Future

The isolation of new genes, the rapid detection of unknown mutations in human DNA, and the identification of differences between genomes require the continued development of many of the techniques mentioned in this chapter (genomic mismatch scanning, differential expression of mRNAs, representational difference analysis, *etc.*). It is clear, however, that the precise nature and location of a mutation must ultimately be defined by DNA sequencing and functional analysis. Many different strategies are being developed to make direct sequencing of DNA from the amplified PCR product rapid, accurate, and efficient. These automated methods for sequencing use fluorescence detection technology. Although they are expensive, they represent the "ideal" mutation scanning technique.

The pace of improvements in gene isolation and mutation detection techniques has been extremely rapid over the past few years. Many promising advances are being tested in many laboratories and within the human genome project. A rapid, accurate, sensitive, and inexpensive method of direct sequencing from the amplified PCR product will be the ultimate in automated mutation analysis. The refinement of this direct sequencing technique will be upon us in a short time, and will be the catapult for more widespread preclinical DNA diagnosis.

It is equally important to bear in mind that these new evolving techniques are helping us to understand the biochemical basis for disease and the etiology of fundamental developmental aberrations. The applications of these techniques to clinical medicine will change the way that medicine is practiced in the future. Diagnosis will become pre-symptomatic. At the present time, the clinical sciences are largely an inferential science in which one reasons from a phenotype to a genotype. In the future, physicians will have to identify individuals who are at risk for specific diseases and suggest DNA analysis. Some of us may have pre-neoplastic or pre-cardiac genotypes and appropriate measures need to be put in place to limit the expressor of these deleterious genes. Obviously there is still a large hiatus between diagnosis and therapy. As the second generation of biotech products develops, one will see techniques and maneuvers such as anti-sense technology that are developed to control the expression of inappropriate genes. These techniques include blocking the genetic code using novel classes of molecules to block receptors, and designing organic molecules to interfere with signaling pathways. The importance of animal models for disease created by altering specific genes and the importance of animal models for testing gene therapy cannot be overestimated.[13] Overall we can look forward to an exciting decade which will bring about revolutions in our conceptual knowledge of biology and provide us with unifying principles to compare and analyze the evolution of species.

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