

## Genetics

ONE OF THE MOST SIGNIFICANT medical developments in the past five years has been the completion of the Human Genome Project (HGP). The first draft of the human DNA sequence is now available. The discovery of new genes for a range of human genetic disorders, as well as genes for normal traits, will have far-reaching effects on diagnosis, treatment and prevention.<sup>1</sup>

**Genetic (DNA) diagnosis.** Diagnostic DNA tests are now available for a limited number of genetic disorders. In Australia, these tests are usually accessed through clinical genetics services (listed along with available tests on the website of the Human Genetics Society of Australasia<sup>2</sup>). Emerging technologies, such as gene chips, have the potential to allow analysis of large numbers of genes, as well as thousands of mutations in each of these genes. Thus, the scope for DNA testing will expand. Developments in nanotechnology will lead to miniaturisation of DNA testing, allowing doctors to obtain genetic information at the point-of-care in a way comparable to a "dipstick" urine test. This individualisation of medical practice will be particularly valuable in determining drug doses, and identifying those at risk of drug side effects.<sup>3</sup>

As the HGP will continue to generate large volumes of data, more sophisticated bioinformatic approaches will be essential. In addition, the increasing complexity of counselling issues related to genetic disorders will require doctors and patients to develop new ways of interacting in terms of how doctors provide information. Computer-based resources will be needed to meet the demand for more knowledge, which may be complex in nature for both doctors and patients. There will be increasing reliance on a team approach for managing genetic diseases.

The increased opportunities for DNA analysis are also generating disquiet, because of the implications for privacy and confidentiality, and the potential for discrimination in employment and insurance. Continuing professional and community education is crucial to ensure that DNA testing proceeds appropriately. A challenge will be population DNA screening, which should be undertaken only after evidence-based research shows a clear cost-benefit analysis. Immediate debate is needed on the place of population screening for the mutations responsible for haemochromatosis and cystic fibrosis.

**Genetic interventions.** Somatic-cell gene therapy (the insertion of DNA or RNA into the somatic cells of humans) was first undertaken in 1990 to treat adenosine deaminase deficiency, a rare genetic disorder. Today, the scope for

gene therapy has broadened, and it is being developed as an alternative treatment for cancer and HIV infection. Despite many clinical trials, it has taken a decade for gene therapy to succeed. In 2000, the first report emerged showing potential cures in X1 severe combined immunodeficiency disorder, a rare genetic defect that is usually fatal within the first two years of life. Five children have been treated, with four being able to return home and lead normal lives.<sup>4</sup> Promising results are now coming from gene therapy for haemophilia.

**Disease prevention.** DNA analysis can also be used for predictive (also called presymptomatic) testing for adult-onset disorders, such as Huntington's disease, genetic forms of colon and breast cancer and, more recently, haemochromatosis. Predictive testing allows DNA mutations to be identified before signs and symptoms develop. In genetic disorders with specific therapies (eg, haemochromatosis), this provides the opportunity to treat early and so prevent complications.

The above disorders involve single gene defects or inheritance patterns that are easily defined. Increasingly, predictive testing will be directed at more common but complex disorders with multifactorial inheritance (ie, disorders that result from the interaction of genetic and environmental factors<sup>5</sup>). For example, Alzheimer's disease occurs in both genetic and sporadic forms. The DNA marker *ApoE4* is strongly associated with early-onset disease. However, although this marker is a risk factor, the pathway by which it increases risk is not yet defined. Further understanding of the pathogenesis of Alzheimer's disease, which will become possible once genetic abnormalities in this condition are fully understood, will allow proactive steps to prevent disease onset or progression (eg, removing or avoiding environmental toxins, and specific therapies directed towards DNA-based abnormalities).

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