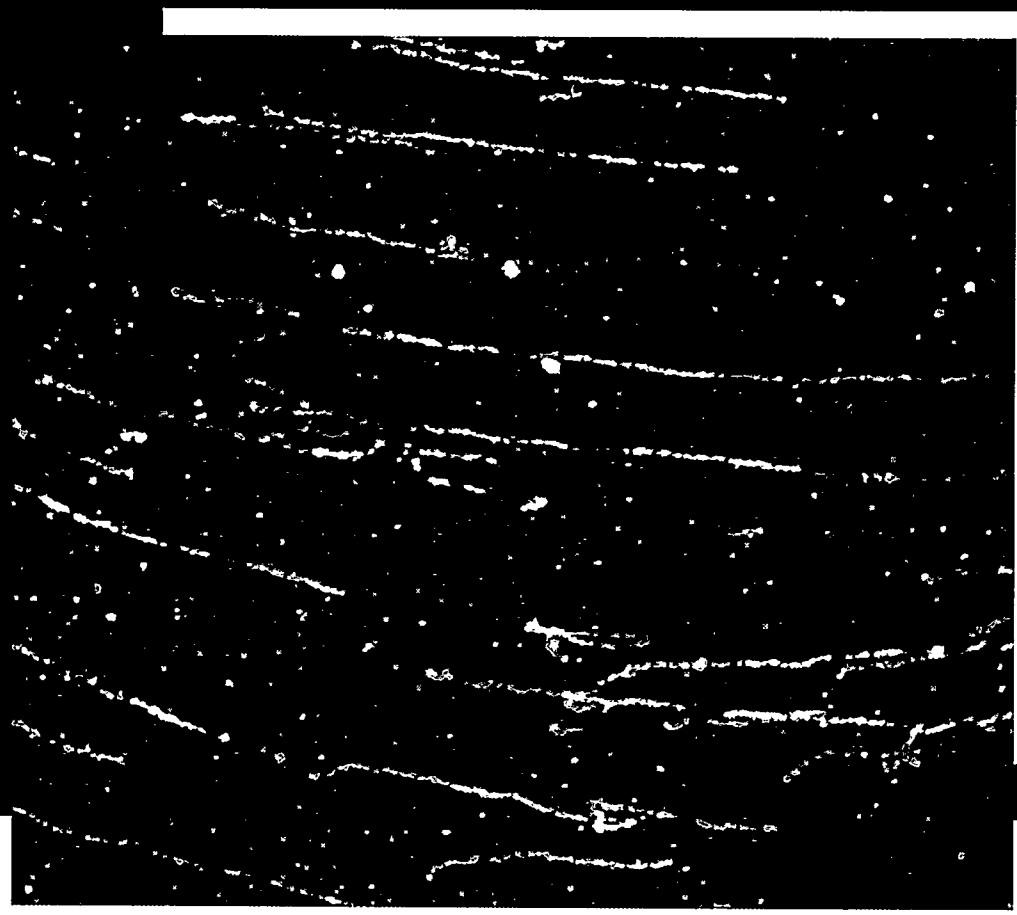
300,000 base pairs) facilitates both mapping and sequencing. Their usefulness was illustrated dramatically in 1993 when the first breast cancer–susceptibility gene (*BRCA*1) was found in a BAC clone after other types of resources had failed. The next year, with major support from NIH, de Jong's PACs contributed to the isolation of the second human breast cancer–susceptibility gene (*BRCA*2).

Mapping

The assembly of ordered, overlapping sets (contigs) of high-quality clones has long been considered an essential step toward human genome sequencing. Because the clones have been mapped to precise genomic locations, DNA sequences obtained from them can be located on the chromosomes with minimal uncertainty.

The large insert size of BACs and PACs allows researchers to visually map them on chromosomes by using fluorescence in situ hybridization (FISH) technology (see photomicrograph below). These mapped BACs and PACs represent very valuable resources for the cytogeneticist exploring chromosomal abnormalities. Two major medical genetics resources have been developed: (1) The Resource for Molecular Cytogenetics at the University of California, San Francisco, in collaboration with the Lawrence Berkeley National Laboratory (LBNL) team led by Joe Gray (*http://rmc-www.lbl.gov*) and (2) The Total Human Genome BAC-PAC Resource at Cedars-Sinai Medical Center, Los Angeles, developed by Julie Korenberg's laboratory (see map, p. 12, and Web site, *http://www.csmc.edu/genetics/korenberg/korenberg.html*).



FISH Mapping on DNA Fibers. The fluorescence microscope reveals several individual cloned DNA fibers from yeast artificial chromosomes (YACs, in blue) after molecular combing to attach and stretch the DNA molecules across a glass microscope slide. Also shown are the locations of two P1 clones, labeled green and red, mapped onto the YAC fibers using FISH. Digital imaging technology can be used to assemble physical maps of chromosomes with a resolution of about 3 to 5 kilobases. [Source: Joe Gray, University of California, San Francisco]