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Commentary on "Integrative Transcriptomics, Proteomics, and Metabolomics Data Analysis Exploring the Injury Mechanism of Ricin on Human Lung Epithelial Cells"

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Ricin toxin (RT) is classified as a potential bio-threat agent in assassinations and terrorism due to its extreme toxicity. Due to aerosol RT exposure is the most lethal route, it is urgent to study its injury mechanism. This work established a RT aerosol lung injury model using A549 cells, which integrates transcriptomics, proteomics, and metabolomics data to study the mechanism of RT injury on human lung epithelial cells. A set of genes, proteins and metabolite were revealed for their potential roles in RT lung injury. The large-scale omics data provided in this study has important significance for the biosafety prevention and treatment of RT intoxication.

The rapid development of microarray, RNA sequencing, and mass spectrometry (MS) technologies has enabled relatively high-throughput analysis of the transcriptome, proteome, and metabolome, which has provided useful tools for acquiring information for molecular profiling, finding new biomarkers, characterizing complex biochemical systems, and clarifying the pathophysiological processes in various diseases. This work integrates bioinformatics analysis methods into the study and opens up a new perspective in the field of RT toxicity mechanism.

RNA-seq analysis was performed to investigate the transcriptome and got an unprecedented number of differentially expressed genes (DEGs). A total of 5872 genes were found to be differentially expressed. According to the results of gene ontology (GO) analysis, the DEGs were enriched in biological processes, mainly including cellular process, metabolic process, biological regulation, regulation of biological process, single-organism process, and response to stimuli. Furthermore, KEGG pathway enrichment analysis results reveal that the altered genes were mainly involved in the TNF signaling pathway, rap1 signaling pathway, pathways in cancer, transcriptional misregulation in cancers, and the Ras signaling pathway. It is worth noting that some of the signaling pathways were well known for their critical roles in cell death and immune regulation. Collectively, these results provide valuable research targets for the follow-up study of the toxicity mechanism of RT.

We employed proteomics analysis technology to study the large-scale structure and function of proteins in A549 cells treated and untreated by RT. A total of 3839 valid proteins were determined to participate in the RT injury process. Notably, we found that the ubiquitin-mediated proteolysis pathway was associated with the RT damage to the cellin the top 10 KEGG pathways, but there has been no literature reported about this. This may be a new interest for the future study of RT injury mechanisms. In addition, protein is the executor of life functions, and changes in its content play an important role in the growth of organisms, environmental stress, and the occurrence and development of diseases. Therefore, finely describing the expression patterns of key genes and comprehensively analyzing the expression of mRNA and protein are the inevitable trend to explore the mechanism of these biological processes. This work suggests a high degree of post-transcriptional regulation in RT treated cells. Interestingly, GO and KEGG analysis of the overlap of the transcriptome and proteome indicated that the ubiquitin-mediated proteolysis was involved in the process of RT injury. The ubiquitin-mediated proteolysis plays crucial role in regulating many biological processes including cellular proliferation, apoptosis, and immune responses. This also indirectly supports the claim that RT can induce apoptosis and inflammation [1-3].

The utilization of bioinformatics software to analyze and predict sequencing data is an emerging technology to explore biological functions. According to the transcriptomics, proteomics, and metabolomics data of RT treated and untreated A549 lung epithelial cells, the gene-metabolism network and protein-metabolism network were constructed to focus the main genes, proteins, and metabolites. The identified gene (OL7A1) and its metabolites (L-tyrosine, piperidine, L-phenylalanine, L-tryptophan, L-arginine, and L-asparagine) were identified as potential markers by integrating genomics, proteomics and metabolomics approaches. Collectively, this integrated multiomic analysis provides a theoretical basis for understanding the systemic mechanism of RT injury on lung epithelial cells.

This work provides a framework for further studies of biological systems, paving the way for the development of new strategies for the prevention, rapid diagnosis, and treatment of RT poisoning, especially of RT aerosol. Further investigations are required to clarify the findings according to the integrative analysis of transcriptomics, proteomics, and metabolomics.

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