Lawrence Berkeley National Laboratory Human Genome Center

http://www-hgc.lbl.gov/GenomeHome.html

Since 1937 the Ernest Orlando Lawrence Berkeley National Laboratory (LBNL) has been a major contributor to knowledge about human health effects resulting from energy production and use. That was the year John Lawrence went to Berkeley to use his brother Ernest's cyclotrons to launch the application of radioactive isotopes in biological and medical research. Fifty years later, Berkeley Lab's Human Genome Center was established.

Now, after another decade, an expansion of biological research relevant to Human Genome Project goals is being carried out within the Life Sciences Division, with support from the Information and Computing Sciences and Engineering divisions. Individuals in these research projects are making important new contributions to the key fields of molecular, cellular, and structural biology; physical chemistry; data management; and scientific instrumentation. Additionally, industry involvement in this growing venture is stimulated by Berkeley Lab's location in the San Francisco Bay area, home to the largest congregation of biotechnology research facilities in the world.

In July 1997 the Berkeley genome center became part of the Joint Genome Institute (see p. 26).

Sequencing

Large-scale genomic sequencing has been a central, ongoing activity at Berkeley Lab since 1991. It has been funded jointly by DOE (for human genome production sequencing and technology development) and the NIH National Human Genome Research Institute [for sequencing the *Drosophila melanogaster* model system, which is carried out in partnership with the University of California, Berkeley (UCB)]. The human genome sequencing area at Berkeley Lab consists of five groups: Bioinstrumentation, Automation, Informatics, Biology, and Development. Complementing these activities is a group in Life Sciences Division devoted to functional genomics, including the transgenics program.

The directed DNA sequencing strategy at Berkeley Lab was designed and implemented to increase the efficiency of genomic sequencing (see figure, p. 45). A key element of the directed approach is maintaining information about the relative positions of potential sequencing templates throughout the entire sequencing process. Thus, intelligent choices can be made about which templates to sequence, and the number of selected templates can be kept to a minimum. More important, knowledge of the interrelationship of sequencing runs guides the assembly process, making it more resistant to difficulties imposed by repeated sequences. As of July 3, 1997, Berkeley Lab had generated 4.4 megabases of human sequence and, in collaboration with UCB, had tallied 7.6 megabases of *Drosophila* sequence.

Instrumentation and Automation

The instrumentation and automation program encompasses the design and fabrication of custom apparatus to facilitate experiments, the programming of laboratory robots to automate repetitive procedures, and the development of (1) improved hardware to extend the applicability range of existing commercial robots and (2) an integrated operating system to control and monitor experiments. Although some discrete instrumentation modules used in the integrated protocols are obtained commercially, LBNL designs its own custom instruments when existing capabilities are inadequate. The instrumentation modules are then integrated into a large system to facilitate large-scale production sequencing. In addition, a significant effort is devoted to improving

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In lieu of individual abstracts, research projects and investigators at the LBNL Human Genome Center are represented in this narrative. More information can be found on the center's Web site (see URL above).

Update

In 1997 Lawrence Berkeley National Laboratory, Lawrence Livermore National Laboratory, and Los Alamos National Laboratory began collaborating in a Joint Genome Institute to implement high-throughput sequencing [see p. 26 and *Human Genome News* 8(2), 1–2].

*Now at Amgen, Inc.