1938

A candidate gene responsible for transient neonatal diabetes. *Y. Makita[1,2], J. Inoue[3], K. Mitsuya[3], K. Imada[4], T. Honma[5], Y. Ito[2], R. Mitamura[2], T. Ishii[2], M. Oshimura[3], A. Hata[2].* 1) Public Health, Asahikawa Medical College, Asahikawa, Hokkaido, Japan; 2) Pediatrics, Asahikawa Medical College, Asahikawa, Hokkaido, Japan; 3) Molecular and Cell Genetics, School of Life Science, Factory of Medicine, Tottori University, Yonago, Tottori, Japan; 4) Pediatrics, Niigata Prefectural Sakamachi Hospital, Sakamachi, Niigata, Japan; 5) Pediatrics, Niigata City General Hospital, Niigata, Niigata, Japan.

Transient neonatal diabetes mellitus (TNDM), a rare form of childhood diabetes (an incidenceof ~1 in 400,000 live births), presents in growth retarded neonates with persistent hyperglycemia. Recovery is usually complete by 18 months of age, however 40% of the patients relapse and develop diabetes again later in life. The association of both paternal uniparental disomy of chromosome 6 (UPD 6) and paternal duplications of 6q24 with TNDM suggested the mechanism of the disease to be overexpression of an imprinted gene in this locus. With an analysis of TNDM patients, the responsible gene is revealed to reside 461 kb region of PAC contig (CEN-dJ210B1-dJ468K18-dJ340H11-dJ197L1). In this region, we found two paternally expressed genes by the method with mouse human hybrid cell lines. One has been reported by the name PLAGL1/ZAC, and the other is newly identified gene, tentatively named X. Total 10 Japanese TNDM patients and their relatives were analyzed with newly developed four microsatellite markers located nearby the two genes to see UPD or duplication. In two out of ten patients, paternal duplication exists throughout the region where present markers locate. However, in one family, only one marker locating centromere side of dJ197L1 is found to be duplicated. Combined with the fact that PLAGL1/ZAC gene is known to be involved in the PAC clones named dJ468K18 and dJ340H11 strongly indicates that the X is a responsible gene for TNDM. Analysis of methylation status of gene X in the remaining 4 patients without any UPD or duplication is now ongoing.

1939

Question of switched I and not misidentificati

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ics, Boston University Sc
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A 3 9/12 year old Afr (A=91.2%; F=3.5%; A_2= cause of elevated Hem was diagnosed in the ch moglobin C. The possibi pre-eclampsia and seizu After confirming all result ity of maternity. Amplific moglobin C and β°Thal v C/β°Thal and the child is

DNA sequence analy (MSUD) and his parents pregnancy. The affected gene which rendered it n Mutation analyses of the no somatic mutations fo confirmed. DNA testing proved maternity and pa Utilizing 16 probes synte viously undescribed mec fected offspring arose fr maternal meiosis I → nor rescue → uniparental dis

1940

Systematic search of molecular variants of the human synapsin 3 gene and association study with schizophrenia. *C.H. Chen[1], M.T. Tsai[2], C.C. Hung[2], C.Y. Tsai[2], M.Y. Liu[3], Y.H. Chen[2], K.J. Hsiao[3].* 1) Department of Psychiatry, Tzu-Chi General Hospital, Hualien City, Taiwan; 2) Institute of Human Genetics, Tzu-Chi Medical College, Hualien City, Taiwan; 3) Institute of Genetics, Yang-Ming University, Taipei, Taiwan.

Human synapsin 3 gene is a newly identified member of synapsin gene family with putative function of regulating synaptogenesis and neurotransimitter release. The gene was mapped to 22q12-13, a possible region that may harbor schizophrenia gene as suggested by several linkage studies. Hence, the synapsin 3 gene was considered a candidate gene of schizophrenia. We systematically searched for mutations in the protein coding and 5'-promoter regions of the synapsin 3 gene in a sample of Chinese schizophrenic patients from Taiwan. Three single nucleotide polymorphisms were identified: g.-631CG and g.-196GA at 5-end promoter region, and g.69GA at exon 1. Further case-control association studies, however, did not find significant differences of genotype or allele frequency distributions of these three polymrophisms between 163 patients and 151 non-psychotic comparisons. Hence, we suggest that the human synapsin 3 gene may not contribute substantially to the pathogenesis of schizophrenia.

B 204

1941

Somatic instability of

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pan.

Huntington's disease (characterized by involunt lying genetic alteration is relation exists between C length through meiotic tr pansion of the triplet repe still unclear. We have g mouse HD gene was rep and mutated huntingtin p peripheral tissues. To de performed using genomi 97 CAG repeats in exon CAG repeat, male) and f pansion through meiotic In addition, a one or two paternal transmission. T through maternal transm icism) in 75 week-old mic eral organs such as the expanded CAG repeat in bility of this mouse mode

1942

AGG Interruptions in the CGG Trinucleotide Repeat Tract of the FMR1 Gene May Contribute to Stability of Fragile X Premutations. *S. Dyack[1], L. Steele[3], G. Koultchitski[3], Y. Yang[3], R. Weksberg[1], P.N. Ray[2,3], C.E. Pearson[2].* 1) Division of Clinical and Metabolic Genetics; 2) Genetics and Genomic Biology; 3) Department of Pediatric Laboratory Medicine, The Hospital for Sick Children, The University of Toronto,Toronto, Ontario, Canada.

Fragile X Syndrome (FRAXA), the most common form of inherited mental retardation

1943

"Mitotic Drive" of Expa

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The expanded CTG re sue-dependent somatic