were exhibiting epigenetic changes were associated with significantly poorer prognosis and a decreased level of survivorship from the disease.

Professor Martin Widschwendter, Head of Department of Women's Cancer at University College London said: "These new findings are important in supporting further research into women's cancer development and prevention. We are working hard to understand the risk factors associated with epigenetic changes in normal breast tissue and how these pre dispose a woman to cancer. The application of these altered epigenetic signatures hold the key developing new interventions that could 'switch off' this epigenetic defect and hold the key to preventing cancer development."

Professor Andrew Teschendorff, Lead Computational Biologist at the Department of Women's Cancer at the University College London said: "These new data show how epigenetic alterations, if detected early enough, could be used to identify women at higher risk of developing breast cancer. Since epigenetic alterations are reversible, it offers the potential to design preventive strategies. Our work further highlights the importance of inter-disciplinary work, combining clinical, biological and statistical expertise to make these findings possible".

Athena Lamnisos, Chief Executive of The Eve Appeal said: "Stopping women's cancers before they start is the ambition of our research programme. In order to do this we need to track cancer development right back to its earliest development and understand how it starts. This research is an important step towards understanding how molecular changes in healthy tissue can be detected. Once we can identify these changes we can then move on to developing ways to revert them."