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Biological Systems

The proper study of mankind may well be the fly, the frog, the bacterium, and the nematode, as well as the rat, the ape, and mankind itself, because studies of specific biological systems have taken a central role in modern biology. This has not always been true; originally biology emphasized taxonomy and the diversity of species. As the number of identified species increased, the similarities among differing species were noted, and more in-depth studies of individual species were appropriate. Gradually certain systems became preferred models for biological systems in general, a tendency which has been accentuated as molecular approaches have become the lingua franca of modern biology.

The concept of selecting a common system for in-depth study emerged slowly. In some disciplines it was once considered poor etiquette to work on a colleague's system: if he or she used the toad, you used the frog. That practice led to great inefficiency, because the details of manipulating any system—how to grow the organism, the chemistry of the cell wall, mating habits—had to be worked out over and over again. Therefore, workers focused on a few systems such as *Escherichia coli, Drosophila melanogaster*, or inbred mice, in which many of the important housekeeping procedures had been elucidated. In this issue of *Science* some of the major experimental systems are described in terms of the state of the art, potential advantages, and possible disadvantages.

Of the systems outlined here, retroviruses, bacteria, and yeast are the simplest, most manipulatable, and most intensively delineated. Retroviruses (Varmus) are revealing per se as well as being useful tools for gene delivery into other systems. Magasanik, while pointing out the past triumphs of using bacteria to understand regulation, metabolism, and genetics, indicates there is much gold still to be mined and gives examples. Yeasts are essentially on a par with bacteria in ease of recombinant DNA manipulation, but—as indicated by Botstein and Fink—it is their complexity, as in cell compartments, cell cycle regulation, and protein sorting, that makes them valuable as eukaryotic models.

Higher on the evolutionary ladder, the nematode, the fly, and the frog have the advantage of complexity beyond the single cell, but represent far simpler species than mammals. Every cell can be identified in the nematode (Kenyon), which makes it ideal for cell lineage studies. Studies in *Drosophila* (Rubin) can now use recombinant DNA, genetic selection, and a history of neurologic and developmental information. The frog (Dawid and Sargent) is a historical system for studying development; the frog oocyte has become a major system for expression of foreign RNA and DNA. Plants have a special role (Goldberg) because of the importance of botanical species and because of their novel developmental processes, among them the capacity for mature cells to regenerate.

Eventually, one must have mammalian studies, and those of the rat, the ape, and the human are three of the most important. Transgenic animals (Jaenisch), particularly transgenic mice, have become major tools for studying the effects of individual genes on the whole animal and permit the generation of precise animal models for human genetic diseases. For understanding of many human responses, primates (King *et al.*) are clearly the best source, but dealing with these large and sophisticated animals makes them a court of last resort; it is always necessary to consider whether alternative systems are available.

Then, of course, there is mankind. Human beings are capable of describing emotional states as well as physical conditions such as pain, they can often provide generations of family history, and they can reveal multitudinous clinical data (White and Caskey). Defensive medicine may thus be an unexpected boon to research. In their Perspective, Sladek and Shoulson present views on the need for caution in attempting to realize the great potential of transplantation of fetal material for human therapy.

The assembly of a *Science* special issue involves the efforts of many, but one editor traditionally takes the lead. In this case, Barbara Jasny came close to editorial heroism in surmounting difficulties that arose in production; she played vital roles in the selection of topics, special assistance to authors, and the editing of final manuscripts.

It is our intention to add some of the systems that have been missed because of the limitations of space in this issue to a final volume on biological systems. We hope, however, that this initial set of articles will be useful to all our readers, from graduate students to research directors to general readers who seek a more thorough understanding of specialty systems.—DANIEL E. KOSHLAND, JR.