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System engineering tools and analysis to leverage signaling pathways of hepatocytes to determine toxicity risk

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Systems engineering recognizes that each system is an integrated whole, even though composed of diverse specialized structures and sub-functions. Hepatocytes are complex cells with numerous subsystems, and the interactions among hepatocytes are complex and not completely understood. Systems engineering looks at systems of all types and emphasizes the relationships and interactions between components. Systems engineering can analyze living systems in terms of design, information processing, optimization, and other explicit concepts, by using various quantitative System Engineering tools that include data analysis, modeling and simulation, signaling processing and graph theory. The application of these tools provides new insight into the intricate workings of hepatocytes. Hepatocytes are complex and yet exceedingly connected systems that make it tremendously challenging to understand the underlying signaling pathways and interpreting numerous and varied high dimensional measurement data. Currently, there is a paradigm shift from apical endpoints in animal testing to perturbation of toxicity pathways in human hepatocyte cells. Gene expression data of PPAR α binding measured over multiple concentrations and times of GW7647 doses along with downstream phenotypes were examined using multivariate data analysis. Associated phenotype changes to hepatocytes showed a correlation with high-dimensional multivariate genomic data - gene expression profiling data. The use of multivariate techniques like principal components analysis, factor analysis, and cluster analysis to analyze gene expression and phenotype data allows for more informed decision-making in toxicity testing.

Biography

James Gigrich is a PhD candidate at George Washington University. He has an MS in Operation Research from Georgia Institute of Technology and a BS in Electrical Engineering from West Point. He was an Associate Professor of Mathematics at the United States Military Academy and currently is the Senior Director of Government Relations and National Security Programs for Keysight Technologies, the legacy Hewlett-Packard Company and a world leader in measurement technologies.

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