Perspectives

Anecdotal, Historical and Critical Commentaries on Genetics

Edited by James F. Crow and William F. Dove

Notes of a Bigamous Biologist

GENETICISTS, like other biologists, have a passionate attraction to organisms but, unlike their colleagues, they are usually monogamous, wedded to one organism for much of their careers. This fidelity is not a manifestation of dreamy romanticism, but rather a consequence of the dedication required to create a standard organism suitable for genetic studies. The emphasis is on "create" because, contrary to the common perception, good genetic organisms are not found in nature; they are shaped by geneticists. There are, however, intrinsically bad genetic organisms, those that have long life cycles and are difficult to study in the laboratory (whales) or those with no sexual stage (Penicillium). Clearly, one must begin with an organism that is easily cultured in the laboratory and has a tractable sexual cycle. But all the rest is hard work. Mutant strains must be designed so that the biochemistry, physiology, and even the genotype can be manipulated at will. Once the organism has been redesigned so that crosses, complementation, recombination and transformation can be carried out with facility, the modified organism can be used by all biologists. Witness the use of bacteriophage lambda, *Escherichia coli,* yeast and Drosophila in genetic engineering experiments by evolutionists, biophysicists, crystallographers and embryologists. None of these standard organisms exists in nature; all have been painstakingly altered to perform the scientist's bidding.

The goal of this single-minded devotion is the creation of a standard organism that can be used to reveal themes fundamental to all organisms or groups of organisms. A great deal is known about all bacteria because of the millions of laboratory hours that have been invested in a single bacterium, *E. coli.* The encyclopedic knowledge about *E. coli,* its genetics and biochemistry make it an invaluable standard, akin to the meter stick, against which other procaryotes and even eucaryotes can be compared. A system of knowledge based on the *E. coli* standard in no way diminishes our interest in other microorganisms. In fact, it intensifies interest and increases the quality of questions that can be posed. The answer to the question, "Is this like *E. coli*?" has profound meaning because the quality and quantity of work on this model organism elevate the criteria for comparison. If the answer is "Yes," then the question has been answered to a first approximation. If the answer is "No," then a new phenomenon has been uncovered. So fruitful has been this approach that geneticists are reluctant to stray from their model systems no matter how alluring another organism seems.

In view of this commitment to sophisticated genetic systems, it is impressive that many *E. coli,* yeast and Drosophila geneticists are initiating studies on the cruciform plant *Arabidopsis thaliana.* The attraction of Arabidopsis is the pioneering of a new paradigm for plants. As has been pointed out in several excellent reviews (Redei 1975; Meyerowitz and Pruitt 1985; Estelle and Somerville 1986), this flowering plant has many attributes that bode well for its use as an object of molecular-genetic research. It is easily cultivated, even in laboratories located in urban centers with erratic climatic conditions. Because of its small size and minimal nutritional requirements, it is possible to grow large numbers of plants in petri dishes or pots without recourse to greenhouse or field. When grown at room temperature and under constant illumination, a generation (seed → plant → seed) takes 5–6 weeks. The plants are self-fertilizing and extremely hardy, needing little tending to produce abundant seed (as many as 10^4/plant). Mutations can be identified among the progeny of plants derived from seed mutagenized with EMS.

In the laboratory, Arabidopsis is compatible with any of the other standard genetic organisms. Its ease of cultivation and modest demands on space relieve the domestic tensions usually engendered by such bigamous relationships. Although the duration of the Arabidopsis life cycle seems at first interminable to the microbial geneticist, it becomes less of a psychological shock as one learns to initiate experiments in parallel rather than in series. Once this new rhythm

has been acquired, the results arrive in the rapid succession to which microbial geneticists are accustomed.

Arabidopsis also has many biochemical features that facilitate the application of the powerful techniques of molecular genetics. It has a remarkably small genome (70,000 kb), only 15 times that of *E. coli*. The small genome coupled with the absence of substantial repeated DNA facilitates the cloning and mapping of genes. Several laboratories are mapping restriction polymorphisms and a high resolution RFLP map should be available soon. Of the handful of genes that have been cloned and sequenced, most are present in only one or two copies and either have but a few short introns or lack them completely. A seemingly trivial coincidence between the base composition of Arabidopsis DNA (41% G+C) and that of *Saccharomyces cerevisiae* provides a crucial route to the cloning of Arabidopsis genes. The identity in base composition between Saccharomyces and Arabidopsis means that the third-position codon biases (As and Ts) in Arabidopsis will be similar to those of Saccharomyces. Therefore, if there is extensive amino acid conservation between a Saccharomyces protein and an Arabidopsis protein, the Arabidopsis gene should have stretches of DNA sequences in common with the Saccharomyces gene. Indeed, several Arabidopsis genes have already been cloned by hybridization to a Saccharomyces gene. Vital information about the function of the newly cloned Arabidopsis gene can be inferred because the function of the cognate Saccharomyces gene is usually known.

Despite these attributes, many problems must be overcome before Arabidopsis can be considered a good genetic system. For one thing, there is a paucity of good genetic markers. Although many mutations have been isolated, few permit selection at the level of resolution required for reversion, recombination, and transformation experiments. This problem could be alleviated if auxotrophic mutations and the corresponding genes could be isolated. Second, there is no rapid method for constructing and maintaining the large numbers of heterozygotes required for the key genetic manipulations of complementation, recombination, and mutagenesis. Because Arabidopsis is naturally self-fertilizing, every outcross requires manual pollination, removing the anthers from one parent and subsequently dusting the stigma of that flower with mature anthers from the other parent. Moreover, the hybrid plant resulting from cross-fertilization will self, producing a genetically mixed population in the next generation. These difficulties could be resolved by constructing a set of strains containing balanced lethal chromosomes. Finally, the transformation system needs to be improved. A procedure for leaf-disc transformation with *Agrobacterium tumefaciens* has been worked out (LLOYD *et al.* 1986). However, transformation with Agrobacterium not only requires the regeneration of plants from transformed cells (a process that takes considerable time) but also occurs by nonhomologous integration events that preclude gene replacements. A more rapid transformation system that did not depend on Agrobacterium might uncover a route to homologous recombination. In the search for a strain that transforms well, many lines from different geographical locations have been introduced into the laboratory. It will be important to converge on one strain so that isogenicity can be maintained.

Progress in overcoming these problems should be rapid because Arabidopsis workers are enthusiastic and cooperative, freely exchanging strains, clones and information. The congenial atmosphere may be attributed to the character of the individual scientists as well as to the fact that, thus far, Arabidopsis has no known practical agricultural or medical value.

The day is not far off when scientists will say, "Is it like Arabidopsis?"

GERALD R. FINK
Whitehead Institute
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139

LITERATURE CITED

ESTELLE M. A., and C. R. SOMERVILLE, 1986 The mutants of *Arabidopsis*. Trends Genet. **2:** 89–93.

LLOYD, A. M., A. R. BARNASON, S. G. ROGERS, M. C. BYRNE, R. T. FRALEY and R. B. HORSCH, 1986 Transformation of *Arabidopsis thaliana* with *Agrobacterium tumifaciens*. Science **234:** 464–466.

MEYEROWITZ, E. M., and R. E. PRUITT, 1985 *Arabidopsis thaliana* and plant molecular genetics. Science **229:** 1214–1218.

REDEI, G. P., 1975 *Arabidopsis* as a genetic tool. Annu. Rev. Genet. **9:** 111–127.