The aim of the study is to validate the etiological role of KIAA0027/MLC1 in childhood-onset megalencephalic leukoencephalopathy with subcortical cysts (MLC) and in schizophrenia, particularly the catatonic subtype, which were reported to be allelic diseases. Among a series of five patients with MLC, four mutant alleles were detected: one case of compound heterozygosity for a splice site mutation and a six-base-pair in-frame deletion, one patient with a homozygous frameshifting insertion-deletion, and a further case heterozygous for a A157E substitution. A systematic mutation screening in 140 index cases with schizophrenia revealed 13 different single nucleotide polymorphisms (SNPs): one SNP in the 5’-UTR, seven SNPs in intronic regions, two synonymous codon variants (T52, Y199), and three coding variants. Two of them, C171F and N218K, were observed in controls at a significant frequency. The L309M variant that was previously supposed to be the causative factor for chromosome 22q(tel) linked-periodic catatonia was found nonsegregating in a further multiplex pedigree. Furthermore, a complicated 33-bp insertion/deletion polymorphism at the 5’-end of exon 11 of MLC1 was found at equal frequency among schizophrenic patients and controls. In summary, our study
provides further evidence for allelic heterogeneity in megalencephalic leukoencephalopathy, excludes MLC1 as a susceptibility locus for schizophrenia, and thereby rules out that MLC and schizophrenia are allelic disorders.