Molecular characterization of Patched-associated rhabdomyosarcoma.

Abstract:
Mutations in the human homologue of Drosophila Patched1 (PTCH1) have been found in several common tumours including basal cell carcinoma, medulloblastoma, and rhabdomyosarcoma (RMS). Medulloblastoma and RMS are also present in the murine model for Ptch1 deficiency. Tumours in heterozygous Ptch1(neo67/+) mice consistently exhibit elevated transcript levels of the proto-oncogene Gli1, of Ptch1 itself, and of the insulin-like growth factor 2 (Igf2). The present study has investigated additional molecular changes in RMSs of Ptch1 mutant mice by means of microarray analysis and protein expression analysis. The data show activation of the cell survival-promoting Akt/protein kinase B (Pkb). Furthermore, RMSs express increased levels of the anti-apoptotic protein Bcl-2 and of genes and proteins known to inhibit cell proliferation, including Gadd45a and p27kip1. Taken together, the data suggest that the formation of RMSs in Ptch1 mutants is associated with the ability of tumour cells to resist apoptosis.