BIOLOGY

Julie Ann Miller reports from the meeting in San Francisco of the first international Congress for Recombinant DNA Research

Standing room only on DNA bandwagon

It was supposed to be an intimate meeting — just a few hundred scientists sharing their latest research using recombinant DNA. But in the end more than 700 researchers and research observers paid a substantial registration fee to hear the all-star cast of speakers. Hundreds more would-be attendees were turned away. Chances for informal exchange, however, were abundant as the participants jammed in the hall waiting for overburdened hotel employees to rearrange the 700 chairs for a luncheon seating, back into a lecture hall configuration and then clear them to make room for pre-dinner poster presentations. Recent classmates, now dispersed through academia and industry, held impromptu reunions crowded between the portable no-host bars and the table where Georgetown University scientists were collecting data for a computer bank of gene sequences. The meeting attracted approximately equal numbers of representatives of the academic and the industrial-financial worlds. The gathering was sponsored not by a scientific society, but by a New York advertising and marketing firm and by a new publication on recombinant DNA research with which it is involved. While the talks occasionally mentioned practical prospects for the newly developed techniques, such as vaccines, drugs and agricultural applications, the emphasis was squarely on the mechanics of creating more and more powerful genetic tools and employing them to puzzle out the mystery still couched in living cells—how the activity of the millions of genes is coordinated and controlled.

Family matters

Not all gene families are as tightly knit as that of hemoglobin. The several genes for each subunit of the blood protein are close neighbors along a stretch of chromosome (SN: 12/27/80, p. 396). But the members of other gene families can be widely dispersed throughout genetic material, reports Brian McCarthy of the University of California at San Francisco. As in some human families, he suspects that the distances between members facilitates their individual expression.

Recognition of families of genes has been one important achievement of techniques using recombinant DNA. Families are comprised of genes sharing much of their nucleotide sequences, so they are thought to have evolved from duplications of a single gene. Members of a family may be active at different stages of development and some members may be "pseudogenes," which have no product at all. Among the gene families described at the San Francisco meeting were those of interferon (SN: 3/7/81, p. 148), the egg protein ovalbumin and transplantation antigens (see below).

McCarthy described two gene families in the fruit fly *Drosophila*. For actin, a protein important in muscle contraction and in movement of intracellular structures, McCarthy finds six genes dispersed throughout the insect's chromosomes. One of the genes is active only during the embryonic stage. Two of the genes have intervening sequences (stretches of DNA that do not code for any protein) in one position, and two others have intervening sequences elsewhere. When he compares the coding sequences of two of the *Drosophila* actin genes with those of actin in other organisms, McCarthy finds that they fall in between the genes characteristic of muscle and of cytoplasmic actin.

Another protein involved in movement is tubulin, a molecule comprised of two subunits. Using a probe DNA copied from a tubulin gene in chick brain, McCarthy finds in *Drosophila* four genes for the alpha subunit and four genes for the beta subunit. The alpha and beta genes are not paired up to facilitate coordinated subunit production. "They are simply scattered in a fashion that doesn't make sense," McCarthy reports. The tubulin genes have various patterns of activity. For example, one is expressed only in sperm and others only in the embryo. Why are there so many genes? Biologists have tended to assume the genes are finely adapted for specific tasks. McCarthy suggests that the greater control possible by individually turning on and off several genes may be more important than their molecular variations.

Cloning the genes for graft rejection

One challenging puzzle of biology has been the set of genes involved in rejection of tissue transplants. Last year the Nobel prize in medicine went to scientists responsible for describing some of the complexities of the genes and their products (SN: 10/18/80, p. 244). Now the powerful tool of recombinant DNA analysis is being focused on these genetic regions, called H-2 in mouse and HLA in the human cell. Because the genes are not active in the egg but are turned on soon thereafter in development, biologists consider their activation a good example of a very early event in differentiation.

"Brute force" was the approach that succeeded in producing bacteria that can reproduce a mouse H-2 gene, Philippe Kourilsky told the meeting. Only 0.02 percent of the messenger RNA in the tumor cells he used carried the relevant genetic information. "Cloning was a trivial matter of work and skill," he says. In their work at the Institut Pasteur in Paris, Kourilsky and colleagues discovered evidence for 10 to 20 genes or "pseudogenes" in an unexpectedly large family. They also obtained information about the gene product — a protein with three domains that spans the cell membrane. Other researchers have cloned in bacteria genes from the corresponding human chromosomal region. Yale scientists find evidence for a family of sequences that are repeated throughout the HLA complex and may be involved in the function of the genes.

The shaping of a fly

One of the most satisfying developmental sequences under study is the control of differentiation of the thoracic and abdominal segments of the fruit fly. A complex of ten genes has been identified; none are required to form the second thoracic segment (which seems to be the most basic style), but more and more genes are activated to direct correct development of the successively posterior segments. A mutant missing all ten genes, for example, develops into a uniform larva where all the segments are like the normal second thoracic segment (this mutant doesn't survive to adulthood). Another mutant has an extra third thoracic segment, and thus an extra set of legs, instead of a first abdominal segment. All the genes in the complex must be operative to form the eighth, most posterior abdominal segment.

David S. Hogness and colleagues at Stanford University are taking a close look at those genes with recombinant DNA techniques. They find that the spontaneous mutations, which turn a segment into a more anterior form, are not due to changes in a single nucleotide, but rather insertion of large segments of DNA into a gene. Preliminary work with fruit fly genes reproduced in bacteria has shown that the messenger RNA they produce does not represent contiguous regions on the fly chromosome. Hogness suggests that they reflect either special splicing of RNA or rearrangements of the genetic material, as in the development of antibody molecules (SN: 1/3/81, p. 6). He says the RNA must be produced at just the right times and places beginning very early in fly development to direct correctly the differentiation of the segments.