Title
MAPPING OF THE BREAKPOINTS PRESENT IN CHROMOSOME 9Q34.3 REARRANGEMENTS IDENTIFIED IN TUBEROUS SCLEROSIS PATIENTS

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Mapping of the breakpoints present in chromosome 9q34.3 rearrangements identified in Tuberous Sclerosis patients.

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We have identified the presence of chromosomal rearrangements in the 9q34.3 region in two Tuberous sclerosis (TSC) families. We previously reported the use of fluorescence in situ hybridization to identify the presence of a chromosome 9q34.3 duplication in a sporadic case of TSC. We have now defined a chromosomal breakpoint flanking the duplication through pulsed field gel electrophoresis (PFGE). We have also utilized PFGE to define the chromosomal rearrangement present in a second TSC family, (TS 33). In TS family 33 we demonstrated the presence of a novel ClaI fragment with probes D9S10 and DBH, indicating that the TSC1 gene mapped within 240kb of DBH and D9S10. We previously reported that the D9S10 locus contains a gene homologous to the Vav oncogene (Smith et al., Ann Hum. Genet. 58: 235-236 1994). In normal individuals, D9S10 and DBH map to the same ClaI fragment. SacII sites lie within this ClaI fragment so that DBH and the D9S122 locus map to a 120kb SacII fragment while D9S10 maps to a 100kb SacII fragments. Using a unique sequence probe which maps adjacent to the telomeric end of the D9S122 locus, we detected a novel fragment in the sporadic case of TSC described above. This finding indicates that the TSC1 gene maps within 120kb of the D9S122 locus. These rearrangements have facilitated fine mapping of the TSC1 locus and their availability will facilitate identification of the TSC1 gene.