Lasker awards honour fruit fly researchers

This year's Albert Lasker medical research awards highlight the remarkable progress made in recent years in basic and medical genetics. The US awards, among the most prestigious for medical and biomedical research, were first made by the Albert and Mary Lasker Foundation in 1944.

This year's basic medical research prize was awarded to Edward B. Lewis of the California Institute of Technology in Pasadena, USA, Christiane Nüsslein-Volhard of the Max-Planck Institute for Developmental Biology in Tübingen, Germany. Both Lewis and Nüsslein-Volhard work on understanding animal development using genetic approaches and both use the fruit fly *Drosophila melanogaster* in their studies. The clinical medical research prize was awarded to Yuet Wai Kan of the University of California at San-Francisco for contributions to the development of DNA analysis for diagnosis of genetic disorders.

Lewis's work, for over 40 years, has concentrated on understanding the role of the *bithorax* gene complex in segmental specification[1-3]. Insects are thought to have evolved from segmented annelids (like the earthworm), and, in the process, developed mechanisms that allow one segment to differentiate structures different from the next (see Figure 1 for an outline). The development and identity of segmental structures in the fruit fly are under the control of two gene complexes (Figure 2,*a*), the *Antennapedia* complex (ANT-C) and the *bithorax* complex (BX-C).

Lewis's work did not begin as an effort to understand animal development. Trained as a classical geneticist under A. H. Sturtevant (who was himself a student of T. H. Morgan, the founder of *Drosophila* genetics), Lewis's early experiments were aimed at understanding the nature of the gene. The classical view is that if two mutations are in the same gene they will 'fail to complement each other'. In other words, if mutations a^1 and a^2 were in the same gene then flies of the genotype a^1/a^2 would be mutant and a^1 and a^2 fail to complement each other and are alleles. If the mutations were in different genes then a^1/a^2 flies would be normal; the mutations are said to complement each other. This is still a useful functional definition, but Lewis showed that sometimes things are different. His study of BX-C showed that while many different mutants in this genetic region behaved as if they were in the same gene and failed to complement each other, other mutant combinations behaved as if they were in different genes and complemented each other. This pattern of complementation was complex and mutants in the locus showed different phenotypes depending on whether the mutations were in *cis* (on the same chromosome) or in *trans* (on different homologous chromosomes) combination with each other. Lewis's work, done long before recombinant DNA technology allowed us to understand these phenomena at the molecular level, showed for the first time that the gene was complex and defined the term pseudoallelism[1]. These experiments on the nature of gene organization are themselves revolutionary and deserving of the highest recognition.

Lewis has, however, carried his experiments much further. He showed that mutations in BX-C had very specific effects on the body plan of the fly[3]. In general, loss-of-function alleles at the

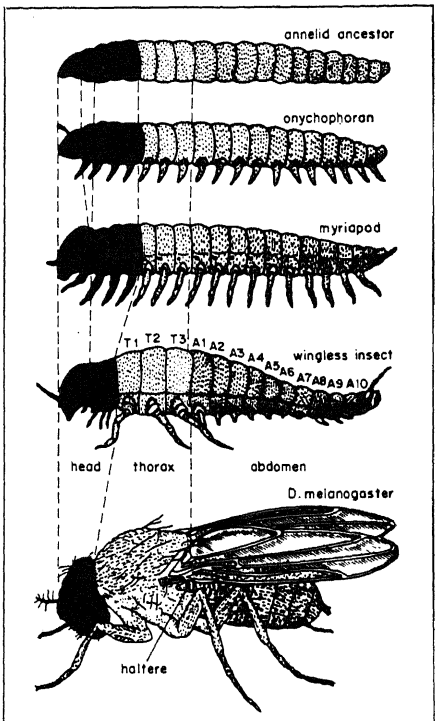

Figure 1. The ancestors of *Drosophila melanogaster*. The specialization of head thoracic and abdominal structures are shown. Flies are thought to have evolved from four-winged insects (not shown). In modern flies the second pair of wings has evolved into halteres, a specialization used to maintain balance during flight. (Modified from ref. 13)

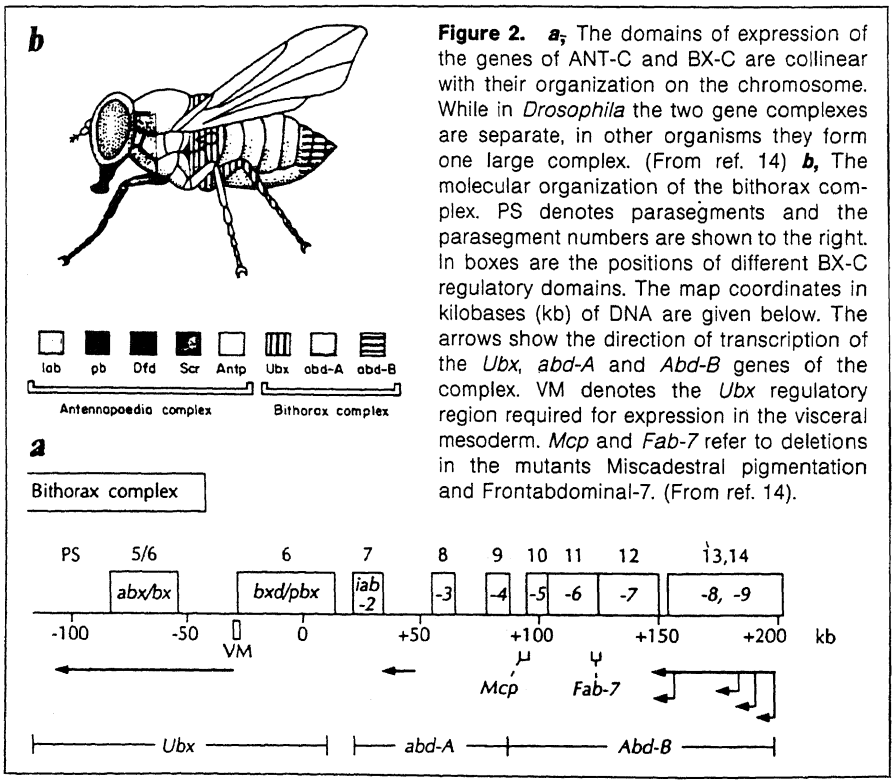

Figure 2. ***a***, The domains of expression of the genes of ANT-C and BX-C are collinear with their organization on the chromosome. While in *Drosophila* the two gene complexes are separate, in other organisms they form one large complex. (From ref. 14) ***b***, The molecular organization of the bithorax complex. PS denotes parasegments and the parasegment numbers are shown to the right. In boxes are the positions of different BX-C regulatory domains. The map coordinates in kilobases (kb) of DNA are given below. The arrows show the direction of transcription of the *Ubx*, *abd-A* and *Abd-B* genes of the complex. VM denotes the *Ubx* regulatory region required for expression in the visceral mesoderm. *Mcp* and *Fab-7* refer to deletions in the mutants Miscadestral pigmentation and Frontabdominal-7. (From ref. 14).