Manipulation of the Immune Response in Cancer

edited by N.A.Mitchison and M.Landy

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PREFACE

Two decades have elapsed since modern tumour immunology emerged as a distinctive speciality. Its growth has paralleled to a large extent the enormous expansion of immunological knowledge and the progressive involvement of immunologists in cancer research. During most of this period in which this intense commitment produced an immense literature on interrelationships between the immune system and cancer it has remained an article of faith that immunology does matter in cancer.

Tumour immunology is now in a phase of re-appraisal. A good deal of the early enthusiasm for immune surveillance and immunotherapy has diminished as detailed and laborious experimental studies have gradually sorted out fact from fiction. Augmentation of the immune response in the tumour bearing host has long been a focal point in seeking to tip the balance in favour of the host, but the modes of immunostimulation that have been available are, on the whole, crude, unselective, and mostly ineffective.

One of the most urgent issues is whether the immune response to tumour specific antigens can be manipulated by more sophisticated methods in such a way as either to increase weak responses or to raise otherwise insignificant responses above the threshold of detection. It makes sense to raise this matter at the present time because recent progress in cellular immunology suggests various basic strategies which might be used for this purpose. Regulation of the immune response which is likely to produce the spin-off of making this kind of manipulation possible has been the principal point of recent basic research in immunology.

With the aim of exploring this issue, the National Cancer Institute, USA supported a meeting held in Oxford in Autumn 1977. This volume reports the outcome of that meeting. It includes texts prepared by principal speakers and an edited version of the transcript of the proceedings. It is divided into seven main sections. Two deal with the present status of tumour specific antigens in animals and man. The third is on cell hybridisation, both as a technique for analysing the phenotype of the malignant cell and also as a way of manufacturing monoclonal antibodies for use as probes of the malignant cell surface. The following two sections concern recent advances in our understanding of effector cells, particularly natural killer cells and macrophages. The last two sections are on immunoregulation. One is devoted to the possible use of soluble factors and the other to manipulation of the immune response mainly

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Our purpose here is to discuss manipulation of the immune response with the aim of preventing and curing cancer. The underlying idea is that cancer cells carry antigens which do not normally provoke an effective immune response, and that these antigens may be made effective by manipulating the response. Our task therefore is to survey what is known of these antigens, and to examine means of making them more effective.

Recent advances in our understanding of both tumour cell membranes and basic response mechanisms make it appropriate to hold this discussion at the present time. Our discussion has been arranged to cover these areas of progress in the following way. As regards cancer cells, the most important advances are (i) partial isolation and characterisation of the antigens of tumours induced experimentally by powerful carcinogens (introduced by Lennox), (ii) identification of unique or stem-cell-specific antigens on the surface of human cancer cells, by means of autologous antibodies (Shiku) or antibodies raised in other species (Metzgar), and (iii) application of the technique of cell hybridisation to the analysis of antigens and other components of malignancy. Cell hybridisation is relevant to our theme in two ways, both as a means of dissecting the components of malignancy (Marshall), or as providing monoclonal antibodies with which to probe the cell surface (Hammerling). As regards the immune response, the choice of subject matter is less straightforward. Immune surveillance of cancer by the T lymphocyte system is a concept which has for a time dominated cancer immunology but which now seems highly restricted in its application. Our discussion accordingly concentrates on non-T cell parts of the immune system: natural killer cells (Kiessling), and macrophages (Alexander). The possibility remains that the T cell system can be made effective by appropriate manipulation. One approach is to use the soluble factors released by macrophages and T cells in vitro (Feldmann). Another is to exploit differences in surface markers and physiological responsiveness between T cell subsets (Cantor,

Gershon).

It has been argued that too much time, energy and money have been dissipated on the immunology of cancer. To this it seems to me that there are two answers. One is that cancer cells do on occasion quite clearly perturb the immune system, however ineffective such perturbation may be in erradication of the cancer. The nature of these perturbations deserves to be examined. The other is that important advances in immunology ought to be tested for application to cancer, and that such testing, if intelligently done, need not be particularly expensive. At any rate, it is in the context of this kind of discussion that the present proceedings should be judged.