BOOK REVIEWS

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Recent scientific advances have shown conclusively that damage to cellular DNA is the initial event in many types of human cancer. The ability of cells to repair such damage represents a major form of protection against carcinogenesis. In the DNA repair syndromes, a genetic deficiency in a DNA repair process results in extreme cancer proneness. Long standing examples are xero-derma pigmentosum and ataxia telangiec-tasia. More recently, hereditary non-polyposis colon carcinoma (HNPCC) has been shown to be associated with defective repair of DNA mismatches. An important biological consequence of unrepaired or incorrectly repaired DNA damage is the generation of mutations. Somatic mutations in oncogenes or tumour suppressor genes are critical steps in the progression of carcinogenesis. Germline mutations are the basis of genetic disease. In the field of human molecular genetics, as the genes underlying more and more genetic disorders are discovered, the need to identify disease mutations for the purposes of diagnosis, prognosis, and understanding of the disorders is mushrooming. Technologies for the Detection of DNA Damage and Mutation is in three parts, which will be of interest to three quite disparate groups of researchers. The first part, on detection of DNA damage, covers a range of highly specialised techniques for measuring different types of DNA damage and their repair. Up until 10 years ago, DNA repair methodology was relatively crude, the techniques available being capable of assessing overall levels of damage and repair in populations of cultured cells. Techniques developed more recently have added much greater sensitivity and specificity. Single cell microgel electrophoresis (more commonly known as the comet assay), described by Singh, is a technique for measuring levels of damage in individual cells. Antibodies generated against different types of damage, such as that produced by UV light (Mitchell), alkylating agents (Thomale et al), and oxidative damage (Melamade et al), have increased the sensitivities of assays and enabled different types of damage produced by complex carcinogens to be measured.

A major advance in the mid-eighties was the development of procedures to measure repair in individual genes. These procedures are described in two chapters by the scientists who devised the techniques (Bohr, and Smith and Hanawalt). A further refinement was devised recently by Pfeifer (the editor of this volume) and Holmquist, who developed methods for measuring repair right down to the level of individual genes. The level of this detail for the first time allows a consideration of the diversity of techniques describe variations on this technique. This collection of up to date repair methodologies will be extremely valuable for advanced research, and as the field of DNA repair, but it is likely to be too specialised to be of much interest to medical geneticists. In contrast, part II describes technologies for the detection of mutations, of central importance to modern medical genetics. A variety of techniques has been developed over the last few years, all of them using variations of amplification of the target gene using the polymerase chain reaction (PCR), followed by some kind of electrophoretic separation to distinguish mutant from normal DNA. Each author is naturally a strong proponent for his own chosen technique, and all the methods (for example, denaturing gradient gel electrophoresis, single stranded conformation polymorphisms, protein truncation test) are described in detail. It would have been useful to have had an overview of the pros and cons of each technique. For the relative novice, a crucial question is the selection of the most appropriate technique to use for the problem being addressed.

Despite the similarity of the title of part III, on mammalian systems for mutation analysis, to that of part II, detection of mutations, this part actually add much different questions and they are of interest to different groups of researchers. The procedures described in part III are used (1) to investigate the mechanisms of mutagenesis in mammalian cells, and (2) in the area of genetic toxicology to determine the mutagenicity of environmental chemicals. The systems used most widely are in cultured cells, namely the p518 shuttle vector and the hprt gene, are described by Seidman and by Maher and McCormick. A shortcoming of cultured cell systems for measuring mutations is that they cannot take account of the incorporation in the mammalian genome of some mutagens. In order to overcome this problem, bacterial genes (lacZ or lacI) have been integrated into mouse genomes. Following exposure of these transgenic mice to mutagenic chemicals, genotypes can be recovered from the mouse genomes from different tissues, and the mutations can be analysed by conventional bacterial molecular genetic techniques. The two systems that have been developed are described by Vlij and Douglas and by de Boer et al. These transgenic mouse systems have only been developed recently, and like all new techniques, they have a number of shortcomings, which are addressed by de Boer et al, together with future prospects and possible developments.

Despite the diverse specialists to whom the three parts of the book are likely to appeal, it is crucial that the book will be the single comprehensive source of the latest complex techniques, and will be of considerable value to many researchers. Most of the chapters are carefully written with theoretical backgrounds, detailed experimental protocols, and, in some cases, invaluable sections on limitations, pitfalls, and troubleshooting. It should find its way onto the shelves of many research laboratories.

A R LEHMANN


This is the sort of book which gets geneticists a bad name. Put briefly, its thesis is easy to state: the sad, mad, bad, and the stupid are spreading the respectable, college educated, middle classes.

The cause is education. Even more clever kids are getting to university where their studies distract their minds from sex (or at least reproduction) whereas the stupid start spreading their genes at a much younger age. Thus, modern society inadvertently selects for the genes associated with stupidity, sadness, badness, and madness. These genes are spreading through the population, explaining the increase in crime, alcoholism, schizophrenia, attention deficit disorder, autism, and so on. This is the "gene bomb" of the title.

We are so lucky that Dr David Comings, a former president of the American Society of Human Genetics and former editor of the American Journal of Human Genetics, was keen enough to detect this genetic epidemic, for otherwise it "could occur so gradually as to go unnoticed until it was too late to correct. However, its eventual effect on the human race could be far more disastrous than the microbial epidemic, "simultaneously increasing the possibility that the IQ of the human race is beginning to turn a corner and evolve backwards to lower levels strikes a raw nerve." Not with me: laughter would seem the most appropriate response.

Let us have a reality check. In Britain today, a higher proportion of the population than ever before benefits from university or other forms of tertiary education; general literacy is higher than it was at the end of the 19th; and a substantial proportion of the young people of the country are adept users of one of the most heralded of genetic products of human genius, the home computer.

We might worry that computer literacy is damaging traditional literacy, but that is nothing new. George Orwell complained in one of his essays that in the 1930s an entire generation was growing up intimately familiar with the workings of the magneto but ignorant of the Bible. It is boring and it is obvious, although apparently not to Dr Comings, that none of these things is consistent with a decline in IQ.

Some of his facts are simply wrong. He asserts, based on the evolutionary divide between humans and other primates, that "higher IQ appeared to require over 100 000 years to evolve." Yet our divergence from the other primates can be dated at least as far back as the cretaceous, nearly two million years ago. Homo erectus was so unintelligent it did not have language, but the point is that the period over which higher IQ developed is arguably 20 times longer than Dr Comings suggests. Consequently we should ask for evidence of declining IQ over a time scale somewhat longer than the half century since the end of the Second World War.
