Gene-expression profiling of the effects of liver toxins

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Gene-expression data from liver tissue or whole blood can be used to classify histopathologic differences in the effects of hepatotoxins. It is hoped that these findings, published in BioMed Central's open access journal, *Genome Biology,* will lead to a more precise way of defining the potential hepatotoxicity of new compounds.

It is already known that toxins can be classified using transcriptomic data taken from the primary target tissue or organ. In this new work, researchers set out to see if expression data from blood could serve as a surrogate for a target organ.

A team from the National Institute of Environmental Health Sciences (NIEHS), part of the National Institutes of Health, and Cogenics, a division of Clinical Data, Inc., produced an extensive set of gene expression data combined with more traditional toxicological measurements, such as clinical chemistry and histopathology, after exposing rats to different known hepatotoxic compounds.

Rodents were treated with one of the eight hepatotoxicants being studied at varying doses designed to induce liver injury (either moderate, severe, or no measurable injury), or with a vehicle control. Data relating to histopathology, clinical chemistry, hematology and gene expression were collected from whole blood and from the liver at different timepoints following exposure.

The researchers confirmed that gene expression data from the target organ can be used to classify and differentiate toxins, and went on to show that classification is also possible using data from whole blood. One of the study's co-authors, Edward K. Lobenhofer says: "These data illustrate the power of gene expression profiling to resolve differences in the physical manifestation of the injury evoked by different toxicants using samples derived from either target tissue or whole blood. Additionally, this study demonstrates the possibility of classifying differences in these types of injury using data generated from blood samples."

The results emphasise the importance of 'phenotypic anchoring' – linking gene expression changes to traditional measures of toxicology. "Our results powerfully underscore the importance of anchoring gene expression data analysis through consistent phenotypic endpoints" says co-author Raymond W. Tennant, Head of the Cancer Biology Group at the NIEHS. "Through phenotypic anchoring we are able to facilitate the identification of genes useful in compound classification."

Source: BioMed Central