LETTER to the EDITOR

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# Single Nucleotide Polymorphisms in *APE1, hOGG1, RAD51* Genes and Radiotherapy Induced Toxicity among Head and Neck Cancer Patients: Comment

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## Dear Editor

we would like to comment on the publication on "Single Nucleotide Polymorphisms in *APE1, hOGG1, RAD51* Genes and their Association with Radiotherapy Induced Toxicity among Head and Neck Cancer Patients [1]." This study, which included 350 patients with head and neck cancer (HNC) who had radiation therapy and experienced side effects like skin reactions and mucositis, sought to investigate the relationship between single nucleotide polymorphisms (SNPs) in DNA repair genes and the harmful effects of radiation on normal tissues. The authors used methods including PCR-RFLP and direct DNA sequencing to precisely look at SNPs in the *APE1, hOGG1*, and *Rad51* genes. The findings showed a strong correlation between severe skin responses and mucositis and the *Rad51* 172G/T polymorphism. Moreover, a correlation was observed between the tumor grade and the hOGG1 polymorphism, whereas homozygous *Rad51* variations were linked to an inadequate response to treatment.

The study presents strong evidence linking the *Rad51* polymorphism to radiation-induced deleterious consequences; nevertheless, a thorough discussion of the therapeutic relevance of these findings is yet lacking. Although the findings are significant, they must be seen within the larger framework of customized treatment. It describes how treatment choices may be impacted by various genetic characteristics. Moreover, the investigation mainly concentrated on a certain subset of SNPs without exploring the possible correlations between supplementary genetic variations in other genes implicated in DNA repair pathways, which could offer a more all-encompassing comprehension of the genetic foundation of radiation damage.

Examining simply a few genetic variants may result in an overlook of the complex genetic landscape that determines radiation sensitivity and treatment. Other SNPs involved in DNA repair (e.g., SNPs in genes like *ERCC1, XRCC1*, and *ATM*) may also have a role in radiation poisoning [2]. Future research should incorporate a broader set of potential genes, preferably through genome-wide association studies (GWAS) or targeted sequencing approaches, in order to identify other genetic variants that may influence radiation sensitivity or resistance in diverse populations.

Several flaws are apparent in this study. First, while the sample size is enough, it may not include all genetic variants, particularly rare genetic variants. Second, the results' generalizability is limited because they are based on a single ethnic and geographic community. Third, the study did not sufficiently account for potential confounding factors that could influence skin and mucosal reactivity, such as patient demographics, treatment regimen, and nutritional condition. This could skew the correlation between detected SNPs and radiation damage. Furthermore, longitudinal study designs may provide additional insight into how these connections evolve over time.

To clarify the biological pathways impacted by these SNPs, future research should concentrate on integrating multi-omics techniques, including transcriptomics, proteomics, and genomes. Examining patient features and gene-environment interactions could yield a more reliable radiation toxicity prediction model. Additionally, investigating the therapeutic potential of tailored radiation therapy or radiation therapy combined with medicines that lower toxicity based on SNP profiles may enhance clinical outcomes. All things considered, incorporating thorough genetic testing into clinical practice for patients with HNC may result in more individualized and successful treatment plans, which can enhance patients' survival and quality of life while undergoing cancer therapy.

*Conflict of interest*

None.

## References

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2. Cavalieri R, de Oliveira HF, Louvain de Souza T, Kanashiro MM. Single nucleotide polymorphisms as biomarker predictors of oral mucositis severity in head and neck cancer patients submitted to combined radiation therapy and chemotherapy: A systematic review. Cancers (Basel). 2024;16(5). https://doi.org/10.3390/cancers16050949.

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