Links Between DNA Damage and Breast Cancer Studied

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Researchers from the Pacific Northwest Research Institute (PNRI) and the National Institute of Standards and Technology (NIST) have uncovered a pattern of DNA damage in connective tissues in the human breast that could shed light on the early stages of breast cancer and possibly serve as an early warning of a heightened risk of cancer.

In the United States, breast cancer is the second leading cause of cancer-related death in women. Breast cancer detection and therapy generally target epithelial cells, the primary locus of breast cancers, but in recent years evidence has accumulated that genetic mutations that develop into cancer may occur initially in a deeper layer of breast tissue, called the stroma. Genetic changes in this connective tissue that supports the breast's network of glands and ducts have been reported to precede the malignant conversion of tumor cells, but the actual role of stromal cells in the early stages of breast cancer initiation and progression is not well understood.

In two recent papers*, the PNRI/NIST team explored the occurrence of damage to stromal DNA caused by free radicals and other oxidants. NIST researchers used a high-precision chemical analysis technique (liquid chromatography/mass spectrometry with isotope dilution) to identify specific DNA lesions, while the PNRI team used a spectroscopic technique (Fourier transform-infrared spectroscopy) to reveal subtle conformational changes to DNA base and backbone structures. Such alterations to the molecular structure can change or disrupt gene expression.

The team identified a unique oxidation-induced lesion in the DNA of breast epithelium, myoepithelium and stroma and found that the highest concentrations of this lesion tended to occur in women in the 33- to 46-years age group, a bracket that corresponds to a known rise in the incidence of breast cancer.

In a second paper, the team studied age-related concentrations of two similar mutagenic DNA lesions and again demonstrated that their occurrence is roughly commensurate with the age at which the incidence of female breast cancer rises. “Collectively,” they observe, “the findings reveal that the structural changes in DNA described may potentially disrupt normal reciprocal interactions between the cell types, thus increasing breast cancer risk.” The findings suggest that lesions measured in the DNA of the stroma, which is readily obtained, may prove to be convenient and sensitive biomarkers for assessing oxidative DNA damage and for signaling an increased breast cancer risk.

*Citation:

K.M. Anderson, P. Jaruga, C.R. Ramsey, N.K. Gilman, V.M. Green, S.W. Rostad, J.T. Emerman, M. Dizdaroglu and D.C. Malins. Structural Alterations in Breast Stromal and Epithelial DNA: The Influence of 8,5'-Cyclo-2-Deoxyadenosine. Cell Cycle Vol. 5, No. 11, June 1, 2006, pp. 1240-1244.

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