Human Genome Project: Progress and Prospect

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Improvement of automated sequencing technology has made tremendous progress in recent years, particularly in the areas of throughput capacity, data quality and operational reliability. As a result, by mid-1999 the international efforts in large-scale sequencing has completed several projects; including about 20 bacterial genomes (those <5 Mb's), yeast (12 Mb), nematode (C. elegans, 97 Mb), 35% of Arabidopsis (~100 Mb), and approximately 400 megabases or 13% of human (~3,000 Mb). Interestingly a major portion of these data (~80%) was elucidated only within the last couple years, indicating a trend that the automated sequencing efficiency has just entered an exponentially growing stage. With that trend continues, the latest released capillary-based equipment can increase the sequencing efficiency by at least 5 folds. Combined with the advanced data management and processing systems, it is increasingly possible that the human genome can be sequenced by 2001 through the efforts involving both public and commercial organizations.

During 1998, commercial company joined the race to sequence the human genome. Founded in May, 1998, Celera Genomics plans to sequence Drosophila, human, rice and mouse genomes starting in the middle of 1999 using whole genome shotgun sequencing strategy. It will likely yield additional novel and rarely expressed genes, as well as millions of polymorphism information. The company is adopting a policy to make its Drosophila and human sequence data available to the research community for free.

With the participation of commercial organizations in genomic sequencing, the annual investment for that activity is now reaching >$400 million US dollars. The combined total throughput is estimated to be >600 Mb/year for 1999, and it will likely continue to grow in the subsequent years. Many large genomes will be sequenced during early 21st century. Thus, with enormous volume of genomic sequence information becoming available, the challenge is shifting towards the downstream sequence interpretation and functional investigations in the modern era of genomes in biological research.

Recent Advances in Cytogenetics

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Chromosomal abnormalities are a leading cause of genetic diseases including congenital disorders and acquired disease such as cancer. One significant technical limitation of conventional chromosome banding analysis is the inability to characterize unequivocally all cytogenetically visible chromosome rearrangements such as unknown marker chromosomes and unidentifiable *de novo* unbalanced translocations. Recently, molecular cytogenetic techniques such as fluorescence in situ hybridization (FISH), chromosome microdissection, and comparative genomic hybridization (CGH) have been widely applied in cytogenetic study. The application of these techniques overcomes the limitation of conventional cytogenetic techniques in identification of complex chromosomal rearrangements. After many efforts, chromosome microdissection has been developed into a useful and reproducible approach to directly detect virtually any kind of visible chromosome rearrangements and to generate different FISH painting probes including whole chromosome, chromosome arm, and band-specific painting probes for cytogenetic study. CGH is an approach to analyze the entire genome for regional variations of DNA sequence copy number (gain, loss and amplification of DNA sequences) in a single experiment. This technique has been widely applied to detect recurrent copy number changes and highlight chromosomal regions containing genes that contribute to cancer development and progression. The application of these techniques will greatly facilitate cytogenetic study.