

## DTEX™ GENE EXPRESSION ANALYSIS

It is well accepted that gene expression and activity of Phase I and II metabolic enzymes and drug transporters play a pivotal role in defining the ADME properties of xenobiotics. Drug discovery researchers typically rely on *in vitro* assays using hepatocytes, or other cells, to screen their compounds for undesirable metabolic and gene induction/suppression profiles. However, current methods do not take into account donor specific variability in basal or drug-related gene expression changes. In addition, commonly used activity based assays are limited to a small selection of enzymes and transporters, which may provide investigators an incomplete assessment from which to select drug candidates for further development. To address these concerns, NoAb BioDiscoveries has developed its DTEX™ Gene Expression Analysis solution.

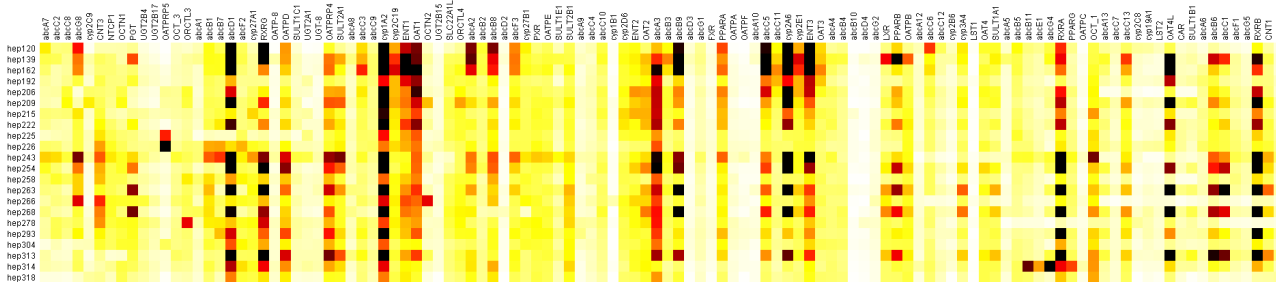
DTEX™ is a proprietary microarray-based technology that allows investigators to simultaneously survey the gene expression levels of over 140 ADME associated genes. Since all genes on the DTEX™ microarray are involved in drug metabolism, conjugation or transport, investigators can interrogate comprehensive basal level and drug-related ADME gene expression changes.

DTEX™ can help investigators answer the following questions:

### 1. Are my hepatocytes qualified for downstream studies?

Basal levels of DTEX™ gene expression vary substantially between different lots of primary hepatocytes. For downstream induction, inhibition or toxicity studies, it is important to use DTEX™ to qualify hepatocytes to ensure not only comparability between lots, but also that the optimal lots are used in evaluating drug treatment effects.

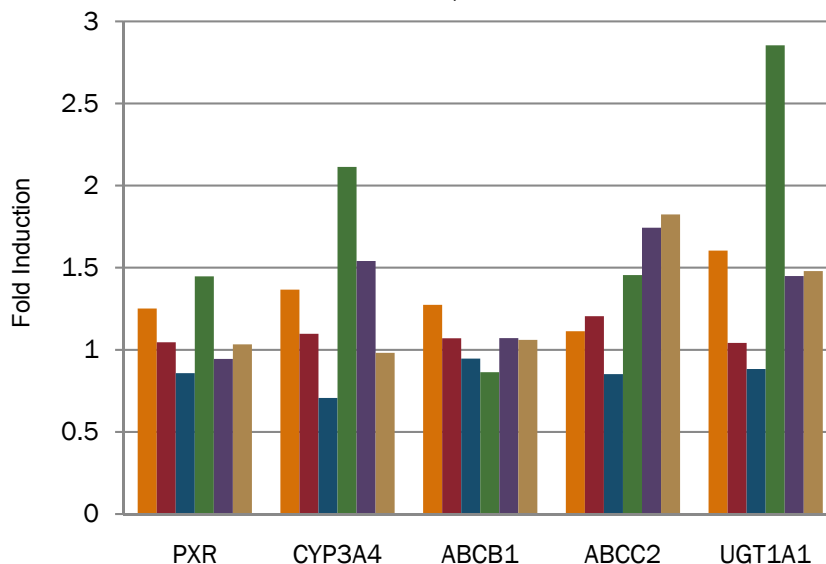
Figure 1. Relative levels of DTEX™ gene expression in 22 human hepatocyte samples [range 0-22x actin]



### 2. Does my drug show an undesirable ADME gene expression profile?

Figure 2. Coordinated induction of DTEX™ gene expression in rifampicin treated hepatocytes from six independent donors.

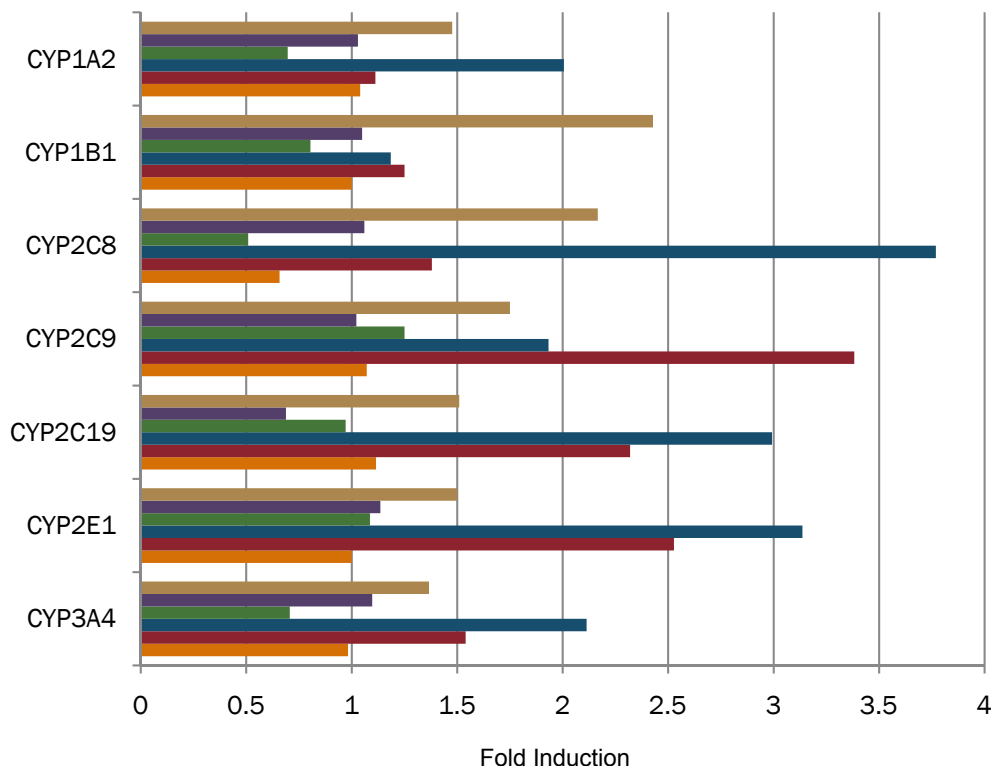
DTEX™ gene expression analysis confirms donor specific variations in drug-associated gene expression profiles. Genes on the DTEX™ array include all known members of co-regulated, drug metabolism, conjugation or transport pathways. In this way, DTEX™ gene expression analysis provides a comprehensive survey of potential drug-drug interaction concerns.



### 3. Do I have a reliable and complete CYP induction profile?

Drug associated induction of DTE<sup>x</sup>™ genes varies substantially between different lots of primary hepatocytes. When examining CYP induction of your compounds, it is crucial to use hepatocytes that are responsive and comparable. DTE<sup>x</sup>™ gene expression can be used to obtain reliable induction/suppression profiles for all key CYPs - including CYPs for which activity assays are commercially unavailable.

Figure 3. Induction of CYP gene expression in rifampicin treated hepatocytes from six independent donors.



### Experimental Procedure

In a typical experiment, investigators can choose to supply total RNA for DTE<sup>x</sup>™ gene expression analysis or they can select to have NoAb prepare, treat, and extract total RNA from a selection of cells, cell lines, or tissues. Samples are processed using the DTE<sup>x</sup>™ microarray, and a Summary Data Report consisting of normalized data, color matrix plots, hierarchical cluster plots, and fold induction tables is provided. Drug effects on selected genes can also be confirmed by QPCR.

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