PCR (10), differential screening and subtractive hybridization (11), differential display (12), SEREX (13) or Proteomics (14). In the SAGE approach, short sequence tags unique to each transcript are generated and concatamerized. Upon sequence analysis, approximately 25 or more independent tags can be identified from each sequencing lane while the expression intensity of a gene directly corresponds to the number of distinct tags counted.

"Genome-wide" expression pattern discovery aims at elucidating gene interactions, pathways, and recognition of gene groups acting in concert (15). For this purpose, high-density off-the-shelf arrays or customized arrays are available. In this instance, precise quantification of gene expression is of interest and therefore, glass- or silicon-based arrays are better suited.

For functional analysis of new genes, a limited group of genes are of interest, and one would like to obtain more information in different biological scenarios by testing the expression intensity in numerous biological samples. The exact expression level is of interest, thus low to medium glass-based arrays are the right choice.

Expression arrays used for drug validation, diagnostics, pharmacogenomics, or toxicogenomics can be envisaged in a two-step scenario. In a first step, when little is known about a disease, a drug, or toxicological endpoints, expression analysis with high-density arrays or an alternative method as described above with appropriate controls should be performed (8,16–18). This analysis leads to the recognition of a subset of genes which can be correlated with a disease, metabolic deregulation and/or intoxication, or with the effects/side-effects of a class of drugs. Although attractive, the genome-wide transcriptome analysis has, at present, several drawbacks: First, the immense cost associated with studying genome-wide expression is the major shortcoming of this approach, especially when dose and time studies are being investigated in parallel. It is therefore, not surprising that genome-wide expression studies are not conducted with the usual replicates of experimentation though standards for quality have been defined (see MIAME for further details). Second, data mining and analysis are difficult and complicated because a lot of redundant data can be generated with only 5–10% of randomly selected genes showing differential expression. Third, high-density arrays rely on EST libraries, which are not of best quality, and it is strongly recommended to corroborate the results by additional techniques.

5. CASE STUDY: ELUCIDATION OF TERATOGENIC MECHANISM(S) OF TOXICITY OF A DEVELOPMENTAL DRUG, EMD 82571

The drug EMD 57033 has been characterized as a calcium sensitiser and was developed to treat coronary heart disease. Calcium ions play a pivotal role in the control of the myocardial contractility, and a rise in contraction force can be elicited by either increasing the transient free Ca^{++} concentration and/or