GENETIC VARIATION IN THE *TSC1* AND *TSC2* GENES IN 24 TSC FAMILIES FROM INDIA

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Tuberous sclerosis complex (TSC) is an autosomal dominant disorder with loci on chromosome 9q34.3 (TSC1) and chromosome 16p13.3 (TSC2). Genes for both loci have been isolated and characterized. Clinical symptoms of TSC include cortical tubers, subependymal nodules, mental retardation, seizures, autism, shagreen patches and angiofibromas on the skin, cardiac rhabdomyomas, retinal hamartomas, and angiomyolipomas in the kidneys. Several mutations have been reported in both TSC genes in patients mainly from the western and Japanese populations. However, there is no report on the mutation analysis of *TSC* genes in patients from the Indian population. We report here the mutational analysis of the *TSC1* and *TSC2* genes in 24 TSC families from India. Using PCR-SSCP and DNA sequence analyses, we have screened all 21 coding exons of the *TSC1* gene and all 41 coding exons of the *TSC2* gene in seven familial and 17 sporadic TSC cases. We have also sequenced promoters of both the *TSC* genes in 24 probands. We have identified a total of 12 mutations. Of these, seven mutations are novel. We have identified a single previously known deletion in the *TSC1* gene. Of 11 mutations identified in the *TSC2* gene, 3 are deletions, 2 are insertions, 3 are missense, 2 are splice site and 1 is a nonsense mutation. In addition, we have also detected three and eight variants/polymorphisms in the *TSC1* and *TSC2* genes respectively. Of these, three are novel SNPs. There was no correlation between the types of mutations (missense, nonsense, etc.) and the severity of the disease. As observed in the western and Japanese populations, the mutations were scattered across the *TSC2* gene. DNA sequence analysis of promoter regions of both TSC genes in 24 families did not show any variation. (This work was financially supported by a grant from DBT, New Delhi to AK and SCG and a CSIR JRF to MA).