Book Reviews

Extrachromosomal Genetics

Mitochondrial Genes. Papers from a meeting, Cold Spring Harbor, N.Y., May 1981. PIOTR SLONIMSKI, PIET BORST, and GIUSEPPE ATTARDI, Eds. Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y., 1982, xx, 500 pp., illus. \$65. Cold Spring Harbor Monograph Series, vol. 12.

Mitochondrial genomes have been intensely studied by a dedicated group of workers for the past decade and a half. In recent years conferences have been held annually and a published collection of papers has usually resulted. One may rightly ask whether all this research activity and publication has been justified. In my opinion this new volume from Cold Spring Harbor answers the question resoundingly in the affirmative. The book is a treasure trove of reviews and short papers that show that the mitochondrial genome must have evolved under constraints quite different from those that apply to its stately partner, the eukaryote nucleus, or its more conservative cousin, the chloroplast genome.

The book is divided into five parts each of which reflects work done on mitochondrial genomes in a group of organisms (animals, yeast, filamentous fungi, protozoans, and higher plants). This comparative approach is particularly helpful since mitochondrial genomes vary greatly in size and structure, although the functions for which they code (that is, mitochondrial tRNA's, rRNA's, and specific components of the electron transport chain) are highly conserved.

Mitochondrial genomes of multicellular animals are small (15 to 16 kilobase pairs), and sequencing studies show that mitochondrial genes are extremely densely packed within them. Complete sequences for bovine, human, and mouse mitochondrial genomes are discussed and compared (Anderson *et al.*, Van Etten *et al.*). There are 13 long open reading frames, all of which lack intervening sequences. Three of these are known to code for three subunits of cytochrome oxidase (COI, COII, and COIII), one for cytochrome *b*, and one for adenosine triphosphatase subunit 6. The protein products of the eight remaining unidentified reading frames (URF's) remain to be determined. The sequences of the two mitochondrial rRNA genes and 22 tRNA genes have also been determined. The protein coding sequences are separated from each other by tRNA genes. The origin of the heavy (H) strand is maintained as a novel three-stranded structure owing to synthesis of short H-strand pieces that displace the parental H strand to give a D loop (Van Etten *et al.*). The origin of the L strand is more prosaic but does contain an impressive hairpin. On the H strand, sequences coding for discrete transcripts (17 in number) saturate the entire length of the strand except for a region corresponding to about 7 percent of the genome around the origin of replication (Attardi *et al.*). The organization of these transcripts faithfully reflects the arrangement of the rRNA genes, the reading frames, and their interspersion with tRNA genes. Human mitochondrial mRNA's either start directly at the initiation codon or have a few nucleotides preceding the codon. Whenever a tRNA gene is situated 5′ to an mRNA coding sequence, the coding sequence starts immediately after the tRNA gene. Most mRNA's terminate in uracil or adenine, and it has been proposed that the truncated ochre codon formed in this way is completed by polyadenylation. There is also good reason to believe that tRNA sequences act as signals for processing. Those H-strand transcripts that code for tRNA and mRNA are made once or twice per cell generation, but rRNA transcripts are synthesized 50 times per cell generation. The strand contains only one URF and seven tRNA genes yet is transcribed at two to three times the rate of the H strand.

The second section of the book, devoted to yeast mitochondrial genomes, contains a number of reviews and papers on the intervening sequences of the cytochrome *b* gene (such as those by Jacq *et al.*, Mahler *et al.*, and Schweyen *et al.*). There are two forms of this gene in *Saccharomyces cerevisiae*; in the long form there are six exons (B1 through B6) and five introns (I1 through I5) whereas in the short form the first three introns (I1 through I3) are missing and exons B1 through B4 are fused. Introns I1 and I5 have blocked reading frames in all three registers, but introns I2, I3, and I4 all contain open reading frames in phase with the exon preceding each of them. These introns code for *trans* acting elements (maturases) important for processing the respective introns from cytochrome *b* mRNA. Intron I1 and presumably I5 are processed by nuclear coded enzymes, and I4 (identical to I1 in the short form) makes a product that is also required for processing the fourth intron in the COI gene. Like the cytochrome *b* gene, this gene can exist in long and short forms that result in the presence or absence of five optional introns (Grivell *et al.*). In the long form the first four introns contain open reading frames in phase with upstream exons and probably specify carboxylterminal parts of proteins with maturase activity. Nuclear genes are also important in processing these mitochondrial transcripts, and nuclear mutations affecting these processes have been identified (Dieckmann *et al.*, Michaelis *et al.*).

Yeast petite mutants may retain any part of the mitochondrial genome. Although this implies that any region of the mitochondrial genome in yeast has the potential to be an origin of replication, one might expect specific origins to be used preferentially in wild-type yeast. To see if this is the case mitochondrial DNA sequences retained in petite mutants (suppressives) whose mitochondrial genomes clearly replicate more efficiently than wild-type mitochondrial genomes have been characterized (Bernardi, Blanc and Dujon). Several potential origins of replication have been identified in this way. A recombinant plasmid carrying one such sequence apparently uses that sequence as an origin of replication.

The last two papers of the second section (Clark-Walker and Sriprakash, Wolf *et al.*) present comparative studies of mitochondrial genomes from other yeast species, and many of the papers in the section on filamentous fungi relate to this topic. For me these parts of the book were particularly interesting from the comparative evolutionary viewpoint. Some examples will show why. The yeasts *Torulopsis glabrata* and *Kloeckeria africana* have small mitochondrial genomes compared to *S. cerevisiae* (Clark-Walker and Sriprakash). Sequence rearrangements are prevalent when the three genomes are compared. Introns in cytochrome *b* are either small or absent although COI in both yeasts

contains an intron and *K. africana* has a 4.3-kilobase-pair inverted repeat. The *Neurospora* mitochondrial genome is reported to contain a gene homologous to the yeast mitochondrial gene coding for the dicyclohexylcarbodiimide-binding protein despite the fact that in *Neurospora*, in contrast to yeast, the gene that is actually expressed for this protein is nuclear in location (van den Boogaart *et al.*). The *Neurospora* large rRNA gene contains an intervening sequence capable of coding for a protein of 258 amino acids, but splicing of this intron depends on nuclear gene products (Yin *et al.* and Garriga *et al.*). In *Aspergillus*, the genes coding for the large rRNA and cytochrome *b* each have single introns whereas the CO1 gene contains two (Küntzel *et al.*, Davies *et al.*). Amplification of specific parts of the mitochondrial genome appears to be responsible for senescence in *Podospora* (Belcour *et al.*).

The fourth and fifth parts of the book are brief and deal respectively with the mitochondrial genomes of Protozoa and higher plants. In trypanosomes a single, giant mitochondrion contains the kinetoplast DNA. The kinetoplast DNA consists of thousands of circles joined together in a single massive network. Of these, 95 percent consist of minicircles of 0.8 to 2.5 kilobase pairs and the rest of maxicircles (true mitochondrial genomes) of 20 to 38 kilobase pairs (Simpson *et al.*). Minicircles are first released from the center of the network for replication and following replication reattach to the periphery of the network (Englund *et al.*). Thus the replicating network grows from the periphery toward the center.

Higher-plant mitochondrial genomes are the largest known. A heterogeneous population of circular molecules ranging from 0.5 micrometer to 30 micrometers has been identified corresponding to a maximum size of 112 kilobase pairs. Restriction enzyme digests are surprisingly complex and yield minimum sizes of 227 to 757 kilobase pairs. A heterologous probe from yeast has been used to identify the COII mitochondrial gene in maize. The gene contains a 794-base-pair intron (Leaver *et al.*). Isolated mitochondria from maize make 18 to 20 polypeptides (Leaver *et al.*). These include COI, COII, and the dicyclohexylcarbodiimide-binding protein. If one estimates the total molecular weight of these proteins plus the mitochondrial tRNA's and rRNA's, the coding capacity accounted for is only 22 kilobase pairs. Cytoplasmic male sterility in maize (cms) is very likely caused by alterations in mitochondrial DNA, and correlates can be found among polypeptides made by the isolated mitochondria.

In conclusion, this book summarizes a wealth of interesting information about mitochondrial genomes, and I recommend it highly to anyone interested in this subject.

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Developmental Neurobiology

Neuronal Development. NICHOLAS C. SPITZER, Ed. Plenum, New York, 1982. xxiv, 424 pp., illus. $45. Current Topics in Neurobiology.

Developmental neurobiology is particularly interesting at the present time because of the recent development and exploitation of new preparations and techniques. This book is a collection of 11 scholarly essays, each of which focuses on a particular subject in the field.

Five of the papers deal with development in invertebrate systems. Two of these are comprehensive reviews that describe the advantages of the particular invertebrate, the organization of the adult nervous system, and what is known about neural development in the organism. In the first of these papers, Stent, Weisblat, Blair, and Zackson detail their studies on cell lineages in the leech using a novel tracer technique. The second paper, by Goodman, reviews somewhat later events in grasshopper development, including the lineage and differentiation of particular identified neurons. Both papers underscore the importance of cell lineage in invertebrate neural development and provide superb introductions to the leech and grasshopper for anyone who is not an invertebrate aficionado or a linealogist. An additional paper on analysis of development in the nematode *Caenorhabditis elegans*, another invertebrate system that is proving useful, might have been appropriate. The other papers that describe invertebrate development are less global and focus on particular developmental issues. Palka describes the use of genetics to perturb normal developmental processes in *Drosophila*. His paper also serves as an excellent introduction to the subject by defining the issues relevant to genetic manipulation of development, the advantages of *Drosophila*, and the terminology used by *Drosophila* geneticists. Palka then details a number of such genetic experiments and points out the lessons that can be learned from each. Flaster, Macagno, and Schehr describe the neuronal organization of the compound eye of *Daphnia*, its development, and the mechanisms that allow the formation of appropriate connections between the eye and the lamina. Edwards describes the development of sensory neurons in the cricket and the role of pioneer fibers in establishing peripheral axon pathways. The growth cone or the growing tip of the axon is responsible for pathway selection, and Letourneau summarizes current knowledge of growth cone structure and function, concentrating on knowledge gained from examining the growth cones of vertebrate neurons in culture.

The remaining papers in the book are not so easily categorized. Jacobson has applied tracer techniques similar to those used in the leech to the developing amphibian embryo and presents evidence suggesting that founder cells that arise early in development and whose descendants will form compartments play an important role in establishing the primary morphological pattern of the vertebrate central nervous system. Information concerning the possible role of cell lineages in the vertebrate nervous system may come not only from studies of cell injection such as these but also from the application of monoclonal antibody techniques. Barald describes how such antibodies have been raised against ciliary ganglion cells: two antibodies are able to detect a subpopulation of crest-derived cells that are otherwise identical to their neighbors. Cell death and synapse elimination serve important functions in vertebrate neural development, and these phenomena are well reviewed in two additional papers. Berg describes the occurrence of cell death, outlines the case that nerve growth factor functions as a trophic factor, and details recent work on the search for other target-derived trophic factors, in particular those that would act on parasympathetic neurons. Van Essen reviews synapse elimination at the neuromuscular junction, makes reference to the existence of the process elsewhere, and presents a case in support of the idea that polyneuronal innervation is controlled by bidirectional signaling between nerve and muscle. Finally, Cowan and Finger describe the heretofore largely ignored ability of the embryonic central nervous system to regenerate and regulate.

Although this collection of papers does not constitute a complete review of the field of developmental neurobiology, it covers a relatively broad range of