

Application of biological markers to carcinogen testing. Environmental Science Research Volume 29. H. A. Milman and S. Sell (eds). Plenum Press. 1983. Pp. xi + 516. Price \$69.50 (US).

This book presents the proceedings of a symposium on the "Application of Biological Markers to Carcinogen Testing" held in Bethesda, Maryland, USA in November 1982. In some ways the title is misleading as the majority of investigations presented are concerned with the nature of neoplastic processes rather than the detection of novel carcinogens. This is partly conceded in the Chairman's introduction to the round table discussion summarising the proceedings.

The book is divided into eight main parts covering *in vivo* tests; *in vitro* tests; oncofetal antigens and hormones; monoclonal antibodies; carcinogen-induced modification in DNA; viruses and finally a general poster session. Each topic is preceded by a Chairman's overview to set the scene.

The *in vivo* section includes aspects of liver, pancreatic and intestinal tumour identification, development and frequency. These set the tone for many of the later papers with the message that individual biological markers tend to be unreliable. However a combination of changes in cell and tissue architecture with histochemical, antigenic and other markers can yield useful qualitative and quantitative information related to neoplasia. There are also timely warnings in this section concerning reliance on species-specific changes in tumour incidence in cancer bioassays and the effect of diet on background tumour incidence.

The *in vitro* section contains papers on the response of primary cultures of rat hepatocytes to 2-acetylaminofluorene; a new assay measuring *in vitro* transformation of diploid human fibroblasts; the identification of genotoxic and epigenetic carcinogens and an evaluation of chronic rodent bioassays and Ames assays as models for predicting human carcinogens. The latter paper states (reviewers additions in brackets) the interesting conclusion that "combined with either rodent (rat or mouse) bioassay or with one or two other *in vitro* tests, the technique (Ames test) is equivalent to or more reliable than the combined mouse/rat model in predicting human carcinogens".

The section on enzymes covers both changes in the levels of various marker enzymes and changes in isozyme profiles occurring in neoplastic tissues. These papers demonstrate that altered levels of some enzymes occur in tumours, dependent on the tissue of origin and degree of malignancy. More distinctive are alterations in isozyme patterns where sometimes a reversion to a fetal pattern is observed.

An interesting oncofetal antigens and hormones section contains papers on alphafetoprotein and hepatic carcinomas; prostaglandins and cancer and changes in human chorionic gonadotropin (hCG) blood levels associated with gestational trophoblastic tumours and germinal tumours of the testis. By measuring differential blood: cerebrospinal fluid ratios of hCG can help to

pinpoint the site of primary tumours or ascertain whether CNS metastases are present.

The section concerned with monoclonal antibodies and immunoanalytical methods is perhaps the most exciting part of the book in terms of potential impact. There are chapters on the detection of thymine dimers; the influence of chromatin structure on the binding of the metabolites of benzo(a)pyrene; and use of antibodies directed against DNA modified by alkylating N-nitroso compounds. The chromatin structure work is particularly elegant and includes a cautious appraisal of the visualisation of the sites of adducts in polytene chromosomes from the salivary glands of *Chironomus thummi* larvae.

Among the potential uses of monoclonal antibodies raised to carcinogen modified DNA are; i) the detection of low levels (subthreshold?) of carcinogen-DNA adducts ii) the rate of change of numbers of adducts with time iii) the measurement of the effects of cellular differences in DNA repair and/or metabolic capability iv) the identification of individuals at particular risk v) prediction of individual responses to chemotherapy.

The section on carcinogen-induced modification in DNA includes work on the use of hypersensitive and repair deficient mammalian cell lines for the identification of carcinogens; detection of radiation induced thymine derivatives in cellular DNA; aberrant methylation of DNA as an effect of cytotoxic agents and the identification of carcinogen-DNA adducts by immunoassays. The paper concerning methylation includes the discussion of the hypothesis that some carcinogens could act by stimulating S-adenosylmethionine dependent methylation of DNA leading to cyto-toxicity and extra replication of damaged cells, i.e. lack of DNA adduct formation may not mean lack of DNA damage.

The Chairman's overview to the virus section is in the form of a presentation on the integration and expression of the polyoma virus oncogenes in transformed cells. Also contained in this section is a presentation on the activation of cellular *onc* (c-*onc*) genes. These papers are now somewhat historical as so much work has been done in these areas since 1982. The final paper is concerned with the Hepatitis B virus as an environmental carcinogen.

The general presentation of the book is clear but reflective glossy pages and microscopic print on some of the figure and table legends create some difficulties for the reader.

There is a wealth of information and ideas in this volume from experts in a variety of fields. Although many details are out of date, both the specialist and student of cancer research will benefit from access to this book to expand knowledge of unfamiliar but relevant topics and to gain insight into possible new directions to explore.

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