TOXICOGENOMIC APPROACH TO PREDICTING ADVERSE DRUG RESPONSES

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Toxicogenomics can provide an understanding of the relationship between genetic variability and individual response to pharmaceutical agents. For many drugs, the existence of hypersensitive sub-populations is usually only discovered after the compound has been extensively prescribed and a population base of sufficient size has been exposed to the agent.

To show the feasibility of this approach for identifying individuals who will have an adverse response to a drug, hypersensitivity to penicillin was chosen as a model for the initial studies. It is estimated that up to 10% of patients who receive penicillin have an adverse reaction. Using differential display, gene expression patterns of sensitive versus normal individuals were used to detect novel genes that may be responsible for adverse drug reactions.

Over 200 candidate genes were differentially expressed between penicillin sensitive and resistant individuals. These genes fall into several functional categories including immune response, cell proliferation, apoptosis and energy regulation. Customized cDNA microarrays have been designed so that large populations of sensitive and non-sensitive individuals can be quickly screened and key candidate genes can be chosen for clinical risk cards.

These studies demonstrate the feasibility of this approach for the identification of candidate genes that may be used to predict adverse response to drugs.