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Allelic association study of NlaIII and MspI polymorphisms of catechol-O-methyltransferase gene and schizophrenia Y.-R. Lee[1], C.-H. Chen[2,3], M.-Y. Liu[4], F.-C. Wei[5], H.-G. Hwu[5], K.-J. Hsiao[1,4]. [1]Institute of Genetics, [2]Division of Neuropsychiatry, School of Medicine, Yang Ming University; [3]Division of Psychiatry, Cheng Hsin Rehabilitation and Medical Center; [4]Department of Medical Research, Veterans General Hospital-Taipei; [5]Hung Chi Psychiatric Hospital, Taipei; [6]Department of Psychiatry, Taiwan University Hospital, Taipei, Taiwan.

Catechol-O-methyltransferase (COMT) catalyzes transmethylation from S-adenosylmethionine to catecholamine neurotransmitters, and was thought to be involved in the pathogenesis of mental disorders in light of biogenic amine hypothesis. Recent studies also reported suggestive linkage of schizophrenia with chromosome 22q11-13, to which COMT gene was mapped. To elucidate if COMT gene is a susceptible gene of schizophrenia, we carried out a case-control association study in a Chinese population from Taiwan. The allelic and genotypic frequencies of two restriction fragment length polymorphic (RFLP) markers of COMT gene, namely NlaIII at exon 4 and MspI at exon 5 were compared between patients and normal controls. The NlaIII RFLP at exon 4 alters amino acid from valine to methionine at codon 158, and is associated with genetically determined thermostability and enzyme activity of COMT. The MspI RFLP at exon 5 is a novel silent mutation at codon 199, which was identified recently in our laboratory. No differences of allelic frequencies and genotypic frequencies of NlaIII and MspI polymorphisms were detected between schizophrenic patients (n=177) and normal controls (n=99). Our results suggest that the NlaIII polymorphism at exon 4, and the MspI polymorphism at exon 5 of COMT gene do not underlie the genetic susceptibility to schizophrenia.

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(mean LOD score=2.99) and exclusion (mean LOD=-2.63) of a disease gene with age-dependent penetrance, assuming a 10 cM map of markers with heterozygosity of 75 percent.

Approximately 200 highly polymorphic microsatellite markers have been typed to date. The highest LOD scores achieved have been 1.77 and 1.42 for markers D5S1457 and D8S1104, respectively. Additional markers in these two regions have not provided evidence of linkage. Multipoint analysis of markers on chromosome 1q and proximal 1p has strongly excluded the region containing the alpha-tropomyosin gene (TPM3), mutations in which are known to be associated with autosomal dominant nemaline inclusion myopathy.

Mendelian disorders, linkage disequilibrium (LD) based strategies in the Finnish population have proven instrumental in the mapping and identification of the genes and their underlying mutations. There is no reason to believe that genes predisposing to complex diseases would not similarly show LD in isolated patient populations. We have collected 208 (175 simplex, 33 multiplex) SLE families from Finland. Extensive genealogical studies showed a slightly increased prevalence of SLE in the eastern part of Finland, suggesting one or a few founder mutations in that sub-population. More than half of these families have been linked as distant relatives by tracing church and community records as far back as the early 17th century. Physiological studies of SLE patients and mice have shown the interleukin 10 (IL10) and interferon A and B (IFNA/B) levels to be dysregulated. Genetic studies of murine SLE models have also implicated the respective genomic regions to contain major susceptibility loci. Therefore, the human homologous regions on chromosome 1 (*IL10*) and 9p22 (*IFNA/B* cluster) have been examined for shared genomic segments indicative of LD with intragenic (promoter-associated) and flanking microsatellite markers. As part of this study, *IL10* was mapped to an 8 cM region in 1q31, and the phyical order of the genes and their flanking linkage markers in 1q31 and 9p22 has been refined further.

in this family. The hearing impairment gene among one
to chromosome 7q31, the DFNB4 locus. Pendred syndr
syndromic deafness, is also linked to this locus. If the
defective gene with different mutations, this information a
be very helpful for understanding the function of the gene, c
gene among another subgroup of this family is linked to
but the size of the subgroup is not large enough to support
score. At the allelic level, there are three alleles segrega
subgroup that links to the DFNB4 locus. This suggests t
gene are abundant in the Caucasian population.

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A highly informative polymorphism in the human neurotensin receptor gene on chromosome 20. F. Le, X. P. Zeng, and E. Richelson. Laboratory of Neuropsychopharmacology, Mayo Clinic Jacksonville, 4500 San Pablo Road, Jacksonville, FL32224, U.S.A.

The growing evidence suggests that neurotensin and the neurotensin receptor play important roles in the etiology of some neurological and psychiatric disorders, including Parkinson's disease and schizophrenia. Thus, the gene for the NTR, which was mapped by others to chromosome 20q13, may be used as a candidate gene for genetic analysis of the association between the neurotensin receptor and neuropsychiatric diseases. We reported a highly informative double tetranucleotide microsatellite repeat polymorphism in the neurotensin receptor gene. This repeat was found among an almost exclusive CT region (~360 bp), in which there actually existed two tetranucleotide microsatellite repeats. The first microsatellite had nine perfect "CCTT" repeats and the second had seventeen perfect "CTTT" repeats. Further study found that this microsatellite repeat was very polymorphic, with 23 alleles found in DNA samples from 105 unrelated individuals, which we examined. Many alleles had very low frequencies, among which eleven were below 2%, eight were between 2-8%, and only four were over 10% (range 11.90 - 12.86%). The estimated heterozygosity was 0.914 and PIC (polymorphism information content) value is 0.906. Additionally, Mendelian inheritance has been demonstrated in two three-generation pedigrees for this polymorphism. Therefore, this is a highly informative polymorphism, which will be very useful as a genetic marker for genetic study of association between the neurotensin receptor and some neuropsychiatric disorders. (Supported by Mayo Foundation for Medical Education and Research, and grant MH27692 from N.I.M.H.)

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Identification of a polymorphism upstream alternatively spliced exon 5a by SSCP and CFL

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Paired box (PAX) genes, a family of transcription fa gene expression by interacting with DNA regulatory seq currently consists of nine genes, PAX 1 to PAX 9. aniridia have been associated with mutations in the PA The focus of the present study has been to better define identify new ocular phenotypes associated with alterati SSCP and a novel mutation detection assay CLEAVASI (CFLP) analysis have been used to identify sequence va of pediatric patients with developmental eye anomalies to be highly dependent on the electrophoresis conditi detection of mutations in DNA fragments up to 300 ba the CLEAVASE I enzyme which has single-strand end 5' end of hairpin structures. The new CFLP technique comparable to direct sequencing, for the detection deletions and insertions. CFLP will allow longer frag analyzed.

In a comparison of SSCP and CFLP analysis of the gene exon 5a, a patient with optic atrophy produced an 5a was directly sequenced revealing that the child is h adenine nucleotide approximately 50 bp upstream of not have the variant SSCP or CFLP pattern. Direct s exon 5a revealed that she is homozygous for the 1 bp d is a neutral polymorphism. The results for other pres pending. The identification of this previously unpubli as it may be encountered by others.