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Gamma-radiation induced DNA methylation and gene expression alterations in human cancer cell lines – an epigenetic connection

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Background: Ionizing radiation induces cellular damages through both direct and indirect mechanisms, which may include effects from epigenetic changes. DNA methylation is a fundamental epigenetic event associated with tumor progression. Hypermethylation of CpG islands at active gene promoters leads to transcriptional repression, whereas hypo-methylation is associated with gene over expression.

Objectives: To identify relative sensitivity and resistance to γ -radiation and to determine the effect of γ -radiation on gene-specific methylation pattern in human tumor cell lines that may be associated with altered gene expression.

Methods: Effect of radiation on gene-specific methylation as well as expression changes were identified using microarray hybridization analysis in radio-resistant and radio-sensitive cell lines which was further validated by bisulfide genomic sequencing. Systems biology approach was used to identify the activation of several novel signaling pathways which are silenced by DNA methylation.

Results: Our study demonstrates that γ -radiation alters DNA methylation at gene-specific level and differential expression leading to transcriptional activation of genes which are silenced by epigenetic mechanisms.

Conclusion: These results provide important information on alterations in DNA methylation and possibly associated with altered gene expression due to radiation effects and may reveal correlations between responses and either diagnosis or prognosis, and such *in vitro* validation marks an important step in the development of potentially informative radiation exposure biomarkers.