assembled so far, two are from the chromosome 16 region, the rest are from the chromosome 4 region. Five of the thirty clones formed a contiguous contig (M-K-D-B-C) for the chromosome 4q22 region, while the other are scattered in the genetic interval of D4S1544-D4S1564. The precise locations of these clones await further mapping. We have submitted a contiguous stretch of 456 kb of non-overlapping sequence to the public database. To present the data to the public, we have registered our Yang-Ming Genome Center (YMGC) to HGSI (Human Genome Sequencing Index: http://www.ncbi.nlm.nih.gov/HUGO/) and provided URL (http://genome.ym.edu.tw/ and http://www.genome.org.tw/) for Internet browsing.

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The DNA sequence of human chromosome 22

A.R. Hunt on behalf of the Sanger Centre
Chromosome 22 project group

One the 1 December 1999 an international consortium of sequencing centres completed the sequence of the first human chromosome, chromosome 22 (Dunham et al Nature 402, 489-495 (1999). Presented here will be a brief overview of the work with specific emphasis on the Sanger Centre's sequencing effort.

Chromosome 22 is the second smallest of the human autosomes. The short arm (22p) contains a series of tandem repeat structures including the ribosomal RNA gene cluster, and is highly similar to the short arms of chromosomes 13, 14, 15 and 21. The long arm (22q) is the portion of the human chromosome 22 that contains the protein coding genes and was targeted for sequencing.

Extensive clone maps of chromosome 22 were derived by adopted a clone by clone approach using cosmids, fosmids, bacterial artificial chromosomes (BACs) and P1-derived artificial chromosomes (PACs). The sequence-ready map covers 22q in 11 clone contigs with 10 gps and stretches from sequences containing known chromosome 22 centromeric tandem repeats to the 22q telomore.

The sequence was then determined for a representative set of clones that completely covered the map by a method of shotgun subcloning into M13 and pUC vectors and sequencing using fluorescent dye primer and dye terminator chemistries. Resulting sequences, ca 1500 reads/100kb, were assembled using the automated script phrap2gap. The assemblies were then viewed and assessed in the resulting database and directed sequencing performed to close gaps and resolve ambiguities (finishing'). The major problems encountered during completion of the sequences were CqG islands, tandem repeats and apparent cloning biases. Directed sequencing using oligonucleotide primers, very short insert plasmid libraries, or identification of bridging clones by screening high complexity plasmids or M13 libraries solved these problems.

The completed sequence consists of 12 contiguous segments (the additional gap being intractable to sequence) covering 33.4 million bps separated by 11 gaps of known size. This sequence is estimated to cover 97% of 22q, and is complete to the limits of currently available reagents and methodologies. The largest continuous contig is >23 million bps, and to our knowledge at the time of writing, this is the largest continuous sequence ever determined.

For further chromosome 22 related information visit: http://www.sanger.ac.uk/HGP/Chr22/

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The Resource Center of the German Human Genome Project: Screening Service

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As the central infrastructure unit of the German Human Genome project the Resource Center/Primary Database (RZPD) has been funded by the Federal Ministry of Education and Research (BMBF) since 1995. It Is jointly operathed by the MaxPlanckInstitute for Molecular Genetics (Dept. Hans Lehrach) in Berlin and the Deutsches Krebsfnrschungszentrum (Dept. Annemarie Poustka) in Heidelberg.

The screening service of the Resource Center carries out gene identification experiments upon requests of national and international research groups in academy and industry. Probes are send by the customers via mail and the screening service takes over the entire issues of planning and carrying out hybridisation experiments, data analysis and data management. More than 200 cDNA and genomic libraries of different species currently stored at the Resource Center can be requested for screening experiments by hybridisation or PCR. Experiments are planned and performed individually depending on the demands of the user (e.g. species to species hybridisations, cross species hybridisations, hybridisations with complex probes). Identified clones are directly send to the user. Since 1996 when the screening service took up Its work, the number of requests increased steadily. Currently, we perform about 400 requests per year leading to the isolation of approximately 2000 positive cDNA or genomic clones / year.

With roughly half of all human genes represented in EST databases, the focus of human genome research Is shifting towards expression profiling of these genes to correlate gene expression with phenotype. The Unigene set of all human genes and gene sets of other model organisms which are made available through the Resource Center provide unique and powerful tools for the complex analysis of genes and gene networks. Thus, we currently implement this new technology In routine application in order to offer expression profiling as a service for the customers of the RZPD.

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Isolation and the Complete Sequence of the Human 6-Pyruvoyl-tetrahydropterin Synthase Gene Containing BAC clone 321H15.

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Hyperphenylalaninemia (HPA) may be caused by deficiency of phenylalanine hydroxylase or tetrahydrobiopterin (BH), the essential cofactor for the aromatic amino acid hydroxylases. 6-Pyruvoyl-tetrahydropterin synthase (PTPS) deficiency is a major cause of BH-deficient HPA (MIM 262640). About one third of southern Chinese HPA are caused by BH deficiency and this frequency is more prevalent than that of Caucasian HPA population. Mutation analysis on PTPS gene indicated that three mutations, 155A>G, 259C>T and 286G>A mutations, account for about 80% of Chinese PTPS deficiency. The 155A>G mutation accounts for 54% of the southern Chinese PTPS mutation, but only one (2.8%) of the northern Chinese PTPS mutant allele was found to be 155A>G. No restriction fragment length polymorphism (RFLP) or short tandem repeats (STR) marker has so far been described on PTPS gene. To identify the polymorphic markers for linkage analysis, a Bacterial artificial chromosome (BAC) clone containing PTPS gene was isolated by PCR method with PTPS gene specific primers and sequenced completely by random shotgun approaches. This BAC clone, 321H15, was mapped to chromosome 11q22.3 by fluorescence in situ hybridization and was 83kb in length. The STS WI-30933 (WIAF-82) of Unigene Hs. 181795 was located up-stream to PTPS gene and a microsatellite marker, D11S1347, was located down stream to PTPS gene. An Unigene cluster Hs. 182503 was found to locate down stream distal to PTPS gene. The PTPS gene was fine mapped to between WI-30933 and D11S1347 with 8kb and 26kb distance, respectively. The D11S1347 marker could be applied to trace if there are common founder of 155A>G, 259C>T and 286G>A mutations in Chinese PTPS-deficient HPA.

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