embryonic cells. This, in itself, provided an interesting scenario for studying the differences between ostensibly malignant cells and their normal counterparts. However, it also meant that EC cells, which can be grown in large numbers and made to differentiate in culture, might serve as an invaluable, accessible source of material for analysing the characteristics of developmental changes which usually occur only in very small populations in the embryo. The supposed equivalence of EC cells and early embryonic cells was further endorsed by the demonstration that EC cells injected into a mouse blastocyst participate in subsequent development and contribute to apparently normal tissues in live chimaeras. Apart from its implications with respect to the suppression of malignancy, this experiment added a new perspective to the role of EC cells in biology. If they would also colonize the germ line of chimaeras then appropriate *in vitro* selection should allow the introduction of specific mutations into mouse stocks. In fact, EC cells have produced few real insights into normal embryogenesis and, as they hardly ever give rise to viable gametes in chimaeras, their potential as vehicles for gene transfer has never been realized. Nonetheless, they were a prototype and a critical spur to finding cell lines that could be used to propagate introduced genetic changes through the germ line.

Embryonic stem cells (ES cells) are cell lines derived directly from mouse blastocyst outgrowths and, while very similar to EC cells, they are far superior in their capacity to form chimaeras. Not only is their tissue distribution in chimaeras more uniform and substantial but they consistently produce extensive germ line colonization. Already it has been shown that selection in culture does not necessarily jeopardize their chances of forming functional gametes and recently two different laboratories have produced chimaeric offspring transmitting preselected mutations in the hypoxanthine phosphoribosyl transferase gene. Whatever the genetic manipulation, be it selecting specific mutations, generating new mutations by retroviral insertion, transfecting particular DNA sequences or attempting homologous recombination, ES cells offer a unique experimental system. The cells in the dish can be turned back into a mouse.

It is timely, therefore, for a practical manual (of the recipe variety) on the management and manipulation of EC and ES cells, and *Teratocarcinomas and Embryonic Stem Cells* is broad in its coverage of relevant techniques. The production of teratocarcinomas from transplanted mouse embryos, transplantation of the tumours themselves and the derivation of EC cell lines from solid murine tumours is well described by Ivan Damjanov and his colleagues. There is another chapter by Andrews, Oosterhuis and Damjanov on human germ cell tumours and the isolation of cell lines from them. This gives a good brief classification of the different human tumours and a useful list of available human teratoma cell lines. In terms of making or working with these tumour cell lines, the authors are at pains to emphasize some of the difficulties. Michael Rudnicki and Mike McBurney do an honest job of introducing the niceties of maintaining EC lines *in vitro* and present the basic methods for inducing and monitoring their differentiation. On a more biochemical level, John Heath deals with the analysis of growth in cultured EC cells and their differentiated derivatives. This includes methods for developing serum-free medium, techniques for measuring cell proliferation and methods for identifying and isolating growth factors produced by EC cells.

Perhaps the chapters that will be most thumbed in the next few years are those describing the isolation and manipulation of ES cells. Liz Robertson has provided a comprehensive description of the various ways ES cells can be recovered from blastocyst outgrowths. The protocols are clear and easy to follow and there are a number of helpful photographs depicting not only correct ES cell morphology but also representatives of other cell types, not potential stem cells, which may appear during the isolation procedure. The selection of genetic variants and fusion hydrids is well covered by Martin Hooper with a useful rationale for preferred strategies and their various pitfalls. It will be an encouragement to many that the problems raised by the presence of feeder layers during selection procedures may now be a thing of the past; Buffalo rat liver cell conditioned medium, the preparation of which is described, supporting equally good growth of EC and ES cells. Methods for introducing DNA into stem cells, including calcium phosphate precipitation, electroparation, microinjection and viral infection, are reviewed by Robin Lovell-Badge. As well as giving details of these various techniques he also provides some useful protocols for extracting DNA and RNA and for doing RNA protection assays. Finally, it falls to Allan Bradley to explain how to turn the stem cells back into a mouse. He describes simple and efficient methods for making and analysing aggregation and blastocyst injection chimaeras with EC or ES cells, and his chapter also includes some sensible tips on choice and maintenance of mouse stocks.

All in all, *Teratocarcinomas and Embryonic Stem Cells* looks like an extremely useful manual for those interested in EC and ES cells. While some of the more complicated procedures, such as micromanipulation, and the subtleties of tissue culture are probably best *learnt* from individual experts, this book will prove a good ally and source of practical reminders when it comes to setting up the various systems oneself. Not only are the instructions clear but, equally important, most chapters warn of possible complications and advise what to do when things go wrong. These are the qualities of a good guide.

Rosa Beddington
Imperial Cancer Research Fund Laboratories
Developmental Biology Unit
Department of Zoology
South Parks Rd, Oxford OX1 3PS, UK

Oncogenes and Growth Control

P. Kahn and T. Graf (editors)
Berlin: Springer–Verlag, 1986

Circumstantial evidence is accumulating, bit by bit, to convict growth factors and their signalling systems as accomplices in developmental processes. For example, growth factors from cows' brains turn out to have striking effect on the differentiation of frog embryos and certain developmental mutants in *Drosophila* turn out to be lesions in genes whose products look a lot like growth factors (dodecaplegic) or their receptors (sevenless). This recently discovered ability to cross taxonomic barriers (often considered the hallmark of 'important' molecules) inspires confidence in the general significance of these agents which, for the last twenty years, have principally been denizens of the plastic dish and the sole preserve of mammals.

There are, in fact, sound reasons for suspecting an involvement of growth factors in morphogenesis and differentiation. A realization has emerged in recent years that growth factors are powerful pleiotropic regulators of cell phenotype and behaviour, aside from their ability to promote cell multiplication Growth factors (along with their receptors and the baggage of signal transduction apparatus) have been found to regulate differentiation in systems as diverse as haemopoesis, muscle, epithelia and adipocytes, and are widely expressed in developing embryos and tissues. Perhaps the most striking aspect is the selective induction of gene expression in response

to growth factor signals which in many respects resembles the changes in gene activity of 'classical' differentiation. Furthermore, as knowledge of growth factor action increases, they also seem to fit nicely into the theoretical framework of signals and interpreters-of-signals developed by pattern formationists, with the advantage of being equipped with a body of understanding on their molecular mechanisms of action.

So where does the embryologist, seeking after knowledge and inspired by these thoughts, turn for information? Unfortunately there are few simple field guides to be recommended to the general reader. This may be because the area is growing so quickly, and encompasses so many diverse apsects that few have had the nerve (or the time) to try. However, *Oncogenes and Growth Control* edited by Kahn and Graf, comes close to fitting the bill. It comprises 46 chapters on diverse aspects of growth factors, oncogenes (now inexorably conjoined), signalling systems and receptors. Each chapter is admirably brief (ideally suited to those, like me, with the attention span of a five year old) and succintly summarizes a single topic. The reviews are mostly just that, pointing the reader towards the primary data rather than regurgitating it, and generally close with an outline of current preoccupations and likely developments. This fragmentation technique works well, encouraging readers to dip into the book at random and link different topics together for themselves rather than ploughing through a predigested version of somebody else's views. Again, because of the number of chapters, the coverage is generally good, and most of the major topical themes are dealt with. The editors have done a praiseworthy job with that often ugly creature, the multiauthor book, as the general standard of each chapter is uniform and good. They exhibit a light touch with their own contributions, which are confined to short overview pieces at the beginning of each section which can be read in their own right. The child-like jacket design is also delightful, and will hopefully find favour as a summary slide (copyright permitting), replacing the 'integrated circuit' design currently fashionable.

The drawbacks? well, as usual, the volume is cunningly priced to discourage a casual individual purchase and, perhaps inevitably, it essentially offers a snapshot of a rapidly moving field and will soon become outdated. Perhaps a paperback second edition will emerge next year?

John Heath
Department of Biochemistry
University of Oxford
South Parks Road
Oxford, OX1 3QU, UK

Organogenesis of the Kidney

L. Saxen
Cambridge: Cambridge University Press, 1987

It is a great pleasure for me to review this book. As the Preface to the book makes abundantly clear, its writing was a labour of love, summarizing and celebrating a quarter-century of devoted and rewarding study of kidney development by Saxen and his colleagues at the northern end of the European Developmental Axis.

The book is straightforward in its organization and clear in its presentation. There are successive chapters on the ontogenesis of the vertebrate excretory system, the experimental methods used to study kidney development, the important advantages of the kidney for study of morphogenetic tissue interactions, the status of knowledge about experimental tubulogenesis, and the special problem of renal vascularization and glomerular formation. The account will certainly be useful to those interested in the kidney, it is essential reading for those working in the intersecting plane of mechanisms of organogenesis and differentiation in complex developmental systems. Both will appreciate the fact that the volume is clearly and amply illustrated and provides an abundant bibliography.

Chapters 3 and 4 contain a detailed analysis of available information bearing on possible mechanisms of induction of nephric tubules, particularly the distance over which these mechanisms may act. As Saxen notes, interpretation of this information remains problematic and the situation is too complex to be adequately conveyed in a brief review. It is sufficient to say that the author makes available the explanatory options and notes that more than one may be operative.

The options include: free molecular diffusion of the agents involved; diffusion limited in some fashion to short range; interaction of cell-surface-associated molecules; interaction through matrix molecules; and molecular transfer 'through intercellular channels'. In the opinion of the Helsinki group, as I understand it, matrix molecules are likely to be involved but available evidence does not preclude participation of diffusible molecules as well. The uncertainty of the evidence dervies from the properties of various filter samples that have been used to block or transmit the inductive stimulus. I add my own view that, given current molecular techniques, more discriminating and precise approaches than filter barriers are called for.

In his concluding remarks (p. 143 onwards), Saxen makes clear that the book is a progress report that summarizes substantial advance but still lacks definitive conclusions. A diagram (Fig. 6.1) depicts 'much of our present knowledge of various molecular and structural events linked to the early, post-inductory development of the secretory nephron – but it is still not easy to find causal relationships within the general framework'. It was, of course, the hope of finding such relationships that generated my own interest in the kidney more than 30 years ago. It submit that hope springs eternal and this book renews it. The kidney remains an ususually favourable target for experimental studies on the detailed mechanisms of organogenesis and the extensive contributions of the Helsinki group have enlarged the foundation for continuing progress.

As to the precise nature of those mechanisms, few today doubt that much of the answer lies in the molecular information at the interface of embryonic tissues of differing developmental history. In what form the critical information exists and over what distances it can be transmitted is still not clear and there are differing interpretations of the available indications. But what is most important to understand is the informational code of the materials in the transitional interspace, particularly in their native combinations and resultant configurations

Nonetheless, information about the nature of these and similar materials in other circumstances is growing apace. Such matrix molecules as the collagens, laminin, and fibronectin are well characterized and others are being steadily added to the list. The concept of intercellular matrix being much more than structural packing no longer needs defense. For those interested in penetrating further into this fundamental biological problem, this book and the developing kidney provide a potentially most rewarding challenge.

Clifford Grobstein
University of California, San Diego
La Jolla, California 92093, USA

Developmental Biology

Virginia Walbot and Nigel Holder
New York: Random House, 1987

Another new undergraduate biology text, the title of which includes the word 'Development,' has in recent years arrived on my desk every few months. Depending on one's point of view, it either is or is not surprising that each has a distinctive character, a different concept of what the field of development encompasses, a particular flavour. Of course they all share