

Biological research was initiated at Los Alamos National Laboratory (LANL) in the 1940s, when the laboratory began to investigate the physiological and genetic consequences of radiation exposure. Eventual establishment of the national genetic sequence databank called GenBank, the National Flow Cytometry Resource, numerous related individual research projects, and fulfillment of a key role in the National Laboratory Gene Library Project all contributed to LANL's selection as the site for the Center for Human Genome Studies in 1988.

Center Organization and Activities

The LANL genome center is organized into four broad areas of research and support: Physical Mapping, DNA Sequencing, Technology Development, and Biological Interfaces. Each area consists of a variety of projects, and work is distributed among five LANL Divisions (Life Sciences; Theoretical; Computing, Information, and Communications; Chemical Science and Technology; and Engineering Sciences and Applications). Extensive interdisciplinary interactions are encouraged.

Physical Mapping

The construction of chromosome- and region-specific cosmid, bacterial artificial chromosome (BAC), and yeast artificial chromosome (YAC) recombinant DNA libraries is a primary focus of physical mapping activities at LANL. Specific work includes the construction of high-resolution maps of human chromosomes 5 and 16 and associated informatics and gene discovery tasks.

Accomplishments

- Completion of an integrated physical map of human chromosome 16 consisting of both a low-resolution YAC

contig map and a high-resolution cosmid contig map (pp. 37–39). With sequence tagged site (STS) markers provided on average every 125,000 bases, the YAC-STS map provides almost-complete coverage of the chromosome's euchromatic arms. All available loci continue to be incorporated into the map.

- Construction of a low-resolution STS map of human chromosome 5 consisting of 517 STS markers regionally assigned by somatic-cell hybrid approaches. Around 95% mega-YAC-STS coverage (50 million bases) of 5p has been achieved. Additionally, about 40 million bases of 5q mega-YAC-STS coverage have been obtained collaboratively.
- Refinement of BAC cloning procedures for future production of chromosome-specific libraries. Successful partial digestion and cloning of microgram quantities of chromosomal DNA embedded in agarose plugs. Efforts continue to increase the average insert size to about 100,000 bases.

DNA Sequencing

DNA sequencing at the LANL center focuses on low-pass sample sequencing (SASE) of large genomic regions. SASE data is deposited in publicly available databases to allow for wide distribution. Finished sequencing is prioritized from initial SASE analysis and pursued by parallel primer walking. Informatics development includes data tracking, gene-discovery integration with the Sequence Comparison ANalysis (SCAN) program, and functional genomics interaction.

Accomplishments

- SASE sequencing of 1.5 million bases from the p13 region of human chromosome 16.
- Discovery of more than 100 genes in SASE sequences.

Center for Human Genome Studies

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In lieu of individual abstracts, research projects and investigators at the LANL Center for Human Genome Studies 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].

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