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Bioinformatics Analysis for the Roles of long non-coding RNAs in the Immune Responses of Mouse Peripheral Blood Mononuclear Cells Exposed to Low-Dose Ionizing Radiation

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Recent advances in sequencing technologies enabling more in-depth genomic and transcriptomic analyses have revealed that many long non-coding RNAs (lncRNAs) are functionally associated with human diseases.[1,2] However, the expression levels of lncRNAs are low in abundance, which poses several challenges for their identification and analysis.[3,4]

We read with great interest the article by Qi and colleagues.[5] The authors revealed for the first time the profile of differentially expressed lncRNAs involved in the responses of the single and chronic low-dose ionizing radiation (LDIR) through the integrated analysis of microarray data which is profound.

The microarray data analysis strategy of this study should be carefully considered and further clarified. According to the authors' description, they seem to use unadjusted *P* values and fold change of expression values when defining significantly differentially expressed lncRNAs. However, due to the characteristics of lncRNAs and high false positives caused by multiple comparisons, it seems that a specialized high-level microarray analysis method may be more suitable, especially when the number of detected lncRNAs is large. Only accurate screening of differential genes can ensure the reliability of pathway enrichment analysis results.

A study comparing several data analysis schemes revealed that linear modeling with empirical Bayes moderation showed good control of the false discovery rate and reasonable sensitivity when defining significantly differentially expressed lncRNAs.[6] In our opinion, the authors might consider using linear models for microarray analysis (Limma), an R/Bioconductor software package that analyzes microarray data using linear models, to test the results.[7,8] Referring to Limma results, choosing appropriate expression fold changes and false discovery rate < .05 as the cutoff is a robust method to analyze the changes of gene expression.

We agree on the importance of comprehensive identification of lncRNAs in single and chronic LDIR responses. More rigorous microarray analysis strategies will be required for insights into these complicated data sets.

Declaration of Conflicting Interests

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References

1. Derrien T, Johnson R, Bussotti G, et al. The GENCODE v7 catalog of human long noncoding RNAs: analysis of their gene structure, evolution, and expression. *Genome Res*. 2012;22(9): 1775-1789. PMID: 22955988; PMCID: PMC3431493. 10.1101/gr.132159.111.

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2. Kopp F, Mendell JT. Functional classification and experimental dissection of long noncoding RNAs. *Cell*. 2018;172(3):393-407. PMID: 29373828; PMCID: PMC5978744. 10.1016/j.cell.2018.01.011.
3. Volders PJ, Helsens K, Wang X, et al. LNCipedia: A database for annotated human lncRNA transcript sequences and structures. *Nucleic Acids Res*; 2013;41:D246-D251. PMCID: PMC3531107; PMID: 23042674. Epub 2012 Oct 5. 10.1093/nar/gks915.
4. Raithel S, Johnson L, Galliart M, et al. Inferential considerations for low-count RNA-seq transcripts: A case study on the dominant prairie grass Andropogon gerardii. *BMC Genom*. 2016;17:140. PMID: 26919855; PMCID: PMC4769568. doi:10.1186/s12864-016-2442-7.
5. Qi Z, Guo S, Li C, et al. Integrative analysis for the roles of lncRNAs in the immune responses of mouse PBMC exposed to low-dose ionizing radiation. *Dose Response*. 2020 18(1): 1559325820913800. PMID: 32269503; PMCID: PMC7093697.doi: 10.1177/1559325820913800.
6. Assefa AT, De Paepe K, Everaert C, Mestdagh P, Thas O, Vandesompele J. Differential gene expression analysis tools exhibit substandard performance for long non-coding RNA-sequencing data. *Genome Biol*. 2018 19(1):96. PMID:30041657; PMCID: PMC6058388.doi:10.1186/s13059-018-1466-5.
7. Law CW, Alhamdoosh M, Su S, et al. RNA-seq analysis is easy as 1-2-3 with limma, Glimma and edgeR. *ISCB Comm J*; 2016, 5: 1408. PMID: 27441086; PMCID: PMC4937821.doi:10.12688/f1000research.9005.3.
8. Ritchie ME, Phipson B, Wu D, et al. Limma powers differential expression analyses for RNA-sequencing and microarray studies. *Nucleic Acids Res*. 2015;43(7):e47. PMID: 25605792; PMCID: PMC4402510. Epub 2015 Jan 20. doi:10.1093/nar/gkv007.