

Chapter XLVI

Basic Principles and Applications of Microarrays in Medicine

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ABSTRACT

The simultaneous expression of a large number of genes is a critical component of normal growth and development, and the maintenance of health. Microarray technology is used to understand fundamental aspects of growth and development, as well as to explore the underlying genetic causes of many human diseases. Systematic analysis of microarray data will yield insight into molecular biological processes and the functions of thousands of gene products in parallel. This approach allows for better understanding in cellular signaling, disease classification, diagnosis, and prognosis. Microarrays allow scientists to analyze the expression of many genes in a single experiment quickly and efficiently. One important goal of computational analysis of microarrays is to extract clues from microarray data and translate the information into biological understanding diseases in medicine and dentistry. There are different platforms or types of DNA microarrays that are commercially available: Glass DNA microarrays and high-density oligonucleotide microarrays. DNA microarray experiments generate large quantities of genome-wide data. To extract useful information from expression profiles, computational tools that compute, statistically validate and display data can be used. An important step in the computation of microarray data is normalization. The purpose of the normalization process is to identify and remove the effects of systematic variation in the measured fluorescence intensities other than differential expressions. There are different methods for the normalization of data: total intensity normalization, regression normalization, normalization using ratio statistics, and variance stabilization (VSN). A major goal of microarray data analysis is to identify differentially expressed genes. Selecting marker genes is an important issue for disease classification based on gene expression data.

The selection of marker genes is critical in tumor classification using gene expression data. Many methods have been proposed to select differentially expressed genes, including parametric and nonparametric tests, and others.

INTRODUCTION

The proper and harmonious expression of a large number of genes is a critical component of normal growth and development, and the maintenance of proper health. Disruptions or changes in gene expression are responsible for many diseases.

Biomedical research evolves and advances not only through the compilation of knowledge, but also through the development of new technologies. Using traditional methods to assay gene expression, researchers were able to survey a relatively small number of genes at a time. The emergence of new tools enables researchers to address previously intractable problems and to uncover novel potential targets for therapies. Microarrays allow scientists to analyze the expression of many genes in a single experiment quickly and efficiently. They represent a major methodological advance and illustrate how the advent of new technologies provides powerful tools for researchers. Scientists are using microarray technology to try to understand fundamental aspects of growth and development, as well as to explore the underlying genetic causes of many human diseases.

Since many genes contribute to normal functioning, research efforts are moving from the search for a disease-specific gene to the understanding of the biochemical and molecular functioning of a variety of genes and how complicated networks of interaction can lead to a disease state, such as oral cancer. With the DNA (deoxyribonucleic acid) microarray-based research, we can look forward to more accu-

rate diagnosis, surgical treatment, and drug-delivery therapy based on an individual patient's genetic profile.

DNA microarray technology has been used for genome-wide gene-expression studies that incorporate molecular-genetics and computer-science skills on massive levels. This technology allows comparisons of gene-expression levels in samples derived from normal and diseased tissues, treated and nontreated tissues, and tissues in different stages of differentiation or development. It uses nucleic-acid hybridization techniques and computers to evaluate the mRNA (messenger ribonucleic acid) expression profile of thousands of genes simultaneously for the purposes of gene discovery, disease diagnosis, improved drug development, and therapeutics tailored to specific disease processes.

DNA microarrays are miniature arrays containing gene fragments that are either synthesized directly onto or spotted onto glass or other substrates. Each spot serves as a highly specific and sensitive detector of the corresponding mRNA. Further computational analysis of microarray data allows the classification of genes by their mRNA expression patterns. Global gene-expression profiles in cells or tissues will provide us with a better understanding of the molecular basis of a phenotype, pathology, or treatment.

Furthermore, there exists an increasing number of applications for protein and antibody microarrays (Feilner et al., 2004) in basic research diagnostics, drug discovery, and in vitro risk assessment of nutrients.

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