

And this, it should be noted, is only the first and easiest step in elucidating the function of the disease gene and the basis of the disease.

Pelletier, Munroe and Housman on the molecular genetics of Wilms' tumour leads on directly from the above chapter, taking the analysis of WT more or less up to date. This nephroblastoma is the most common renal tumour in children, with a remarkably constant rate of occurrence among diverse population groups of about 1 in 10000 children under 15. The cure rate: 5.7% in 1938, 50% in 1950 and nearly 90% in 1989, due to progress in surgical, radiotherapy and chemotherapy techniques, makes a dramatic success story. Of particular interest, several other disease conditions are often associated with Wilms' tumour, giving the so-called WAGR syndrome which includes aniridia, genito-urinary anomalies and mental retardation. These have been jointly located in chromosome 11p13 by a visible deletion. From these beginnings, more than 325 markers have been mapped to the short arm (p) of chromosome 11, making it one of the most densely marked of all the human autosomal regions. Concentration on 11p13 has suggested a candidate gene for WT containing four zinc fingers of the Cys-His variety at the carboxyl terminus, with other characters of a DNA-binding protein.

Ghosh and Todd consider multifactorial disease, with lessons from type-1 diabetes (IDDM). Schizophrenia, Alzheimer's disease, hypertension and atherosclerosis are other examples in which presumed genetic and environmental influences contribute to both onset and progression of the disease, with the number of genes and their types of interaction to be sought out. A mathematical approach using likelihood, comparative mouse-human mapping where similar diseases are found in the mouse, use of large numbers of markers in both species, and other approaches suggested by the much easier search for QTLs (quantitative trait loci) in plants and animals of agricultural interest are promising, but we are evidently at an early stage in this very important field. Ghosh and Todd's article, with its many references, is well worth study.

Goodfellow, Hawkins and Sinclair give an excellent account of their many problems and final success in cloning TDF, the mammalian sex-determining gene on the Y chromosome. This article brings out the unexpected difficulties that can be experienced in the supposedly straightforward tasks of constructing maps of the human Y and pinpointing the position of TDY, chromosome walking and searching the cloned sequences for likely candidate genes, and proving equivalence between target and a candidate gene. This must have been rather like climbing Everest with under-tested apparatus, and I was relieved to find the climbers had got down again. Do not miss this chapter, especially if you intend to embark on chromosome walking and even jumping.

Reith and Bernstein fill us in on the molecular

biology of the *Dominant white spotting (W)* and *steel (Sl)* loci in the mouse. Both loci lead to defects in haematopoiesis, melanogenesis and gametogenesis, and *W* is allelic with *c-kit*, a proto-oncogene that encodes a receptor tyrosine kinase (RTK), while *Sl* encodes the ligand for the Kit receptor. Much new work on these two classic mammalian developmental loci is described, which I have not the space to summarize here. Rather, I want to draw the reader's attention to the article by Snyder and Silver on the mouse *t*-complex responder locus.

This transmission ratio distortion system, as is well known, consists essentially of several distorter (D) genes and one responder (R) gene, all in a 20-cM region of chromosome 17, containing a number of other irrelevant loci. Research by several groups has not, until recently, approached an explanation of how the transmission distortion is produced. The R, not the D genes, has the central role in this system: males heterozygous for both D and R genes transmit a very high proportion of R sperm to their progeny, whether R and D are on the same or opposite chromosomes, while R heterozygous on its own is only transmitted in 10–30% of sperm instead of around 90%. Snyder and Silver describe how the search among candidates for the Responder gene has identified the previously known gene *Tcp-10b*^t. This gene contains 10 exons and generates two transcripts whose expression differs, during spermatogenesis. The full-length transcript comes from the total of exons, while a novel transcript (only produced in the round spermatid stage, not in the pachytene spermatocyte) splices out exon VIII and uses a cryptic splice donor in exon IX to join with the acceptor of exon X, out of frame. The authors' model to explain transmission ratio distortion on the basis of this amazing discovery may tax those who find the rest of the book too easy to follow, though no other model yet seems more feasible.

From my brief discussion of the contents of the six chapters in this book, the reader may well conclude that it should at least be in his departmental library, and would stimulate his molecular genetic students. One would like to see it in soft covers with a lower price so that it could find its way to a number of laboratory shelves. The authors are all to be congratulated on making their chapters so absorbing to at least one reader.

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Major Genes for Reproduction in Sheep (2nd International Workshop, Toulouse, July 1990). Edited by J. M. ELSÉN, L. BODIN and J. THIMONIER. (Coll. les Colloques no. 57.) 1991. Pp. 462. 250.00 FF. ISBN 2 7380 0337 0.

Although major genes are by no means unknown in

animal production systems, their role in genetic improvement has been subsidiary to the standard quantitative methodology. Up to now, this has been true of sheep reproduction, as for all other traits. But genetic research in this area is now in danger of being hijacked by major-gene thinking, as if there was nothing else to do. Perhaps there is not, because major genes, where you have them, can completely swamp any other genetic variance. This is patently true for sheep reproduction, and whatever other use you may have for genes of large effects, they certainly provide an array of attractive experimental tools.

The fuss started with the discovery of the Booroola gene in Australia. It was not until 1980 that a classification system based on repeated counts of ovulation rate (initially, of lambs born) allowed acceptable segregation ratios to be established. By now, there is no doubt that it is indeed a single autosomal gene, with an additive effect on ovulation rate. The Committee on Genetic Nomenclature for Sheep and Goat have assigned to it the symbol *Fec* (imaginatively, *Fec* for 'fecundity'), although *F* is still in use. Symbols are becoming important, because already we have also *FecC*, *FecI* and *FecJ*, contributed respectively by Cambridge, Iceland and Java. It is not known whether these genes are alleles of (perhaps identical with) the Booroola, or whether they are at separate loci. More genes yet, be they alleles or loci, may be in the offing. There are putative genes of the same kind reported from the Romney breed in New Zealand, the Olkuska in Poland and, more tentatively, the Belclare in Ireland. If you aspire to international travel and you take up sheep reproduction you will be spoilt for choice.

All this and more may be gathered from this volume, which reports the proceedings of the Second International Workshop held in Toulouse in 1990. The first had been held in Australia in 1980, and at that time Australasia had a monopoly of the contents. This time round, we have contributors from 17 countries, reflecting the heavy traffic in live sheep, semen and embryos over the intervening period. Everyone now seems to have access to Booroola or Booroola-like material, and it was timely to bring together a summary of the research in the area.

That research has in fact been extraordinarily diverse. Some people simply want more lambs, and we have accounts of the exploitation of these major genes in all sorts of breeds and crosses in all sorts of places. The technical term seems to be 'introgression', though it may not yet have penetrated the bucolic vernacular of some of the countries involved. Anyway, the results are much as expected. Given the need for laparoscopy to identify female carriers, and for progeny testing to test putative males, progress is inevitably slow. I also suspect that some schemes are too small to be efficient. Nevertheless, gains can be shown, and we have examples. The successful development of a probe, or even a worthwhile marker, would be an immense

boon. But so far, stalwart individuals are left to demonstrate the application of Mendel's first law, and it still seems to work.

We have 16 chapters describing the work of the physiologists on the manifold effects of these genes. Some of the effects are very clear. There is no doubt that the Booroola gene elevates plasma FSH during oestrus. But then we come up against a blank. It has not been resolved whether this is a direct effect of the gene on FSH secretion from the hypothalamo-pituitary or whether it is indirect through feedback secretions from the ovary. This is just one example of the difficulties that physiologists have found in what is admittedly a complex system of hormone secretions, release factors, receptors and inhibitors. Various levels are altered to various degrees, when often any one of them might have a domino effect on the others. I am at a loss to summarize this section, so I shall merely give quotations from two chapters which I hope are not grossly unfair to the others: 'the mechanism as to how the F gene influences ovulation rate remains unknown' and 'there is no method to type carriers and non-carriers of the F gene in the male'. The grammar of the second of these cannot be faulted.

The need for probes or markers was mentioned earlier, and the molecular biologists, like the physiologists, cannot be blamed for lack of effort. The 8 chapters, collectively, provide an excellent indirect review of the popular methodologies in the field. You can even learn that VNTR means 'variable number tandem repeats' to some, and 'very numerous' to others. But despite the extensive application of DNA probes, cDNA libraries, RFLPs, minisatellites, Southern blots, DFP and the rest, the answer so far seems to be that they have found nothing concrete. But they may yet. One further quotation seems to me to present a balanced view of the prospects. 'The identification of the F gene product will probably need a large scale effort and extensive cooperation. One may, however, be fairly confident of the chances of success in this endeavour.' I like the measured use of the word 'fairly' in that statement.

To make sure that there is something for everybody in this volume, the last section is on the statistical aspects of the detection of major genes. Four chapters cover the field well, and offer some useful suggestions. They ignore, however, what is possibly an even more difficult statistical exercise. Before any major gene can be sensibly incorporated into a breeding programme, we need accurate information on the effect of all three genotypes, at a two-allele locus, on each and every production trait. This itself is a massive field exercise, and the task of summarizing and utilizing this essential information requires the appropriate statistical treatment. If nothing else, a chapter on this would have alerted the practitioners to the difficulties.

In summary, despite some largely negative results in parts, this volume nevertheless provides an excellent review of genetic research on reproduction in sheep.

Some of the activities will be of direct interest to workers in other areas. Unfortunately, you will find the book very difficult to use as a reference volume. The individual contributions carry no summaries, and there is no index. I suspect that this is a cunning device to prevent an over-casual review. At least, that is my excuse to the Editor of this journal, who understandably has been complaining that I have been slow to produce it.

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Genetics and Evolution of the Domestic Fowl. By LEWIS STEVENS. Cambridge University Press. 1991. Pp. 306. Hardback £50.00 (\$89.95). ISBN 0 521 40317 0.

This book meets a need which is easily neglected, but where success will help ensure the future growth of science in this area. Students of genetics, molecular biology, development or quantitative genetics are offered a glimpse of the unique potential of poultry as study material.

Specialists in this subject have been endowed with two great landmarks of progress. Hutt's *Genetics of the Fowl* (1949) marked the prominent role of poultry studies in early genetics, and was so comprehensive that it remained the standard text for four decades. *Poultry Breeding and Genetics* (edited by

R. D. Crawford, 1990) brought together authorities in every aspect of the subject. The synthesis of molecular, Mendelian and quantitative genetics is unique among vertebrate species.

Non-specialists too often complete their education unaware of the relevance of the fowl to their studies. This book offers a stimulating description of how the most advanced technologies can be applied to a species which has a long tradition in science, a vast knowledge base and great scientific and commercial value.

Dr Stevens writes, in the tradition of F. B. Hutt, as an enthusiast as well as an expert. The strongest chapters are those on 'The transmission of inherited characters' and 'Immunogenetics of the domestic fowl'. The appendix on 'Oncogenes' deserves to be developed into a full chapter. The only obvious weakness is in molecular embryology, where the readily accessible embryo is widely used to study gene expression in development.

The book should be recommended to biology students from agriculture to molecular biology. By offering such students a bridge into the specialist poultry literature, *Genetics and Evolution of the Domestic Fowl* will help to ensure that studies of poultry will stay at the forefront of vertebrate genetics.

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