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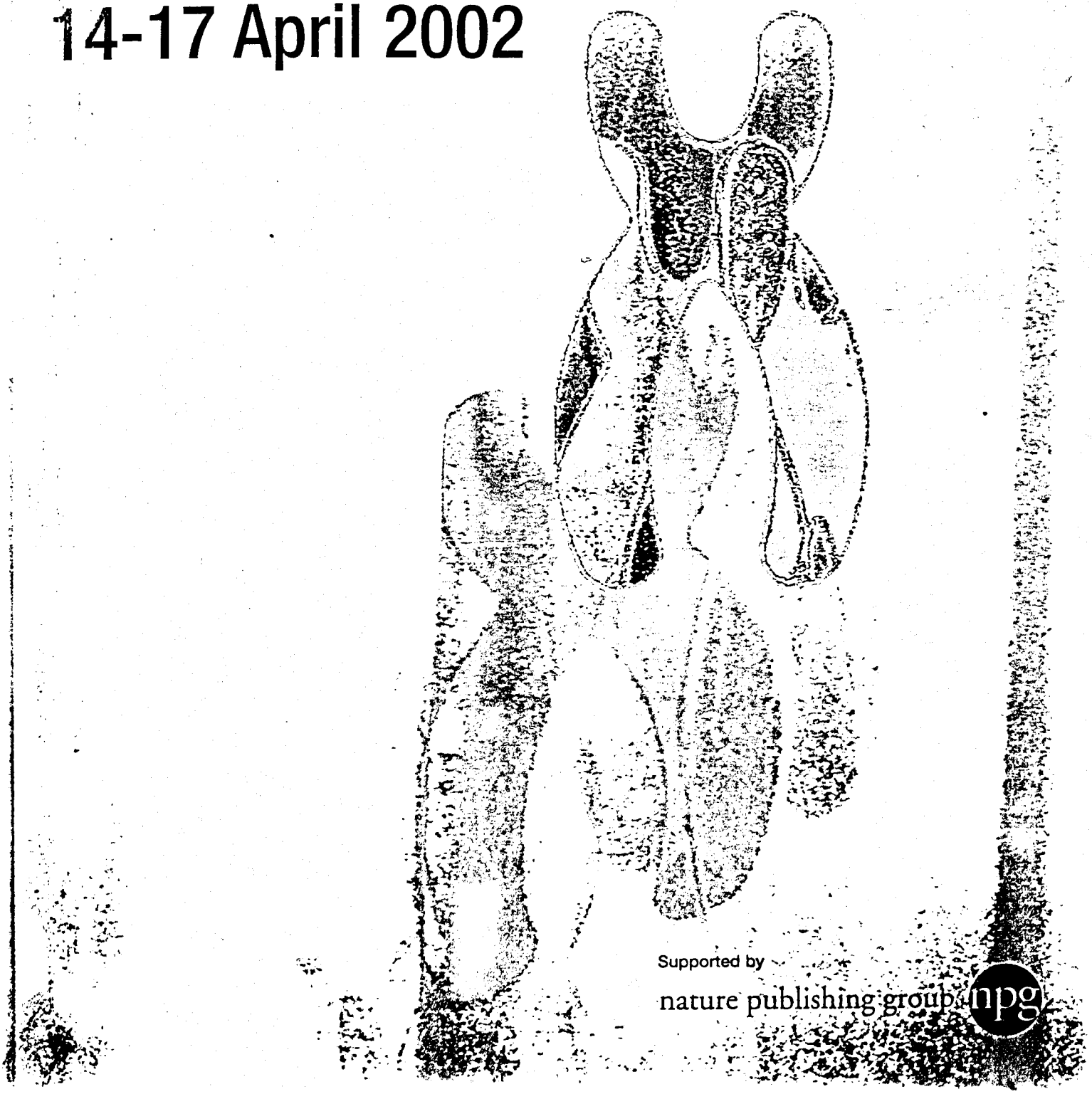

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scored at first time, among which 91% were diagnosed by metaphase chromosome analysis. Several features of this method, including high efficiency, no affection on cell dispersion or significant increase of the background autofluoresence, minimum cross-contamination, etc. have suggested its suitability for large-scale analysis. Among our identified carriers, most were neonates initially suspected for characteristic cardiovascular malformations or suggestive dysmorphic features. Rare features such as bifid thumb, umbilical and inguinal hernias, and interstitial pulmonary fibrosis were also noted. 22q11 deletion has also been identified among available parents and grandparents, none of which were previously diagnosed. There had been one mother carrier who had no overt clinical problems. One father carrier had no cardiac abnormality, no dysmorphic appearance, and no nasal speech. Most strikingly, we have identified a 22q11 deletion in a patient presenting as 'isolated severe scoliosis'. The patient, a 19-year- old male, was referred to an orthopaedic clinic due to progressive scoliosis accompanied with worsening back pain. Past history revealed bilateral pes cavus, umbilical hernia, unexplained learning difficulties and onset of measles. Other abnormal findings included pain in the right ankle, small hand muscle wasting and very long fingers, lax elbow joints and widespread stretch marks. Initial spinal X-ray and magnetic resonance imaging demonstrated a severe S-shaped thoraco-lumbar kyphoscoliosis and bilateral acetabulae protrusio. A pelvic X-ray further revealed bilateral absence of sacroiliac joints. On the bone scan, radionuclide Tc99m uptake within the spine was surprisingly 'normal' considering the degree of the curvature. Renal retention of Tc99m was noticed incidentally. Retrospectively, the patient was found to be mildly dysmorphic with low front hairline, narrow palpebral fissures, pinched nares, and high palate. Echocardiography revealed a normal heart except for an aortic root of 3.7 cm in diameter (upper limit of normal range). As at least a quarter of 22q11 carriers do not have a cardiovascular abnormality clinically and the characteristic facies can be easily missed in the absence of typical malformations, we call for a yet higher index of suspicion for this important genetic abnormality. FISH for 22q11 deletion should be offered to a yet wider range of patients.

POSTER NO: 320

Assessment of electronic data collection from PubMed for the establishment of Chinese Gene Variation Database (CGVdb)

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In order to collect genetic mutations and other variations information in the Chinese population for clinical application and medical genetic research, a Chinese Gene Variation Database (CGVdb) (http://www.CGVdb.org) was established. The content and structure of this ethnic mutation database follow the guidelines recommended by HUGO Mutation Database Initiative (MDI).

A semi-automatic electronic data collection method was developed to help us to collect the genetic mutation and polymorphism study reports from publicly available NCBI PubMed database. These mutation and variation reports related to inherited genetic diseases in Chinese population, but not including somatic mutations, are defined as Chinese gene Variation Reports (CVRs). By our customized search string composed of PubMed MeSH terms and search field tags, we can limit the results to the papers we want. To evaluate the effectiveness of our electronic data collection method, we have established a standard data set which contains those papers expected to be true CVRs by manual reviewing all the papers published in 18 selected journals related to human genetics, which includes 9 journals published in U.S. and Europe, 5 journals published in Mainland China and 4 journals published in Taiwan, in the period of 1997 and 1998. The total number of papers in PubMed of this 18 journals in the period of 1997 and 1998 is 6,942. Manual review has found 108 CVRs. However, our electronic data collection method detected 265 papers from PubMed. By comparison of the standard data set and the result of our electronic data collection method, 3 False Negatives (FN, rate : 0.03), and 160 False Positives (FP, rate : 0.60) were found. Using the electronic data collection method, 1012 reports were found in the period of 1997 and 1998 from searching all the papers contained in PubMed. Among them, 256 CVRs and 756 False Positives (FP rate : 0.75) were found. This result indicated that the total CVRs in the PubMed database from 1966 to 2001 can be estimated to be around 1330 from the 5258 reports detected by our electronic method on Jan. 31, 2002. The 3 FNs occurred in the standard data set were attributed to the patient origin was not described in the title nor in the abstract. To find this kind of paper, searching through the full text database is needed. Our next step to improve this electronic data collection method will be fine tuning the search string to lower the FP rate as much as possible while keeping the FN rate below 0.03.

POSTER NO: 321

Isolation and the Complete Sequence of the Human BAC Clone 395N09: The Complete Genomic Sequence of Dihydropteridine Reductase Gene and its mutation in Chinese Hyperphenylalaninemia

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Dihydropteridine reductase (DHPR) regenerates the quinonoid dihydrobiopterin to tetrahydrobiopterin (BH4), the essential cofactor required in aromatic amino acids hydroxylation. Defect in DHPR will result in BH4-deficient hyperphenylalaninemia (HPA, MIM 261630). In this study, a bacterial artificial chromosome (BAC) clone 395N09 that contained the DHPR gene was isolated by BAC library screening using PCR method with DHPR gene specific primers. This BAC clone (395N09) was mapped to chromosome 4p15.31 by fluorescence in situ hybridization and sequenced completely by random shotgun approaches. The finished sequence of 395N09 clone was 130138 bp in length with error rate less than 0.01 in 10kb (GenBank No. AB053170). The DHPR gene is located at nt 33,044-58,725 of 395N09, and is 25682bp in length. Four STS markers SHGC-145965, GDB:181534, T24026, and 1394 are located within DHPR gene. Four STS markers D4S2926, stSG35942, RH100005, and SHGC-50879 are located down stream to DHPR gene. The STS marker D4S2926, 20kb down stream to the DHPR gene, is a dinucleotide repeat marker and could be applied to linkage analysis for the DHPR gene to trace the transmission of a mutation. The 395N09 clone overlapped with two draft sequences, RP11-46E22 (GenBank No. AC074179) and RP11-333I7 (AC018596), and filled the gap between these two sequences listed in the Human Genome Project working Draft (http://genome.ucsc.edu/).

To identify the molecular defects of DHPR Chinese DHPR deficient HPA, 7 exons of the DHPR gene were amplified by PCR and sequenced accordingly. A novel mutation of the DHPR gene, designated 697A>C, was identified in a Chinese patient suffering from DHPR deficiency. The 697A>C transversion leads to amino acid change from Thr to Pro at codon 233 (T233P). The 697A>C were linked to the heterozygotes determined by DHPR activity in blood and none of 100 alleles of unrelated normal Chinese were found to have this 697A>C substitution. These data indicated the 226C>T substitution might not be a polymorphism but a mutation causing PTPS deficiency.

POSTER NO: 322

Haplotype and R778L Mutation Analysis in Chinese Patients with Wilson Disease

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Wilson disease (WD), an autosomal recessive disorder of copper transport, is characterized by biliary excretion and by impaired incorporation of copper into ceruloplasmin. Toxic accumulation of copper causes tissue damage, primarily in the liver, brain, and kidneys. Here, haplotype analysis using three microsatellite markers, D13S314, D13S301, and D13S316, has been a useful indicator of specific mutations. Based on the analysis of haplotypes of D13S314, D13S301and D13S316, size of segments was 134-157bp, 128-156 bp, and 136-154 bp, 19,