

## MUTATION ANALYSIS OF THE *TSC2* GENE IN 23 TSC FAMILIES FROM INDIA

Mahmood Ali<sup>1</sup>, M. Markandaya<sup>1</sup>, S.C. Girimaji<sup>2</sup>, A.K. Shukla<sup>3</sup>, S. Sachhidanand<sup>4</sup> and A. Kumar<sup>1</sup>

<sup>1</sup>*Department of Molecular Reproduction, Development and Genetics, Indian Institute of Science, Bangalore-560012, India;* <sup>2</sup>*Dept. of Psychiatry, NIMHANS, Bangalore 560029, India;* <sup>3</sup>*Department of Radiology, KIMS, Bangalore 560002, India;* <sup>4</sup>*Department of Dermatology, Bangalore Medical College, Bangalore 560002, India.*

Tuberous sclerosis complex (TSC) is an autosomal dominant neuro-cutaneous disorder with loci on chromosome 9q34.3 (*TSC1*) and chromosome 16p13.3 (*TSC2*). Genes for both loci have been isolated and characterized. Pathologically, tuberous sclerosis complex is a disorder of cell proliferation, differentiation and migration. Clinical symptoms of TSC include cortical tubers, subependymal nodules, mental retardation, seizures, autism, shagreen patches and angiofibromas on the skin, cardiac rhabdomyomas, retinal hamartomas, ungual and peringual fibromas, and cysts and angiomyolipomas in the kidneys. More than 350 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 *TSC2* gene in 23 TSC families from India. Using PCR-SSCP and DNA sequence analyses, we have screened all 41 exons and promoter region of the *TSC2* gene in seven familial and 16 sporadic TSC cases. We have identified a total of 12 mutations representing 25% and 75% of familial and sporadic cases respectively. Of these, eight mutations are novel. Of 12 mutations, 3 are deletions, 2 are insertions, 4 are missense, 2 are splice site and 1 is a nonsense mutation. In addition, we have also detected nine single-nucleotide polymorphisms (SNPs) in the *TSC2* gene. Of these three are novel SNPs. There was no correlation between the types of mutations (missense, nonsense, etc.) and the severity of the disease. The mutations were found to be distributed across the gene without any clustering, suggesting that mutation analysis requires scanning of the complete coding sequence of the *TSC2* gene (This work was financially supported by a grant from DBT, New Delhi to AK and SCG and a CSIR JRF to MA).