Book Review

Molecular Diagnostics

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Our understanding of the function of human DNA, known as the human genome, is steadily progressing. Cytogenetic methods have been in clinical use since the 1960s, and molecular tests for almost 2,500 rare monogenic disorders since the 1980s. Recently, genetic testing has also become an important tool in studies of familial cancer predisposition, where the numbers of those benefiting from testing are large compared with tests for rare diseases. In the near future, genetic testing may have an increasing role in determining risks for other common genetic diseases—such as cardiovascular diseases and common multifactorial diseases—and in pharmacogenetics.

Genetic testing/screening makes use of a variety of technologies to identify inherited or acquired modifications in the genetic information of an individual. The technologies used can be cytogenetic, as well as biochemical and immunochemical, to verify the composition of DNA, RNA, proteins, carbohydrates and lipids.

The result of this testing can yield different types of information, such as: (1) confirmation or exclusion of the diagnosis of a specific disease; (2) the magnitude of the risk, or its absence, of developing a disease or reacting adversely to drugs and environmental factors; (3) the magnitude of the risk of biological descendants inheriting a defect.

The tests can be performed on individuals, or on nuclear or extended families. The term 'screening' is usually reserved for the systematic testing of the members of defined populations or high-risk population subgroups for one or more inherited modifications of the genome. As the technology improves and its cost decreases, the genome of individuals may also be screened for a series of related or unrelated inherited variants. Since the composition of the chromosomes and the DNA of an individual are fixed at fertilisation, most tests can be done at any stage of life, either before or after birth (pre-implantation diagnosis, all forms of prenatal diagnosis and neonatal and adult testing). In most genetics centres, the testing of children will be strictly limited to those cases in which a diagnosis is important for management or therapy.

As a result, the possibilities for testing and screening for the genes involved in inherited diseases or susceptibility to diseases have increased spectacularly. In addition, modulators of gene expression — other genes, non-coding DNA sequences, proteins involved in the three-dimensional organisation of DNA and acquired (epigenetic) modifications of DNA — are being identified. This has led to the surprising realisation that even environmental factors, such as food components, might modify DNA function fairly dramatically. This means that most simple tests, as done today, will have to be complemented with tests allowing more precise predictions of the risks, of the progression and of the clinical characteristics of diseases.

High-throughput DNA sequencing has also opened up a series of new approaches to the identification of individual characteristics, which may be relevant for determining the risks of developing diseases or of showing variation in the rate at which we metabolise drugs. Indeed, our DNA contains some distinct individual variation in its composition. Testing for predispositions to particular diseases and pharmacogenetic testing have potential for the future, although much research will still be needed before these approaches can be routinely implemented in practice. For example, despite the recent rush of offers from commercial companies, the comprehensive €1000 genome sequence is not an immediate prospect.

Analysis of individual variants also allows the identification of biological traces collected at crime scenes with great accuracy. Application of this knowledge in forensic cases and in studies of biological descent has become routine.

It is clear that we are only at the beginning of our understanding of the function of all the DNA fragments, but there are already many examples of how DNA analysis can contribute in medicine and in many other fields.

This second edition of the book *Molecular Diagnostics* provides an excellent overview of the techniques that are available today for molecular research and diagnosis of inherited or acquired diseases. With an impressive

number of experts in the field, the editors provide in two sections a comprehensive yet broad overview of the different technologies, including the newer sequencing techniques. Each chapter contains a good description of the context in which the technology can be applied and ends mostly with nuanced recommendations on the precise use of the technology for a particular problem. While some chapters even provide detailed procedures (eg Chapter 3 on enzymatic cleavage), others give excellent references to detailed procedures and compare different methods or products used therein.

The chapters are well illustrated but, for understandable economic reasons, the figures are only presented in grey shades. This is regrettable, in particular for the drawings that require colour—such as in the cytogenetic chapters, where there are examples of fluorescence in situ hybridisation (FISH) results. Coloured illustrations can nevertheless be found in the e-book, but, of course, this must be purchased separately.

Some chapters contain overlaps — for example, those pertaining to the use of microarrays. This is understandable and is not necessarily a shortcoming. Indeed, each chapter has different authors and a different focus. A different application of the same or similar technology is therefore acceptable, presenting a broader view on the advantages and shortcomings of the different technologies.

The splitting of the book into two sections is a bit odd. Section 2 pertains to 'applications of molecular diagnostics and related issues'. This appears to be a way of including everything related to diagnosis without being pure technology in the book. Some of the chapters in this section do not really differ from those of Section 1; others, while of excellent quality as single papers, are actually unable to cover all aspects of the topic — for example, the chapters on patents, on counselling, on quality issues and on safety. It would have been better to put these into a third section under the heading 'related issues'. Also, somewhat surprisingly, since two chapters in Section 2 are devoted to the applications in forensics — not really a clinical diagnostic issue — there is no chapter on genealogical applications of the technology. Of course, a single book cannot cover all issues in detail and this certainly does not decrease the value of the book as a good reference work.

There is a glossary at the end of the book, which gives good definitions of the most important terms used in the book.

While this book will, without doubt, replicate the success of the first edition, it will probably need a third edition in the coming years, since the technology continues to change dramatically and many students will soon not understand why we are still talking about technologies that are no longer used. This is all the more reason to look forward to the advent of the next edition. This is also the case for the references, which generally only go up to 2008, as a result of the need to get the book ready for publication by the end of 2009. Nevertheless, students, as well as expert investigators, will benefit from this edition, since it forms one of the most comprehensive sources for clear and complete explanations of most, if not all, technologies currently available for diagnosis. It should therefore find its place in the library of any research or molecular diagnostic laboratory.

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