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Gene expression following HIV-1 infection

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Paul Kellam

Abstract

The use of cDNA arrays has allowed monitoring of the change in expression of host cell genes during HIV-1 infection.

Significance and context

Global analysis of changes in mRNA levels provides a catalog of genes that are modulated as a result of a biological process. Such analysis, using cDNA microarrays, has recently been applied to the study of host gene responses to virus infection. It is hoped that by undertaking such studies certain pathways will be identified as having critical roles during viral infections.The investigation described by Geiss *et al.* is the first viral study to describe such an analysis using cDNA arrays deposited onto glass slides, and demonstrates the use of such arrays in host-pathogen interaction studies, opening the way for other laboratories to use similar glass- or membrane-based filters to study other viruses. A previous study of host-cell gene expression in response to a virus infection was reported but used Affymetrix array chips. The authors also describe in some detail the methods used for image processing, data normalization and error analysis. Custom software was developed for this quantitative analysis. As the authors describe, with the growing use of array technology it is important that a focus of the data analysis should be to generate both expression ratios and estimates of the uncertainties in these ratios.

Key results

Geiss *et al.* show that in the first three days following infection by HIV, 20 cellular genes were differentially expressed out of a total of 1,500 studied. Changes in gene expression were confirmed by northern blot analysis for a selected set of genes. The 20 cellular mRNAs were from a variety of pathways. The authors comment that some of the genes identified may have a role in host-cell defense mechanisms and/or facilitation of the viral life cycle.

Methodological innovations

The use of cDNA microarrays is beginning to affect most biological disciplines. Although no large improvements in methods are reported relative to previous array papers, the authors point out the differing efficiency of incorporation of the two fluorescently labeled nucleotides, Cy3 (green) and Cy5 (red), during cDNA synthesis. This discrepancy had to be accounted for in the authors' new normalization and data analysis methods.

Conclusions

The authors conclude that by examining the effect of HIV-1 infection on different cell types, utilizing different strains of HIV-1, and using larger sets of human genes, further insights will be gained regarding the complex biology of HIV infection and AIDS.

Reporter's comments

Research into host-pathogen interactions has determined many critical components of the cellular environment that a virus must destroy, modulate or usurp in order for the virus to complete its replicative life cycle. This paper represents the first use of relatively affordable microarray technology to probe the global changes in host gene expression during virus replication. The authors also pay significant attention to data analysis and standardization. This will be essential for future cross-comparison of the effect on host gene expression of infection with different viruses or other pathogens. Studies of this type have the potential to produce a global view of the cell-based mechanisms involved in cellular responses to the myriad infectious agents to which humans and other animals are constantly exposed.

Table of links

Virology

References

1. Geiss GK, Bumgarner RE, An MC, Agy MB, Wout AB van't, Hammersmark E, Carter VS, Upchurch D, Mullins JI, Katze MG: Large scale monitoring of host cell gene expression during HIV-1 infection using cDNA microarrays. Virology. 2000, 266: 8-16. 0042-6822