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POSTER PRESENTATIONS

Clinical Genetics: Molecular Diagnosis *(continued)*

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CARRIER SCREENING AND PRENATAL DIAGNOSIS OF ALPHA-THALASSEMIA BY DUAL RESTRICTION ENZYME ANALYSIS.

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α - thalassemia, the most common genetic disease in some Chinese provinces, is found throughout southeast Asia and the Mediterranean. Heterozygous α - thalassemia patients are often identified by their low erythrocyte MCV and normal Hb electrophoresis. Sometimes we will confuse α - thalassemia -2 with normal person, so we need to test their genotype by restriction enzyme analysis. A dual restriction enzyme digestion protocol was developed using a 3'ζ - globin probe to clearly distinquish the most common α - thalassemia deletions that represent nearly all the α - thalassemia haplotypes in Southeast Asia.

From the carrier studies, fourteen cases were found to have the gentotype of α α /α α , five cases were α α /- 3.7, one case was α α /- 4.2, twenty cases were α α /-- SEA. There were two cases diagnosed to have the genotype of α α /α α , but they had low MCV and normal Hb patterns. From the hematological analysis data, we considered one belonged to iron deficiency anemia and the other was non-deletion α -thalassemia. Of four prenatal diagnosis cases, two were found to have the normal genotype of α α /α α , the other two were --/--, homozygous α -thalassemia.

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Congenital spondyloepiphyseal dysplasia - analysis of the COL2A1 gene. A. Winterpacht, S. Mundlos and B. Zabel*. Department of Pediatrics, University of Mainz, Mainz,FRG.

The evidence that some skeletal dysplasias are caused by mutations of COL2A1, the structural gene of type II collagen, is based on biochemical studies, linkage data, and single, recently reported cases with COL2A1 mutations identified at the molecular level: an exon 46 point mutation together with a probably silent exon 51 point mutation in a lethal short-limbed dwarfism, an exon 31 single base mutation in a family with osteoarthritis/ chondrodysplasia, an exon 48 deletion, and a 45 bp tandem duplication in exon 48 in patients with congenital spondyloepiphyseal dysplasia (SEDC).

By using polymerase chain reaction and single-strand conformation polymorphism (SSCP) analysis we started to look for mutations in the COL2A1 gene of 10 SEDC patients. Investigation of exons 46-31 showed one patient having a mutation in exon 50. The nucleotide sequence revealed a G to A transition at nucleotide 105 resulting in a Valin to Isoleucine conversion. Since the mutation is also carried by the patient's healthy father, it is probably not the cause of the disease, thus representing a rare polymorphism (not present in 30 controls). SSCP analysis proves to be an efficient method for the detection of COL2A1 point mutations as screening of the complete gene is in progress.

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Screening for von Hippel-Lindau disease by DNA-polymorphism analysis. B. Zbar*(1), F. Latif(1), G. Glenn(2), S. Hosoe(1), M. Yao(1), P. Choyke(4), M. Lerman(1), and M. Linehan(3). (1) Laboratory of Immunobiology, NCI-FCRDC, Frederick MD, (2) Cancer Diagnosis Branch, NCI, Bethesda MD, (3) Surgery Branch, NCI, Bethesda MD, and (4) Diagnostic Radiology, Clinical Center, NIH, Bethesda MD.

Von Hippel-Lindau disease is a rare autosomal dominant trait characterized by a predisposition to develop retinal angiomas, hemangioblastoms of the brain and spinal cord, renal cell carcinomas, pheochromocytomas and cystadenomas of the pancreas and epididymis. We evaluated DNA-polymorphism analysis as a method for identifying disease gene carriers by prospectively comparing the results of RFLP analysis with a comprehensive clinical examination. Forty-eight asymptomatic individuals at risk of developing von Hippel-Lindau disease were tested with probes for loci known to flank the VHL gene. The genetic markers tested were RAF1, D3S18, D3S191, D3S571, and D3S627.

RFLP analysis predicted 9 disease gene carriers and 33 individuals with the wild-type (normal) allele among the 48 individuals at risk of developing von Hippel-Lindau disease; the test was not informative in 6 individuals. All (9/9) individuals predicted to carry the VHL gene had evidence of occult disease on clinical examination. There was no clinical evidence of von Hippel-Lindau disease in 32/33 individuals predicted to carry the wild-type allele.

DNA-polymorphism analysis can identify individuals likely to carry the von Hippel-Lindau disease gene.

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Gene diagnosis of Duchenne muscular dystrophy and Becker muscular dystrophy with dystrophin cDNA and genomic clone probes. J. W. Zhang*, G.Y. Wu, Y.J. Zhao, W.M. Chu and J.Z. Liu, Institute of Basic Medical Sciences, CAMS, Beijing, China.

Duchenne muscular dystrophy (DMD), allelic with the milder Becker muscular dystrophy (BMD), is an X-linked myopathy resulting in death of the patients by early adulthood. Some genomic clones and dystrophin cDNA have been used for the DNA diagnosis of DMD/BMD.

Using the 14 kb cDNA, we have tested the DNA isolated from 50 unrelated DMD/BMD families. The results showed that the DNA deletions of Chinese DMD/BMD patients located mainly near the center of the gene.

Using the genomic clone probe P20, we have identified a new Bgl II restriction fragment length polymorphism (RFLP) site. The allelic fragments are 6.1 kb and 7.1 kb long respectively. The frequences of the miner allelic band (6.1 kb) in the 42 normal X-chromosomes and the 27 DMD/BMD X-chromosomes tested were 36% and 30% respectively. The polymorphic information content (PIC) was about 45%. The new RFLP site has been used for detection of carriers and prenatal diagnosis of DMD and BMD.

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Characterization of deletion in Duchenne muscular dystrophy (DMD) by multiplex polymerase chain reaction (PCR). J.Yang(1), S.Zhang*(1), D.Lo (2), Y.Tang (1), Q.Wang (1) and X.Hu (1). (1) Dept. Med. Genetics and (2) Dept. of Neurology, West China Univ. of Med. Sci., Chengdu, China.

The gene for DMD has been mapped to the short arm of X chromosome (Xp21) and majority of the DMD cases are due to gene deletion. Recently PCR with multiple primers is used in detection and characterization of gene abnormalities of inheritable diseases and has proved to be a simple and rapid method in detection of deletions in DMD. Using this multiplex PCR we studied 17 cases of DMD/BMD from Chengdu area with 9 sets of primers by Beggs. In total 9 deletions were observed. Among them one case of deletion was detected only when 18 sets of primers were used. Thus 53% (9/17) of our DMD cases are due to deletions and the latter are concentrated in the 6.5-8.0 Kb region of the cDNA of the gene as well as in the regions corresponding cDNA probes 7 and 8. The preliminary results are in good accordance with the data reported by Chamberlain et al and indicate that the primers used in present study are applicable in detection and characterization of the DMD in Chinese.

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Preliminary studies of the 3'hypervariable region downstream of α-globin gene in Chinese. Y.Yu, S.Z. Zhang, Y.Hu, L.Lo, S.X.Zhang* and H.Li, Dept. of Med. Genetics and Dept. of Urology, West China Univ. of Med. Sci., Chengdu, China.

3'HVR, a hypervariable region downstream to the human globin gene is a DNA fragment with variable number of tandem repeats and has proved to be linked to the gene for autosomal dominant polycystic kidney disease PKD-1. Frequencies of the allelic fragments of 3'HVR has been studied. DNA of peripheral blood cells from 58 unrelated healthy individuals were prepared, digested with restriction enzyme PvuII transferred to Hybond nylon filter and hybridized with P-labelled 3'HVR probe. The size of the allelic fragment were estimated with a self-made curve equation fitting computer program. It has been shown that the size variation of the 3'HVR allelic fragments is between 1.4-8.0 Kb. The allelic frequencies fit positive distribution with about 39% alleles between 2.0-2.6 Kb and 95% alleles between 1.6-7.4 Kb. The results are similar to those reported by S.Reeders and other authors. In addition linkage analysis with 3'HVR probe was applied successfully to 2 APKD families.