produced at Los Alamos National Laboratory (LANL) and Lawrence Livermore National Laboratory (LLNL). These libraries allowed the huge task of mapping and sequencing the entire 3 billion bases in the human genome to be broken down into 24 much smaller single-chromosome units. Availability of the libraries has enabled the participation of many laboratories worldwide. Some three generations of clone libraries with improving characteristics have been produced and widely distributed. In the DOE-supported projects, DNA clones representing chromosomes 16, 19, and 22 have been ordered (mapped) and are now providing material needed for large-scale sequencing.

Sequencing

Toward the goal of greatly increasing the speed and decreasing the cost of DNA sequencing, DOE has supported improvements in standard technologies and has pioneered support for revolutionary sequencing systems. Marked improvements have been made in reagents, enzymes, and raw data quality. Such novel approaches as sequencing by hybridization (using DNA "chips") and mass spectrometry have already found important, previously unanticipated applications outside the Human Genome Project.

Joint Genome Institute

In early 1997, the human genome centers at Lawrence Berkeley National Laboratory, LANL, and LLNL began collaborating in the Joint Genome Institute (JGI), within which high-throughput sequencing will be implemented [see p. 26 and *Human Genome News* **8**(2), 1–2]. The initial JGI focus will be on sequencing areas of high biological interest on several chromosomes, including human chromosomes 5, 16, and 19. Establishment of JGI represents a major transition in the DOE Human Genome Program.

Previously, most goals were pursued by small- to medium-sized teams, with modest multisite collaborations. The JGI will house high-throughput implementations of successful technologies that will be run with increasingly stringent process- and quality-control systems.

In addition, a small component aimed at understanding how genes function in the body—a field known as functional genomics—has been established and will grow as sequencing targets are met. High-throughput functional genomics represents a new era in human biology, one which will have profound implications for solving biological problems.

Informatics

In preparation for the production-sequencing phase, many algorithms for interpreting DNA sequence have been developed, and an increasing number have become available as services over the Internet. Last year, the GRAIL (for Gene Recognition and Analysis Internet Link) and GenQuest servers, developed and maintained at Oak Ridge National Laboratory, processed an average of almost 40 million bases of sequence each month.

As technology improves and data accumulates exponentially, continued progress in the Human Genome Project will depend increasingly on the development of sophisticated computational tools and resources to manage and interpret the information. The ease with which researchers can access and use the data will provide a measure of the project's success. Critical to this success is the creation of interoperable databases and other computing and informatics tools to collect, organize, and interpret thousands of DNA clones.

For additional information on the DOE genome programs, refer to Research Highlights, p. 9; Research Narratives, p. 25; this report's *Part 2, 1996 Research Abstracts*; and the Web site (*http://www.ornl.gov/hgmis*).