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Cervical Smear Tests Could Be Used One Day to Detect Early Breast Cancer

Cervical smear tests one day could be used to detect early breast and ovarian cancer. A European research team recently published in *Nature Communications* an epigenetic signature for breast and ovarian cancer that can be easily assayed in cervical smear samples.

DNA methylation is an epigenetic mechanism to control gene expression. Greater methylation silences a gene, whereas its hypomethylation leads to greater gene expression. DNA hypomethylation of steroid hormone receptor genes is one epigenetic signature often associated with breast cancer. These genes drive growth and are under strict regulation. Steroid hormones can drive tumours with dysregulated progesterone receptor expression. Furthermore, breast cancer-driven DNA methylation changes have been identified in adjacent normal tissue.

While assaying DNA methylation is an easily performed epigenetic test, sample heterogeneity and the choice of surrogate tissue are important factors to consider for clinical implementation. In particular, the surrogate tissue must be hormonally sensitive and reflect changes occurring elsewhere. Given that cervical samples are hormonally sensitive and routinely obtained, the research team examined whether cervical samples could provide an epigenetic signature that indicates cancer risk.

DNA methylation was analysed in 2,818 cervical matched to 357 cheek and 227 blood, and in 42 breast tissue samples from women with and without breast cancer. The training set identified 31 gene areas within progesterone receptor binding sites that were hypomethylated in cervical samples, which were also hypomethylated in the normal breast tissue of women with breast cancer or in BRCA mutation carriers (who show a high incidence of breast cancer). These were compiled into a DNA methylation-based Women's risk IDentification for Breast Cancer index (WID-BC-index) that could identify women with breast cancer with high accuracy (over 80% specific). Since women with breast cancer are also at higher risk for ovarian and endometrial cancer, the signature was tested in samples from women with ovarian cancer and was found to be predictive. They could identify 71.4% of women under 50 and 54.5% of women over 50 with ovarian cancers with 75% specificity.

Overall, the data show that a systemic epigenetic programming defect is highly prevalent in women who develop breast cancer, which can be used as a biomarker for monitoring breast cancer risk as well as that of ovarian cancer. These findings are important because breast cancer is the most common cancer in women, and ovarian cancers are associated with high mortality. Since ovarian cancers are now mostly detected after spreading, detecting the disease earlier may improve treatment.

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Source: Nature Communications

Published on : Mon, 14 Feb 2022