DNA REPAIR AND TUMOUR RESISTANCE

WORKSHOP HELD AT THE PATERSON LABORATORIES, CHRISTIE HOSPITAL, MANCHESTER, ON 11 FEBRUARY 1974

Convenor: B. W. Fox

DNA repair phenomena have been shown to be involved in the development of drug resistance by studies in the methylene dimethanesulphonate sensitive, and resistant lines of the Yoshida rat sarcoma in vitro. A wide variety of techniques are needed to study the various steps of the known repair mechanisms in mammalian cells and these were discussed in detail. The breakage and rejoining of mammalian cell DNA after exposure to drugs and ionizing radiation is monitored by the use of alkaline sucrose gradient sedimentation techniques as first described by McGrath and Williams (1966). Dr B. W. Fox discussed the principles of this technique and that of the constant velocity sedimentation method of Noll currently used in this laboratory. Problems in interpretation of data and possible artifacts of the technique were also described. During repair of DNA strand breaks, mammalian cells insert bases into non-replicating DNA strands by repair replication. The technique for examining this process involves the use of 5-bromodeoxyuridine or 5-iododeoxyuridine in a heavy labelling technique for studying DNA followed by centrifugation in CsCl gradients. Dr A. R. Lehman then described the techniques and problems involved in detecting and monitoring post-replication repair, another known repair process in mammalian cells and the fact that it can be inhibited by caffeine and its analogues in contrast to repair replication.

Following some discussion of the details of the technique itself, Dr D. Scott described the methods employed in the assessment of chromosome damage and its repair. The importance of such determinations is clear if a correlation between the damage to the DNA strand and survival data is to be established. So far, the correlation between the extent of chromosome damage in sensitive and resistant cell lines, and cellular sensitivity as determined by survival curves, is good.

The morning session was completed by a short account of the methods of detection of mutagenic action in somatic mammalian cells, this being a potential assay for the effectiveness of repair. The markers available for mammalian cells were listed and a typical example of the experimental schedule for suspension cells employed was described. In the afternoon, demonstrations were set up for the participants in three of the laboratories. Members were able to see the equipment employed and also to discuss the finer technical points with regard to procedure, sources of materials etc., which are often difficult to obtain. Demonstrations included the linear and constant velocity alkaline sucrose gradient techniques including different methods of gradient manufacture and fractionation, the caesium chloride centrifugation technique, and a discussion on the parameters which affect the gradient structure. A method of detection of radiation sensitive mutants in bacteria was described using a stepped exposure to radiation of a patch of cells. The technique of demonstrating host cell reactivation using phage plaques was described by Dr J. M. Boyle as well as the estimation of dimers and their excision from DNA.

The techniques of chromosome spreading and autoradiography were also shown, together with the basic techniques of soft agar culture of colonies and the identification of mutants.

The first workshop, being in the nature of an experiment, brought out several important points on their future organization and conduct, and it is hoped that using this
information, these workshops can become a useful way of communicating details of technique which would otherwise be both inhibiting and delaying to potential workers in the field covered by the title.

This workshop was supported by the Cancer Research Campaign.

**Book Reviews**

**Pathology of Tumours in Laboratory Animals, Vol. I. Tumours of the Rat.** Ed. V. Turosov. (1973). pp. 214, illustrated. Price £6.00.

The progress of experimental pathology and in particular cancer research is severely hindered by the serious lack of experimental pathologists familiar with the wide range of animal tumours encountered. There is, as pointed out in the foreword to this book, "a lack of satisfactory documentation and standardization of tumour terminology". The Editor recognizes in the introduction "the need for the histological classification of tumours in laboratory animals to be standardized" as "histological terms are sometimes used loosely". The I.A.R.C. is to be commended in undertaking such a project which could be invaluable to cancer research. However, it is necessary to consider whether the present monograph which is the first of a series covering the rat, mouse and hamster, will indeed improve on the prevailing disorder.

This volume, on the rat, contains eleven chapters written by different authors and covers the skin, auditory sebaceous glands, mammary glands, salivary glands, oesophagus, stomach, intestine, pancreas, soft tissues, bone and the haemopoietic system. The chapters vary in length from a short concise account of the tumours of the auditory sebaceous gland to a long detailed and good account of the mammary gland. The length of the chapters reflects the present information concerning each tissue and all are abundantly illustrated.

There is, however, considerable variation in quality of the chapters and there is little consistency in the use of terminology. For example, it is doubtful if there would be widespread acceptance of such opinions as "non-malignant tumours and tumour-like lesions have been induced that do invade all coats..." and "It is therefore better to base the diagnosis of malignancy on cellular and structural abnormalities in growing neoplastic tissues". There is increasing evidence from human pathology that in some situations unsupported morphological criteria may be misleading. In contrast the chapters, for example, on the skin, auditory sebaceous glands, pancreas and soft tissues are good.

The success of a monograph of morphology depends, to a very large extent, on the quality of the illustrations. As with the text there is considerable variation. The illustrations of some chapters are excellent with an adequate descriptive legend for each plate, but the high standard is not maintained and is, in part, due to poor histological technique. There are examples where the illustrations add nothing to the text, either as a result of an incorrect magnification chosen to illustrate the feature selected or poor resolution. In some instances the legends are inadequate in describing the illustration, and in not giving either the staining procedures or the magnification.

In spite of these criticisms the monograph as a whole is to be recommended. Hopefully in the succeeding volumes and editions the Editor will ensure that the faults will be rectified, so bringing every chapter up to the standard of the best. This series will then become an essential part of every pathologist's library.

W. H. Butler

**REFERENCES**

McGrath, R. A. & Williams, R. W. (1966) Reconstruction in vivo of Irradiated Escherichia Coli D.N.A.: the Rejoining of Broken Pieces. Nature, Lond., 212, 534.