

Simultaneous discovery of a gene network and the chemicals to which it reacts: Analysis of hepatocyte expression in the TG-GATEs database

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The Genomics Assisted Toxicity Evaluation system (GATEs) database contains gene expressions from rat hepatocyte cells as measured in 24 samples from 145 *in vitro* dose-response experiments conducted on mainly medicinal compounds currently on the market. Our goal is to see if, for some subpopulation of compounds, there is a coherent set of genes that apparently act in concert when exposed to any compound in this subpopulation. After reducing the gene pool to only those genes with clear dose response curves, we employ the tau-path test to detect association between pairs of genes, when this association is present over only some of the compounds. A graph was formed with nodes representing gene pairs having such association and edges connecting nodes with a common gene. Each edge is weighted by the Tanimoto measure of agreement between the corresponding sets of compounds. This revealed a strongly connected cluster of 26 gene-pairs all connected through the PCSK9 gene which forms a lead segment of many enzymes. Chemicals appearing frequently among the gene-pair subpopulations are analyzed for structural and functional similarities. This work with Rex Hu from Ohio State University, and Wayne Johnson and Glenn Myatt, from Myatt & Johnson, is partially supported through a grant from the NIH.

Biography

Joseph S. Verducci obtained his SB from MIT, his Ph.D. from Stanford, and he did post-doctoral work at Carnegie-Mellon. He is a fellow of the American Statistical Association and former Editor-in-Chief of the ASA journal Statistical Analysis and Data Mining. He is also a recipient of the ASA Statistics in Chemistry award. His current research involves methods of detecting subpopulations over which variables are associated.

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