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Landing on the Genome

This year marks a turning point in the progress of the genome project, as aptly illustrated by this Genome Issue. The first genome of a model eukaryote, yeast, has been fully sequenced, an achievement that has large implications for biology as a whole (Goffeau *et al.*, p. 563). In addition, the structural mapping phase of the human genome project is approaching its goal: The transcript map, the first version of which is presented as a special chart and discussed in a review article (Schuler *et al.*, p. 540), complements previous genetic and physical mapping efforts and is a substantial improvement for all those interested in identifying disease genes. The value of this transcript map in searching for disease genes has long been known, but the means of producing it only became evident in the past few years. The hundreds of thousands of partial complementary DNA sequences available today, together with mapping based on analysis of collections of radiation hybrids, have permitted the localization of 16,000 genes in only 1 year. By next year, we hope that more than half the human genes will be positioned on this map.

Although the transcript map is an important addition to the scaffold for sequencing efforts, we are still in need of sequence-ready maps for most of the human chromosomes. An attractive alternative that obviates this requirement has recently been proposed by J. C. Venter, H. O. Smith, and L. Hood.* Their approach, based on sequencing the ends of large DNA fragments, theoretically allows for rapid assembly of the sequence data. The need for sequencing is becoming more and more urgent, as evidenced by Great Britain's huge investment in sequencing one-sixth of the human genome. Publicly funded pilot sequencing projects have been initiated in the United States, Germany, and Japan; and France is also in the process of setting up a sequencing center. The private sector has entered the sequencing arena and will no doubt contribute substantially to this work, although uncertainties remain as to when and under what conditions the information will be publicly available.

The human transcript map was produced in a semi-industrial manner in a few large genome centers. This was made possible by an unprecedented level of international collaboration under the leadership of the Human Genome Organization. The sequencing of the yeast genome was also the result of a multinational collaboration but was done by a network of academic laboratories with a direct interest in the biology of some of the sequenced genes. The availability of the yeast sequence has probably convinced the remaining skeptics that it is indeed worth knowing the entire sequence of an organism's genome. Yeast biologists can now examine a plethora of genes whose function remains elusive, and the entire yeast protein complement is at hand as well. We are looking forward to the full deciphering of the *Caenorhabditis elegans* genome, which is scheduled for 1998 and will open up opportunities for approaching fundamental questions in neurobiology and developmental biology.

Despite the ever-increasing avalanche of data, we are still frustrated because not all of the information is accessible. For instance, links between different sets of data are difficult to retrieve or are missing from databases. In addition, the question of timeliness of data release is a subject of lively debate, as seen in the pair of Policy Forums in this issue. Should the quasi-raw data be accessible as soon as it is produced (Bentley *et al.*, p. 533), or should it first be validated and properly annotated (Adams *et al.*, p. 534)? The argument for immediate or at least rapid release is not new; major U.S. mapping centers have previously been urged to do so by funding agencies. Data annotation is a never-ending process, and I feel that science has more to gain than to lose from rapid public dissemination of data.

Genomic sequencing is the first step in the establishment of the genetic periodic table, as proposed by E. Lander in his Policy Forum (p. 536). This knowledge will no doubt change our perception of biology, just as in the 16th century the exploration of our planet changed the human perception of the world. New challenges are emerging in this transition from a structural to a functional phase. The approaches that are currently available are limited, and new concepts for addressing the issues of functional genomics and for understanding a living organism as a whole will be required. The 21st century promises to be extremely exciting for all those interested in biology and its applications.

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