

## Progress to Date

### Chromosome 5

Over the last year, the center has focused its production genomic sequencing on the distal 40 megabases of the human chromosome 5 long arm. This region was chosen because it contains a cluster of growth factor and receptor genes and is likely to yield new and functionally related genes through long-range sequence analysis. Results to date include:

- 40-megabase nonchimeric map containing 82 yeast artificial chromosomes (YACs) in the chromosome 5 distal long arm.
- 20-megabase contig map in the region of 5q23-q33 that contains 198 P1s, 60 P1 artificial chromosomes, and 495 bacterial artificial chromosomes (BACs) linked by 563 sequenced tagged sites (STSs) to form contigs.
- 20-megabase bins containing 370 BACs in 74 bins in the region of 5q33-q35.

### Chromosome 21

An early project in the study of Down syndrome (DS), which is characterized by chromosome 21 trisomy, constructed a high-resolution clone map in the chromosome 21 DS region to be used as a pilot study in generating a contiguous gene map for all of chromosome 21. This project has integrated P1 mapping efforts with transgenic studies in the Life Sciences Division. P1 maps provide a suitable form of genomic DNA for isolating and mapping cDNA.

- 186 clones isolated in the major DS region of chromosome 21 comprising about 3 megabases of genomic DNA extending from D21S17 to ETS2. Through cross-hybridization, overlapping P1s were identified, as well as gaps between two P1 contigs, and transgenic mice were created from P1 clones in the DS region for use in phenotypic studies.

## Transgenic Mice

One of the approaches for determining the biological function of newly identified genes uses YAC transgenic mice. Human sequence harbored by YACs in transgenic mice has been shown to be correctly regulated both temporally and spatially. A set of nonchimeric overlapping YACs identified from the 5q31 region has been used to create transgenic mice. This set of transgenic mice, which together harbor 1.5 megabases of human sequence, will be used to assess the expression pattern and potential function of putative genes discovered in the 5q31 region. Additional mapping and sequencing are under way in a region of human chromosome 20 amplified in certain breast tumor cell lines.

## Resource for Molecular Cytogenetics

Divining landmarks for human disease amid the enormous plain of the human genetic map is the mission of an ambitious partnership among the Berkeley Lab; University of California, San Francisco; and a diagnostics company. The collaborative Resource for Molecular Cytogenetics is charting a course toward important sites of biological interest on the 23 pairs of human chromosomes (<http://rmc-www.lbl.gov>).

The Resource employs the many tools of molecular cytogenetics. The most basic of these tools, and the cornerstone of the Resource's portfolio of proprietary technology, is a method generally known as "chromosome painting," which uses a technique referred to as fluorescence in situ hybridization or FISH. This technology was invented by LBNL Resource leaders Joe Gray and Dan Pinkel.

A technology to emerge recently from the Resource is known as "Quantitative DNA Fiber Mapping (QDFM)." High-resolution human genome maps in a form suitable for DNA sequencing traditionally have been constructed by

