

Lawrence Livermore National Laboratory Human Genome Center

Human Genome Center
Lawrence Livermore National Laboratory
Biology and Biotechnology Research Program
7000 East Avenue, L-452
Livermore, CA 94551

Anthony V. Carrano, Director
510/422-5698, Fax: /423-3110, carrano1@llnl.gov

Linda Ashworth, Assistant to Center Director
510/422-5665, Fax: -2282, ashworth1@llnl.gov

<http://www-bio.llnl.gov/bbrp/genome/genome.html>

The Human Genome Center at Lawrence Livermore National Laboratory (LLNL) was established by DOE in 1991. The center operates as a multidisciplinary team whose broad goal is understanding human genetic material. It brings together chemists, biologists, molecular biologists, physicists, mathematicians, computer scientists, and engineers in an interactive research environment focused on mapping, DNA sequencing, and characterizing the human genome.

Goals and Priorities

In the past 2 years, the center's goals have undergone an exciting evolution. This change is the result of several factors, both intrinsic and extrinsic to the Human Genome Project. They include: (1) successful completion of the center's first-phase goal, namely a high-resolution, sequence-ready map of human chromosome 19; (2) advances in DNA sequencing that allow accelerated scaleup of this operation; and (3) development of a strategic plan for LLNL's Biology and Biotechnology Research Program that will integrate the center's resources and strengths in genomics with programs in structural biology, individual susceptibility, medical biotechnology, and microbial biotechnology.

The primary goal of LLNL's Human Genome Center is to characterize the mammalian genome at optimal resolution and to provide information and material resources to other in-house or collaborative projects that allow exploitation of genomic biology in a synergistic manner. DNA sequence information provides the biological driver for the center's priorities:

- Generation of highly accurate sequence for chromosome 19.
- Generation of highly accurate sequence for genomic regions of high biological interest to the mission of the DOE Office of Biological and Environmental Research (e.g., genes involved in DNA repair, replication, recombination, xenobiotic metabolism, and cell-cycle control).
- Isolation and sequence of the full insert of cDNA clones associated with genomic regions being sequenced.

- Sequence of selected corresponding regions of the mouse genome in parallel with the human.
- Annotation and position of the sequenced clones with physical landmarks such as linkage markers and sequence tagged sites (STSs).
- Generation of mapped chromosome 19 and other genomic clones [cosmids, bacterial artificial chromosomes (BACs), and P1 artificial chromosomes (PACs)] for collaborating groups.
- Sharing of technology with other groups to minimize duplication of effort.
- Support of downstream biology projects, for example, structural biology, functional studies, human variation, transgenics, medical biotechnology, and microbial biotechnology with know-how, technology, and material resources.

Center Organization and Activities

Completion and publication of the metric physical map of human chromosome 19 in 1995 has led to consolidation of many functions associated with physical mapping, with increased emphasis on DNA sequencing. The center is organized into five broad areas of research and support: sequencing, resources, functional genomics, informatics and analytical genomics, and instrumentation. Each area consists of multiple projects, and extensive interaction occurs both within and among projects.

Sequencing

The sequencing group is divided into several subprojects. The core team is responsible for the construction of sequence libraries, sequencing reactions, and data collection for all templates in the random phase of sequencing. The finishing team works with data produced by the core team to produce highly redundant, highly accurate "finish" sequence on targets of interest. Finally, a team of researchers focuses specifically on development, testing, and implementation of new protocols for the entire group, with an emphasis on improving the efficiency and cost basis of the sequencing operation.