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Multifactorial Toxicology Experiments: An Integrative Multi-Omics Workflow

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Introduction

Utilizing omics methods, toxicology research can gain a deeper comprehension of the phenomena that underlie the phenotypic changes brought on by various forms of exposure to particular toxicants. However, specialized data analysis software is required to analyse the multifactorial omics studies data. In this work, we propose a new workflow that combines data integration from multiple analytical platforms with factor de convolution. Trimethyltin (TMT) exposure of 3D neural cell cultures was used as a case study. A metabolomics approach that combined four complementary analytical methods (reversed-phase LC, hydrophilic interaction LC, hyphenated to mass spectrometry in positive and negative ionization modes) was used to simultaneously examine the significance of the culture maturation state, the duration of the exposure and the concentration of TMT. We were able to break down and quantify the influence of various experimental factors on the outcome of the TMT exposure using the ANOVA multiblock OPLS (AMOPLS) technique. The maturation state and treatment duration made the most significant contribution to the overall metabolic variability, as demonstrated by the findings. Despite representing the smallest observed modulation among the three factors, the contribution of TMT effects was highly statistically significant. The MetaCoreTM pathway analysis tool revealed that TMT altered neuronal differentiation and signalling processes, biosynthetic pathways and GABAergic and glutamatergic neurons in particular. Combining proteomic data proved this, giving the mechanistic understanding of this toxicant exposure more credence.

Description

Metabolomics is now a well-established part of the omics approaches used to explain neurological disease processes. Since the advent of genomics, epigenomics, transcriptomics and proteomics, it has been accepted as an evolution. Metabolomics provides a comprehensive view of a system's current state as a result of the interaction between the environment and its own genetic, transcript and protein profiles and perturbations. It is the final step in the cascade of events from genes to living organisms. The relevance of systems biology approaches to support decision-making based on a better mechanistic understanding of chemical hazards has recently been highlighted by efforts to harmonize the attempts to include omics in the field of regulatory toxicology. The collection of biological data without the need for prior knowledge is a natural fit for untargeted omics workflows, which may reveal previously unknown modifications to the systems under investigation. For sure, they can possibly turn into an important instrument with regards to the investigation of new systems of poisonousness .While metabolomics can provide a picture of both long-term and instantaneous reactions of the system induced by the stressor under study, proteins require a longer period of time to be either synthesized or degraded [1].

Often, a wide range of investigative methods are required for toxicology studies aimed at revealing the mechanisms of action of various substances. As a result, it is becoming increasingly important to comprehend not only the mechanisms by which these compounds may affect biological systems but also the key events that are shared by various toxicity pathways so that a more rapid assessment of the potential danger posed by compounds can be performed. Adverse Outcome Pathways (AOPs) are the foundation of the Organization for Economic Cooperation and Development (OECD) framework and aim to place mechanistic toxicological data in a context that can be used for risk assessment. These important events are at the heart of AOPs. This idea creates a new obstacle for the analytical strategy, necessitating strategies that can handle multifactorial experimental designs and allow for joint biological interpretation of data from various analytical platforms. The information in untargeted omics analyses typically consists of thousands of variables [2].

Dimensionality reduction techniques have been widely used to summarize, investigate and discover information within such a large number of signals. This is done with both unsupervised and supervised methods, with supervised ones having the advantage of being able to maximize the variance between samples from different experimental groups while taking into account the experimental design (DOE).Even though a few alternatives have been proposed (ASCA, ANOVA-PCA, etc.), classical dimensionality reduction methods fail when multiple experimental factors are involved in the design. They are unable to offer a single model for interpretation in order to circumvent this restriction. ANOVA multiblock OPLS (AMOPLS) was recently proposed as an appropriate tool for studying complex omics datasets by providing a single model to comprehend the system's behavior and taking DOE information into account. Each metabolites cumulative contribution can be evaluated using the models explained variance. As a result, it is possible to specifically link each compound to the manner in which each experimental factor has been influenced. In addition, AMOPLS can be joined to a consensus approach, making it possible to evaluate the contribution of various analytical techniques to the models variability by combining multiple tables from different methods. Consensus AMOPLS was used to combine metabolomics data from various LC-MS platforms in this study [3].

In order to maximize information retrieval from toxicology studies, the current work focuses on a strategy that combines factor deconvolution with multi-omics integration. For instance, phenotypic changes caused by exposure to the heavy metal trimethyltin (TMT) in primary 3D rat neural cell cultures were investigated. Numerous *in vitro* and *in vivo* studies have demonstrated that TMT causes neurotoxicity and neuroinflammation. It was decided that this substance would be an appropriate model substance for studying the effects of neuroinflammation and neurotoxicity based on previous in-house experience with it in the 3D rat model. Three distinct aspects of the experiment were taken into account the degree of maturation of the cultured cells, the time spent exposed and the toxicant's concentration. For the purpose of analysing the contents of the cells, a multiplatform metabolomics strategy used four distinct but complementary LC-MS setups, which were then followed by a confirmatory proteomics analysis. The AMOPLS multivariate analysis, information from metabolomics and proteomic analyses and a pathway enrichment tool were used to decompose and independently quantify the contribution of each experimental factor. As a result, the merged omics signatures were used to identify potential toxicity pathways that link the cellular response to TMT exposure [4].

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A comprehensive workflow for exploring data from multifactorial, multiplatform and multi-omics studies was proposed in this work. It is possible to gain a deeper understanding of the intricate cellular changes caused by exposure to toxicologically relevant molecules by combining complementary biochemical data gleaned from metabolomics. Consider the relative effects of maturation stage, treatment duration and concentration by exposing a known neurotoxicant to a 3D neural model that is undergoing progressive differentiation in culture. A method for comprehensively examining the various responses shown to the same toxic substance is the utilization of DOE to evaluate the relative contribution of various factors of crucial importance to toxicology studies (cell maturation, exposure duration and concentration). AMOPLS enabled us to evaluate the contribution of each effect separately for this purpose. Orthogonal LC-MS methods work together to make it easier to look into the chemical space of the sample and provide more information about changes in metabolism [5].

Conclusion

The findings showed that the neural tissues response to the various TMT concentrations tested was unaffected by either the maturation state or the duration of exposure. However, the concentration of TMT had a significant impact on the system's response, impairing numerous cellular processes associated with neuronal differentiation, homeostasis of biosynthesis and neurotransmission. Lastly, a pathway enrichment analysis platform supported the metabolomics findings by integrating proteomics analyses at the biological level. A good illustration of how systems biology various tools can be successfully combined in an integrative workflow to address the study of multifactorial toxicology experiments is the presented strategy.

References

1. Wilkins, Jordan Maximillian and Eugenia Trushina. "Application of metabolomics in Alzheimer's disease." *Front Neurol* 8 (2018): 719.
2. Bridges, Jim, Ursula G. Sauer, Roland Buesen and Lize Deferme, et al. "Framework for the quantitative weight-of-evidence analysis of omics data for regulatory purposes." *Regul Toxicol Pharmacol* 91 (2017): S46-S60.
3. Rabilloud, Thierry and Pierre Lescuyer. "Proteomics in mechanistic toxicology: History, concepts, achievements, caveats and potential." *Proteomics* 15 (2015): 1051-1074.
4. Tolstikov, Vladimir. "Metabolomics: Bridging the gap between pharmaceutical development and population health." *Metabolites* 6 (2016): 20.
5. Boccard, Julien and Serge Rudaz. "Exploring omics data from designed experiments using analysis of variance multiblock orthogonal partial least squares." *Analytica Chimica Acta* 920 (2016): 18-28.

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