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EDITORIAL

In Transition

In many ways, this has been a year of transition for the Genome Project, and this issue of *Science* highlights some of the changes that are occurring. Emphasis is shifting from physical mapping to large-scale sequencing. As more sequences become available, even databases of entire genomes, researchers are beginning to ask new kinds of questions and look for simpler and more rapid ways to convert nucleotide arrays into an understanding of gene expression. At an increasing rate, information about genes is being translated from the research lab to the clinic and is leading to growing concerns about the uses of genetic information. The Genome issue itself is undergoing some changes with the advent of electronic communication. The special chart in the issue will also appear in the "Beyond the Printed Page" section of *Science*'s home page (http://www.aaas.org/science/science.html). We also will offer electronic discussions in which readers can comment on the two controversial Policy Forums appearing this week. Finally, we will provide links to databases detailing the newly reported sequence of *Mycobacterium genitalium* and the physical map of chromosome 4 of *Arabidopsis*.

The effort to generate a physical map of the human genome has created its own momentum, but at what point should the community decide that the maps are good enough and that it is time to move on to the next goals? Maynard Olson believes that the time is right for a major drive to complete the sequence, but not all of Olson's colleagues will agree with the conclusion in his Policy Forum that the maps and technology are good enough to justify such a frontal assault, or that it is appropriate to divert resources from other projects.

Now that the second complete sequence of a free-living organism, *M. genitalium*, has been published (Fraser *et al.*), the field of comparative genomics is ready for a giant leap. The sequences of other small organisms will soon be available, as discussed by André Goffeau in his Perspective. Comparisons should provide insights into the basic systems necessary for life and for differentiated function.

It has been my experience that investigators who deal with model systems tend to be chauvinistic about their beasts. The authors of this year's wall chart were no exception. As one of the authors told me in the early stages of the project, "When this comes out, everyone will be suffering from worm envy!" For the genome community, the *Caenorhabditis elegans* project has been a paradigm of a group effort to reach a well-delineated goal. It is also a model system with great potential for exploration of developmental biology, cell biology, and neurobiology. The surprising finding that a *C. elegans* gene is a significant homolog of a human gene involved in early-onset Alzheimer's disease is an example of the potential insights into human disease to be gained from the study of model systems.

Demonstration of successful gene therapy in humans is one of the cherished ideals of the Genome Project. Although gene therapy has not yet cured any human disease, considerable progress has been made, as reviewed by Ronald Crystal. Long-awaited results (Bordignon *et al.* and Blaese *et al.*) relating to adenosine deaminase gene therapy for severe combined immunodeficiency are also described in this issue. These studies show that long-term in vivo expression of the transgene can safely be attained in patients, but the interpretation of clinical effects is not straightforward. It is important to emphasize that a clinical trial represents one step in the process, not the end of the road. Information may pass from clinical trials to research laboratories and back again many times before success is achieved.

The health care system in the United States is also in a time of transition and (hopefully) evolution as society discovers technological approaches to treatment of diseases but shudders at the associated costs. Increased costs mean that the prospect of loss of health insurance can be as frightening and damaging to a family as an illness itself. Members of a National Institutes of Health–Department of Energy Working Group and the National Action Plan on Breast Cancer have issued a set of recommendations in a Policy Forum by Kathy Hudson *et al.* for state and federal agencies trying to deal with the new dimension that genetic information adds to the health care problem. If these recommendations were followed, genetic information, including family histories, could not be used to establish insurance premiums or eligibility. Generating the sequences may prove to be the easy part; assimilating the implications of our genetic heritage in a way that will benefit individuals and society is the real challenge.

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