The way forward in multi-omics data analyses

Impact paragraph

As aforementioned in chapter 5 – general discussion, this thesis firstly provides a brief of omics technologies currently available for drug side effect research and then explores different omics analysis approaches as well as the drugs-induced molecular alterations inside the cell. Our main aim is to form different data analyses, while the main theme of this thesis is seated within the drug side effects field because understanding the negative effects of drugs is essential for drug safety. Furthermore, exploring the drug toxic mechanism of known drugs could support the clinical usage of those drugs as well as aid the drug discovery process [1].

This thesis focused on the toxic mechanisms of anthracyclines (ANTs), including 3 common analogs: doxorubicin (DOX), epirubicin (EPI), and idarubicin (IDA), and rifampicin (RIF). ANTs are essential chemotherapeutic agents, but their adverse effects can lead to heart failure in cancer survivors. RIF is an important antibiotic for tuberculosis but can cause liver injury. Despite their adverse effects, these drugs are still popular today [2-4]. Although different research had tried to draft the toxic mechanisms of these drugs, their paradigms remain incomplete. In this thesis, we detected several potential targets and phenomena such as altered DNA methylated genes, altered genes, lncRNAs, and proteins' expression under these drug treatments. All these outcomes can be immediately used by risk assessors to evaluate the ANTs-induced cardiotoxicity and RIF-induced hepatotoxicity. These potential targets can be candidate biomarkers to diagnose the particular drug's side effects and help to understand the drug's toxic mechanism. Especially, while many studies mainly focused on the proteome and protein-coding genes, this thesis emphasized the other aspects of the biological system such as DNA methylation and lncRNAs. Epigenetic modifications and lncRNAs have been implicated in cellular processes, and can also be useful tools to reveal drug-induced adverse side effects.

The analysis approaches in this thesis are publicly available, a part of them has been published, and can already be used by other researchers to improvise and analyze the omics data. The usage of high throughput technologies resulting in omics data has been widely accepted in drug toxicity studies. It aids scientists to explore cutting-edge discoveries and promotes reforming the toxicity field. However, the rational recognition of modern omics technologies requires effective and transparent data analysis approaches. This urgent need has appeared not only in the academic research community but also among regulatory agencies and in

the pharmaceutical industry [5]. This thesis portrays different analysis approaches for various omics data types and thus enriches the omics analysis toolbox. Our omics analyses have been published and are accessible to a broad range of users. This also supports the appreciation of omics data and promotes the transparency of omics analysis. Furthermore, it ties to other movements to contribute to the use of omics data in drug development and drug regulatory.

Overall, this thesis discloses several points of interest about both bioinformatics and drug adverse effects perspectives. We displayed the substantial changes in DNA methylation, transcriptome, and proteome as well as parts of the molecular inter-dependences, specifically TF-target relations, beyond the limitation of the data and the need for findings validation. The established omics analysis approaches could take advance of the modern omics technologies to demonstrate the molecular toxic mechanisms and head toward the advanced toxicology field.

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