Screening for Reactive Metabolites Using Genotoxicity Arrays and Enzyme/DNA Biocolloids

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1 INTRODUCTION

Therapeutic drugs and chemicals used in our bodies or in our environment must be guaranteed safe to the people who are exposed to them. Extensive procedures for screening and predicting toxicity have been developed in the pharmaceutical industry. Nevertheless, drugs that are toxic to some subset of the population are not always identified by these procedures. About 30% of drug development failures are linked to toxicity issues, and unfortunately some of these do not come to light until clinical trials or even after the drug is introduced to the market. In addition, drug costs correlate with drug development failures (Caldwell and Yan, 2006). For these reasons, predicting drug toxicity at the earliest stages of development has become a critical goal (Nasser, Kamel and Clarimont, 2004).

A wide variety of strategies have been proposed for early toxicity prediction, including *in silico* methods along with a range of *in vitro* and *in vivo* biological approaches (Nasser, Kamel and Clarimont, 2004; Mayne, Ku and Kennedy, 2006; Kramer, Sagartz and Morris, 2007). Established methods use microsomes, cell cultures, or animal models and tend toward utilization of biochemical end points that are the result of complex responses to the drug (Kramer, Sagartz and Morris, 2007). These methods are typically combined into a panel of methodologies that in many cases provide a reasonably good prediction of human *in vivo* toxicity (Mayne, Ku and Kennedy, 2006). Nonetheless, unpredicted or idiosyncratic drug toxicity can result from interindividual variations in human biochemistry and resulting drug behavior in specific individuals that may be impossible to predict from batteries of toxicity tests and sometimes even from human clinical trials limited to subsets of the population that will eventually use the drug.

Certainly existing toxicity testing and prediction methods are important, viable, and useful. However, there is an unfilled niche for simple, cheap, high-throughput,

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