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Review

# Discovering causes and cures for cancer from gene expression analysis

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**Abstract**

Tumorigenesis is governed by a series of complex genetic and epigenetic changes. Both mechanisms can result in either the silencing or aberrant expression of messages in a cell. Gene expression profiling techniques such as the serial analysis of gene expression (SAGE) or microarray analysis can provide global overviews of these changes, as well identify key genes and pathways involved in this process. This review outlines the current roles of these techniques in cancer research, and how they may contribute to finding not only mechanisms of this disease, but potential targets for therapy.
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*Keywords:* Gene expression profiling; Cancer; SAGE; Microarray

## 1. Introduction

With the exception of a few cancers such as childhood leukemia and testicular cancer, cancer is very much a disease of aging. The incidence of cancers such as prostate, breast, ovarian and melanoma show a sharp increase in onset in older adults. This observed increase in incidence is due to factors such as decreased efficiency in cellular mechanisms (e.g., changes in telomerase activity), hormonal changes, accumulated damage (e.g., excessive sun exposure, smoking) and age-related declines in immune function (reviewed in Beghe and Balducci, 2005). In a population where longevity is ever increasing, cancer incidence will continue to rise, and thus, understanding the molecular mechanisms that underlie this disease is of great importance.

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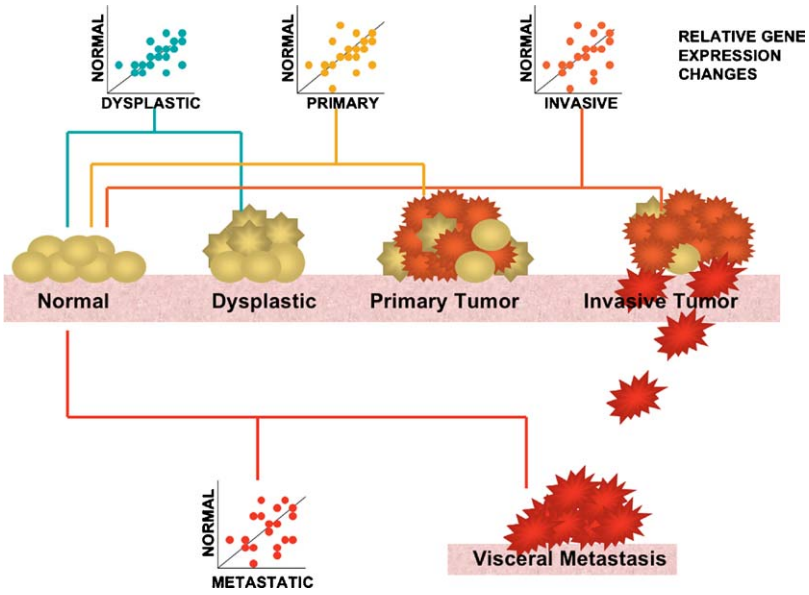


Fig. 1. As a tumor progresses for normal growth to increasingly dysplastic and malignant stages, it undergoes a host of genetic changes. These changes can be accurately profiled by microarray and SAGE technologies.

Microarray studies have provided an avenue for an in depth analysis of global changes in gene expression and cancer research has been the main arena for these types of experiments. The development of additional gene expression profiling techniques such as serial analysis of gene expression (SAGE) have also largely dealt with the analysis of tumor biology as cancer development and progression is dependent on a series of genetic changes, making it an ideal format for these types of studies. As a general rule, cancers begin as a few altered cells in a normal population leading to a dysplastic phenotype. These dysplastic cells undergo further changes to become malignant, and each malignancy is a heterogeneous population of tumor, normal and dysplastic cells. Thus, the gene expression profiles of normal cells, as compared to tumors across the spectrum of progression, become increasingly dissimilar. This progression is represented schematically in Fig. 1. In this review, we will outline the lessons learned from these gene expression profiling studies, as pertains to the classification of tumors, prediction of outcome, treatment response and potential markers and targets for diagnosis and therapy.

## 2. Marker/pathway identification

Currently, microarray analysis is the gene expression profiling technique that has the most expansive set of analytical tools. Because of this comprehensive cohort of statistical analyses, large experiments can be easily examined to provide important clues about tumor progression and outcome, and treatment response. These analyses may be divided into two major types—pattern discovery and pattern prediction. Pattern discovery provides a global