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Truncating mutations of hSNF5/INI1 in aggressive paediatric cancer

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Malignant rhabdoid tumours (MRTs) are extremely aggressive cancers of early childhood. They can occur in various locations, mainly the kidney, brain and soft tissues,. Cytogenetic and molecular analyses have shown that the deletion of region 11.2 of the long arm of chromosome 22 (22q11.2) is a recurrent genetic characteristic of MRTs, indicating that this locus may encode a tumour suppressor gene. Here we map the most frequently deleted part of chromosome 22q11.2 from a panel of 13 MRT cell lines. We observed six homozygous deletions that delineate the smallest region of overlap between the cell lines. This region is found in the *hSNF5/INI1* gene, which encodes a member of the chromatin-remodelling SWI/SNF multiprotein complexes. We analysed the sequence of *hSNF5/INI1* and found frameshift or nonsense mutations of this gene in six other cell lines. These truncating mutations of one allele were associated with the loss of the other allele. Identical alterations were observed in corresponding primary tumour DNAs but not in matched constitutional DNAs, indicating that they had been acquired somatically. The observation of bi-allelic alterations of *hSNF5/INI1* in MRTs suggests that loss-of-function mutations of *hSNF5/INI1* contribute to oncogenesis.