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Radiation-induced genomic instability and LINE-1 hypomethylation in radiographers

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Genomic instability is an important factor in cancer induced by ionizing radiation. Global DNA hypomethylation has been recently proposed as a potential biomarker for cancer risk through genomic instability. However the association between low-dose ionizing radiation exposure and DNA methylation changes is unclear. This study aimed to understand the epigenetic mechanisms associated with low-level radiation exposure and radiation-induced genomic instability (RIGI) among industrial radiographers. Global DNA methylation levels were measured in WBC DNA from 40 industrial radiographers and 32 healthy male volunteers using two assays: (1) Pyrosequencing of repetitive element LINE-1 and (2) luminometric methylation assay (LUMA). The micronucleus-centromere assay was also performed to measure aneuploidy of chromosomes 1 and 4. The mean levels of LINE-1 and LUMA methylation were significantly lower in radiographers than in controls (73.8 ± 1.2% vs 74.4 ± 1.1%, 66.4 ± 5.8% vs 69.1 ± 3.3% respectively, $p<0.05$). LINE-1 and LUMA hypomethylation was not significantly correlated with the last 1-year, the last 3-year, or the total cumulative radiation doses in radiographers. However, LINE-1 hypomethylation was significantly correlated with the cumulative radiation dose without recent 3-year exposure ($r = -0.39$, $p<0.05$). Also, LINE-1 hypomethylation was a significant contributor to total aneuploidy by the cumulative radiation dose without recent 3-year exposure (45% variation of total aneuploidy, $p<0.05$). The obtained data indicate that LINE-1 hypomethylation is associated with the delayed genomic instability induced by radiation, which may allow an expansion of knowledge in understanding the epigenetic changes as a molecular event of radiation-induced genomic instability and/or radiation-induced carcinogenesis, to use as biomarkers for a prediction of risk of low-dose radiation exposure. However additional studies with a larger number of subjects and other repetitive elements using different assays are needed to fully understand the relationship between genomic DNA hypomethylation and radiation-induced genomic instability.

The funding obtained from the UGP provided great opportunities for me to generate preliminary data for my research. With these interesting findings, I was able to present a poster in 3rd Biennial Western Regional IDeA Conference, and received a Best Poster Award. I am currently working on a manuscript for peer-reviewed publication. This study would be the first paper

publishing the relationship between epigenetic alteration and chromosomal instability among healthy radiographers occupationally exposed to low-levels of radiation. Furthermore, I am also preparing a grant proposal to the NIH with this preliminary data for my future studies; development of biomarkers for intrinsic radiosensitivity of healthy individuals which may allow the monitoring of occupational or environmental radiation exposure and can also assist the stratification of patients for response to radiotherapy.