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Book Review

Cancer Chemotherapy
Edited by John A. Hickman and Thomas R. Tritton
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It is a pleasure to recommend this compact volume on cancer chemotherapy. The editors emphasize in their preface that this volume is not about refining dosages, schedules and combinations of existing drugs in the clinic since there are many outlets for this type of work. Instead, they have focussed on new mechanistic possibilities where the next generation of drugs are likely to emerge and contribute to cancer chemotherapy in the clinic over the next decade.

While no one volume can be comprehensive in this enormous area of endeavour, the editors have chosen 14 fascinating areas of research, reviewed by appropriate experts.

The first chapter is on oncogene inhibitors. Quite rightly, many basic researchers are concentrating on subverting the signals from growth promoter genes (oncogenes) or alternatively try to re-establish growth control that has been subverted by the loss of tumour suppressor genes. Certainly we are now in an era where some of the targets for this approach can be clearly identified and hopefully major advances will come from this area.

The second chapter is about the fascinating area of apoptosis as a potential end-result of any successful anti-cancer therapy. Two experts in the field, Caroline Dive and Andrew Wyllie, emphasize that the regulation of cell death is of course as essential in organized growth and embryogenesis as is cell growth. It may well be that resistant tumour cells are those that have the pathway for apoptosis blocked, and understanding the mechanisms involved may well result in major breakthroughs and the development of new therapies. As the authors point out, apoptosis derives from the Greek word for the falling of leaves from trees or petals from flowers; perhaps a new spring will arise from this autumnal image.

The third chapter concentrates on the cytoskeleton, which is a rapidly evolving area of research and an important target for cytotoxic drugs. Clearly with the wide range of natural products which have activity against the microtubules, ranging from the vinca alkaloids through to taxol and the dolostatins, we are likely to see major new agents coming from this area of research.

Chapter 4 concentrates on one area of signal transduction, the tyrphostins, as potential antiproliferative agents. It is likely that there are going to be exciting agents which interact with tyrosine kinase but, as always with clinical cancer development, the selectivity for therapeutic effect against tumour rather than normal tissue will remain critical.

Chapters 5 and 6 cover areas which have held considerable promise but which perhaps are going through a period of relative neglect. In the first, neuropeptide growth factors and antagonists are reviewed, and in the second, the ether lipids. Currently the focus of attention is in other areas of research.

Chapter 7 concentrates on protein kinase C, its isotypes and multidrug resistance. Compounds which interact with the various isoforms of protein kinase C may produce major anti-cancer agents of the future. In the meantime, interesting inhibitors of the multidrug resistant phenotype are already being explored in the clinic.

Chapters 8 and 9 focus on the topoisomerase enzymes. Topoisomerase II, as a target of a range of established anti-cancer agents, has been the subject of a great deal of work over the last decade. More recently, attention has been on topoisomerase I and, with the advent of two camptotecin analogues in the clinic, topotecan and irinatecan, this target is of great interest and screening of agents with activity against topoisomerase I is likely to identify further promising anti-cancer agents.

Chapters 10 and 11 focus on DNA sequence specificity of anti-cancer agents. In the first, John Hartley and Robert Souhami review what is known about the DNA sequence specificity of a wide range of anti-cancer agents. This fascinating work emphasizes how little is known about the ultimate target of anti-cancer agents and the basis of antitumour selectivity when this is seen in the clinic. In Chapter 11 there is a major review of what is known about the mechanism of action of neocarzinostatin, which has been studied for the last 15 years. The potential of the enediyne antibiotics is clearly emphasized.

In Chapter 12 the vascular epithelium of tumours as a target for anti-cancer chemotherapy is reviewed by John Lazo and colleagues. This new area of anti-cancer drug development is important and the first of the semisynthetic analogues of fumagillin (AGM-1470) has already started clinical testing.

Chapter 13, while interesting, focuses on prostatic carcinoma and mainly on hormonal approaches to disease control. A summary of this type of information is available through a range of other sources.

The final chapter reviews the current development of cytokines and haemopoietic growth factors and their applications in oncology. This is a clear summary of this exciting area by two recognized experts in the field. Surprisingly, no comment is made on the potential of linking haemopoietic growth factors together, thereby potentially amplifying their effect, as in the fusion product, PIXY-321, which is a complex of GM-CSF and IL-3.

This volume is an excellent summary of a wide range of exciting areas of cancer research brought together in a very readable and well presented form. I highly recommend it for anybody interested in the development of cancer chemotherapy.

E. S. NEWLANDS
CHARING CROSS HOSPITAL, UK