Selection (S) and/or promotion (P) of chemically initiated hepatocarcinogenesis accelerate an already ongoing process. Selection and promotion could be additive or synergistic as evidenced by the analysis of the kinetics of appearance of malignant tumours in the triphasic protocol. Selection (S) and promotion (P) could, at least partly, imply genetic events leading to changes in gene expression, ploidy and possibly chromosome structure that provide growth advantages to some cell populations. It remains however to be demonstrated that such cells are the "initiated cells" which by clonal proliferation constitute the "preneoplastic lesions" from which the malignant tumour(s) arise.

The Application of Monoclonal Antibodies

Reported by: M.I. COLNAGHI
(Istituto Nazionale per lo Studio e la Cura dei Tumori, Via G. Venezian 1, 20133 Milano, Italy)

The topic of research in this seminar devoted to monoclonal antibodies (MoAbs) attracted a large number of presentations indicating widespread interest in this subject. In fact, following Professor R.W. Baldwin's masterly Mühlbock Memorial Lecture, there were many interesting presentations dealing with this topic on various occasions throughout the 3-day meeting and concluding with this seminar on the application of MoAbs. Overall, this provided an up-to-date assessment of the status of the art of a wide spectrum of applications of MoAbs in oncology.

The results presented in this field of research appeared to arouse a general feeling of optimism which can be justified as follows: a) the ability of several MoAbs to define differentiation markers is no longer questionnable and this will certainly contribute towards increasing our understanding of malignancy; b) it has been demonstrated that some of these MoAbs are capable of predicting tumour progression and therefore special attention is now being devoted to improving and developing them as valuable prognostic tools; c) there is also no doubt as to the usefulness of several MoAbs in diagnostic procedures where they have allowed improvement of conventional methodologies in areas such as histopathology, cytology, in vivo tumour localization and detection of micrometastases in vitro.

As far as therapeutic approaches are concerned, a more cautious attitude is required, mainly due to two particular problems: a)the available monoclonal reagents are apparently never strictly tumour specific, and b) the expression of the relevant epitopes on tumour cells is often heterogeneous. Although in diagnostic and prognostic approaches the difficulties these factors present are not so limiting, in therapeutic applications (particularly those in which in vivo manipulations are concerned) there are much more serious limitations. For example, in the case of in vitro therapeutic applications, such as bone marrow purging in the context of autologous bone marrow transplantation, these limitations can be overcome by using an operationally tumour-specific pool composed of a cocktail of several different MoAbs with complementary reactivities, as opposed to the use of a single reagent. So far this alternative has been giving promising results. The same type of approach could also be adopted for in vivo therapeutic applications, but in this case it is much more difficult to attain operational specificity. Furthermore, the antigenic nature of murine MoAbs, which at present represent the majority of reagents available, imposes yet another limitation. The use of human MoAbs would definitely help to resolve this problem, but their production still involves a number of difficulties. A possible solution could be offered by application of genetic engineering techniques for the generation of what are now called 'chimeric' antibodies: reagents composed of an appropriate antigenic binding site of murine origin, whereas the rest of the antibody molecule is human. These 'chimeric' molecules should theoretically be less immunogenic than their murine counterparts.

It therefore seems that the optimistic feeling referred to above can be justified by the fact that we are now conscious of the difficulties involved in using MoAbs and, in addition, methodologies are available to surmount the problems presented in their diverse applications in cancer diagnosis and therapy.

Leukocyte Adherence Inhibition Techniques in Cancer Detection

Reported by: T. SANNER
(Laboratory for Environmental and Occupational Cancer NHIK, The Norwegian Radium Hospital, Oslo, Norway)

The leukocyte adherence inhibition (LAI) assay was developed by Dr. W. Halliday about a decade ago. The test is based on the finding that sensitized peripheral leukocytes from patients with cancer exhibit a reduced ability to adhere to a glass surface when incubated in vitro with extract from a tumour of the same type. The test provides an assessment of cellular immunity and has primarily been used in relation to cancer. At an International Workshop on LAI in Buffalo, N.Y. in 1978, coded samples were analyzed and a successful demonstration of an in vitro assay of specific antitumour immunity in humans was achieved for the first time.

Although the experimental procedure of the LAI test is simple, there are a number of unknown factors which may influence the results, and the test in its present form is not suitable for use in routine laboratories. However, in specialized laboratories the test may be a useful diagnostic tool. With the use of LAI techniques several important findings which may throw light on tumour immunology in general, and lead to the development of a simpler test system, have been made during recent years. It was therefore considered timely at this meeting to attempt to summarize the present

status of the use of LAI techniques in cancer diagnosis.

D.M.P. Thomson (from Montreal, Canada) reviewed some of the earlier work with the LAI technique and discussed the physiological phenomenon underlying the response. By the use of different mouse strains he has determined that the responses obtained correlate with immunocompetence and chemotaxis. He further described research on a new organ-specific cancer neoantigen (OSN). This antigen is shed by tumour cells and was isolated from spent tissue culture medium of a human lung cancer cell line and it has also been found in the human foetus. The antigen has a molecular weight of 40,000 Daltons. Similar antigens appear to be present also in tumours from other organs and evidence was presented that this is a general tumour associated antigen with organ specificity. Dr. Thomson's findings may provide more specific antigens for use in the LAI test and provide new insights concerning tumour antigens.

V. Holan et al (Prague, Czechoslovakia) studied patients with carcinoma of the larynx and found that the leukocytes from some patients only reacted with one or a few extracts of individual tumours. The pattern of reactivity was different in individual patients suggesting that histocompatibility antigens could play a role. A significant difference in adherence was observed in experiments where leukocytes from normal non-immunized rats were tested with syngeneic or allogeneic tissue extracts and it was concluded that a significant proportion of leukocytes recognize allogeneic histocompatibility antigens without previous sensitization.

Several reports were devoted to LAI measurements on leukocytes from patients with different types of cancer. D. Eljuga et al (Zagreb, Yugoslavia) found that most of their patients with breast cancer responded in the LAI assay against breast cancer extracts, while no responses were obtained with extracts from benign breast tumour tissues (fibroadenoma) or a colorectal carcinoma. T. Sanner et al (Oslo, Norway) also reported a high percentage of responses in patients with cancer of the breast. Some of their patients have now been followed for more than seven years after initial LAI measurements and the start of treatment. No correlation was found between the results of the LAI assay prior to diagnosis and the subsequent development of the disease. F. Kalafut et al (Bratislava, Czechoslovakia) followed the LAI response in patients with malignant melanoma of the uveal tissue. They found that the test was positive in about 85% of their patients. Of interest, when the test was repeated 3 to 6 months after excision of the tumour from the eye, the LAI response had dropped in about 50% of the patients. All these patients have survived, and after a mean time lapse of 3 years, no metastases have been observed. These results suggest that the LAI response measured after a certain time following treatment may have prognostic value.

H. Kotlar and T. Sanner (Oslo, Norway) discussed a new test for the detection of an antitumour immune factor present in the serum of cancer patients. The experimental procedure of this test is similar to the original LAI test and it has been called the humoral leukocyte adherence inhbition (H-LAI) test. In the H-LAI assay trypsinized leukocytes from control persons are used as indicator cells and the effect of addition of serum from the patient under study and the relevant antigen on the adherence of the indicator cells are determined. With the H-LAI test responses were obtained in 70 to 90% of patients with breast, ovary and lung cancers. These response rates agree well with the results obtained in the original LAI test. The advantage of the new test is that it can be performed on small amounts of serum which can be frozen and stored for long periods. H. Kotlar also reported results from a small retrospective study using coded serum samples from persons who have later developed lung cancer. In this study, responses were found 1 to 5 years prior to the clinical diagnosis of the disease. It has been found that the serum factor responsible for the observed reaction in the H-LAI test is a glycoprotein with molecular weight of about 70,000 Daltons. Mechanistic studies indicate that the T8-subpopulation of the T-lymphocytes is essential in the H-LAI reaction. This new LAI assay appears to be the humoral counterpart to the original cellular LAI test.

Three studies from Budapest, Hungary which confirmed the usefulness of the H-LAI test were presented. G. Kövesi and B. Fekete used myelin basic protein as a general cancer antigen and found that 97% of their patients with cancer in the head and neck region reacted while no false positive results were obtained among 27 control persons. M. Horvath and B. Fekete reported data on lung cancer patients and found that they all responded in the H-LAI assay. The response decreased to normal values 7 to 20 days after operation. T. Kubasova et al discussed an interesting modification of the H-LAI assay where they used a radioactive amino acid mixture to label the indicator cells. The H-LAI index was calculated from the radioactivity of adherent cells. The results showed high specificity and reproducibility. Hopefully, this seminar will stimulate further research upon the use of the LAI system which may contribute to a better understanding of tumour immunology in general and to improved methods in early cancer detection.

Cellular Transformation in Vitro

Reported by: N.E. FUSENIG
(Institute of Biochemistry, German Cancer Research Centre, Im Neuenheimer Feld 280, 6900 Heidelberg, F.R.G.)

In this seminar the presentations and discussions concentrated on the phenomenon of spontaneous malignant transformation in cultures of rodent and human cells. Particular emphasis was placed on the analysis of phenotypic and genetic changes occurring during the transformation process and on the elucidation of their possible causal relationship with certain stages of the development of tumourigenic cells.