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DNA microarray technology and integrative viral genomics ▼

Viral DNA microarray technology provides a new opportunity to identify and integrate host–drug interaction pathways. The identification of viral sequences (genotypes) and viral and cellular genes of which RNA levels change (phenotype) in an infection can provide key insights to viral replication strategies and potential drug interactions.

The first generation of a viral-DNA chip for genome wide expression measurements was reported for the human cytomegalovirus (hCMV) genome[1]. Subsequently, similar and different viral DNA microarray approaches have been applied to the global analysis of other viral systems[2–4]. It is noteworthy that the patterns (signature) of viral gene expression are influenced either directly or indirectly by expression of cellular proteins and, as a consequence, quantitative and qualitative differences in the profiles of viral gene expression vary depending on the host-cell background expression levels[3]. Accordingly, changes in cellular gene expression after infection add a further level of complexity to this host–pathogen dilemma (reviewed in Ref. 5). Therefore, a better understanding of how to inhibit a virus transcription–replication cycle can only be fully appreciated by future studies that aim to integrate host-cell gene expression with viral gene expression.

In current drug discovery programs, viral DNA microarray analysis of gene expression can provide a rapid confirmation for an anticipated mechanism of action for drug inhibition[1]. Such known viral expression profiles of drug inhibition can be used to identify and determine the mechanism of action of potential new lead drugs. Using microarrays for genotyping and the identification of drug resistance mutation(s) could further enhance this empirical approach. In the future, it might be possible to perform such experiments *in silico* using classification methodology of expression profiles from drug inhibition studies with those obtained from a database of gene expression profiles of virus mutants.

In addition to mutants generated in the laboratory, naturally occurring mutations in virus-infected patients have important implications for therapy and the outcome of clinical drug studies. Thus, viral genotyping methods for detecting the prevalence of drug-resistance mutations, or virulent strains or isolates from patients are of high priority. In the past few years, a wide variety of different microarray technology platforms have been applied to viral genotyping. These include DNA microarrays for HIV, hepatitis C virus, poliovirus and influenza viruses[6]. Moreover, a global diagnostic microarray approach is likely to disclose many key clinical features that could help to tailor drug regimes. Potentially, integrative microarray viral databases could dramatically enhance the comparative analysis of antiviral strategies and might help to identify pan-active and specific antiviral drugs.

Clearly, an integrative approach combining viral and host DNA microarrays is required for a more rigorous pharmacogenomics approach to viral biology and the development of anti-infectives. In the future it is conceivable that this might well become a standard not only in the discovery of antiviral drugs, but might also have a role in choosing treatment options for infectious diseases.

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