occur' (p. 3). This is a very different attitude from that of those searching for relatively universal mechanisms. The comparative approach fosters broader thinking and is likely to lead to a heightened appreciation of the different strategies used by different organisms, but it does make the book more difficult for the uninitiated student. The amount of data and its complexities becomes overwhelming, especially in cases where the experiments have been done in somewhat different ways with the different species. It is also sometimes difficult to know where to find some topics. The discussion of the *Xenopus* transcription factor TFIIIA, for example, is within the lampbrush chromosome section (p. 376–380). Especially in Chapters III–V, subjects are often intermingled in ways that make assimilation of the material more difficult than it could be.

It must have been a special challenge to Dr Davidson to try to select important material for inclusion from the onslaught of publications in the *Drosophila* and *Caenorhabditis* fields. It is impossible for rapidly published reviews to keep up with the current results in these areas and, therefore, it would be completely unfair to expect such a polished book to include the latest about *C. elegans* cell lineages or new 'striped' *Drosophila* genes. It is good, for this reason, that much of the *Drosophila* and *Caenorhabditis* work described addresses issues that have, in some sense, matured. Thus, measurements of mRNA complexity at different stages are presented, there is a fold-out copy of the complete *C. elegans* cell lineage, and there is a survey of the different classes of *Drosophila* genes that have been studied for their involvement in embryogenesis. The classes of fly genes are presented in terms of differential gene expression rather than from the perspective of interacting gene networks that control development; as in most of the book, genetic circuitry is not emphasized. Considering its length (about 35 pages) the review of *Drosophila* developmental genetics covers a lot of ground. However, it is my blatantly biased view that in future editions of the book this section would have to be expanded dramatically. The molecular analysis of development has progressed from bulk measurements of transcripts to the study of individual genes and, now, using *Drosophila* and *Caenorhabditis*, from the question of *which* individual genes to study to the goal of studying *all* of the genes involved in a particular developmental process.

There are some errors that may mislead and some unnecessary jargon. Calling something 'interspersed cytoplasmic RNA' (p. 364) is confusing. The striped expression of the *ftz* gene is not reduced to half the usual number of stripes in progeny of mutant *bicoid* mothers, contrary to the statement on p. 289. Nor is the control of *Ubx* expression by the abdominal genes of the BX-C a *cis* effect as is stated on p. 297. These latter issues are ones with which I am especially familiar; I suspect there are fewer slips in some of the other areas that are closer to Dr Davidson's own work. There are other cases where either I miss the reasoning or perhaps the statement is as controversial as it sounds. In *C elegans*, development differential zygotic genome function is observed when the embryo has only a few hundred cells, and it is claimed that 'This property directly predicts the importance of *early cell lineage* in determining the fate of the descendant blastomeres' (p. 194). I do not understand the reasoning behind this claim. Elsewhere it is stated, in reference to the flexibility of early amphibian development, 'Nor can the initial specification processes depend on sequential cascades of genomic regulatory events' (p. 257). Yet why should such a cascade be incapable of flexibility?

The massive amount of material discussed makes the book an imposing task to read, and I see its usefulness more as a reference source than for a course text. How could the amount of material have been usefully reduced to make the remaining text more easily consumed? There are occasional sections where the information presented is of unclear importance and could have been condensed. On pages 58–69, for example, there is a lengthy discussion of the symmetric transcription of repetitive DNA sequences in *S. purpuratus* (and *Xenopus*) embryos that comes to the conclusion that no function can be ascribed to the RNAs. In this instance, the drive to be comprehensive could have been reigned in and a number of others. However, there is no escaping the basic difficulty that the field is vast and therefore the book has to be long. The absence of other books that have the same sorts of goals is probably due at least in part to a lack of authors willing to rise to the task. Other books such as Adam Wilkins' *Genetic Analysis of Animal Development* cover only some of the issues discussed in Davidson's book, although Wilkins' book does much more justice to the power of genetics.

Despite the large amount of material, is there anything missing that should be there? I looked for more advice and guidance from an author with such an exceptional historical perspective. History should help to guide the experimentalist. We would like to hear how to recognize which of the current approaches to developmental biology are most likely to be successful, based on lessons from the past. Wilson (1925, p. 1041) quotes R. Lankester (1877) as stating 'Though the substance of a cell [an egg] may appear homogeneous under the most powerful microscope, it is quite possible, indeed certain, that it may contain *already formed and individualized*, various kinds of physiological molecules.' Of the mass of available data, how are the important facts and ideas to be distinguished from the details? Are we indeed focusing too much on just a few organisms and how are we likely to err in doing so? The implicit answers to some of these questions lie within the book, but a direct assessment of where we stand and how we should best proceed would have been useful. Perhaps science is so different now that what worked for E. B. Wilson would not be as effective anymore, but I suspect that Dr Davidson would agree that Wilson would be every bit as successful in science now as he was 90 years ago. The integrated discussion of classical experimentation and modern developmental biology research is unique to Dr Davidson's and guarantees its lasting value.

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Teratocarcinomas and Embryonic Stem Cells: A Practical Approach

E. J. Robertson (editor)
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Thirty years ago teratocarcinomas were little more than pathological oddities, of passing interest to some oncologists but quite unknown to most biologists. Their emergence from obscurity was largely due to the work of Roy Stevens and Barry Pierce who, between them, gradually impressed on their audiences the special features of these obscure tumours. At a gross level, there was something immediately fascinating in the monstrous form of some teratocarcinomas, the jumble of hair and teeth, skin and brain tissue, intestine and skeletal elements all chaotically cohabiting in a single tumour. But it was the 'life cycle' of teratocarcinomas that was especially intriguing, particularly in the context of the major advances in manipulating early mammalian embryos which occurred in the 1960s.

The stem cells of teratocarcinomas (embryonal carcinoma cells, EC, cells) share many morphological, biochemical and behavioural characteristics with their natural progenitors: germ cells and early 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.

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Oncogenes and Growth Control

P. Kahn and T. Graf (editors)
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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

Embryonal carcinoma and embryonic stem cells Multipotential cell lines can be derived from early mammalian embryos by two methods (Fig. 1). The first (reviewed by Stevens, 1983) depends upon either the natural occurrence of germ cell tumours in specific mouse strains or the induction of teratocarcinoma tumours from the primitive ectoderm of embryos transplanted to ectopic sites. The continued growth of these tumours is due to the existence of a tumorigenic, pluripotential stem cell population, the embryonal carcinoma (EC) cells.Â In Teratocarcinomas an d Embryonic Stem Cells: a Practical Approach (ed. E . Robertson), pp. 183-206. Oxford: IR L Press. The recent derivation of human embryonic stem (ES) cell lines, together with results suggesting an unexpected degree of plasticity in later, seemingly more restricted, stem cells (so-called adult stem cells), have combined to focus attention on new opportunities for regenerative medicine, as well as for understanding basic aspects of embryonic development and diseases such as cancer. Many of the ideas that are now discussed have a long history and much has been underpinned by the earlier studies of teratocarcinomas, and their embryonal carcinoma (EC) stem cells, which present a malignant surro