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Stopping hedgehogs

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The Hedgehog (Hh) pathway has been associated with embryonic cell fate and the development of neoplasia. Medulloblastomas contain mutations in the transmembrane proteins Patched (Ptch) or Smoothed (Smo) that result in ligand-independent activation of the Hh pathway. In the August 30 *Science*, Berman *et al.* report the use of cyclopamine, a plant-derived antagonist of the Hh pathway, to block medulloblastoma growth (*Science* 2002, **297**:1559-1561). They studied cells derived from cerebellar tumours from mice with a mutant *Ptch* allele. Cyclopamine specifically inhibited Hh signalling and medulloblastoma proliferation in cell cultures. Cyclopamine treatment also inhibited the expression of cell-cycle genes and increased the expression of neuronal markers. Cyclopamine-derivatives blocked growth and survival of freshly resected human medulloblastoma cells. Furthermore, Berman *et al.* showed that cyclopamine could block the growth of medulloblastoma allografts *in vivo*. These results open up the possibility of using Hh antagonists as therapeutic agents to treat patients with medulloblastomas.

References

1. The Hedgehog and Wnt signalling pathways in cancer.
2. *Science*, [<http://www.sciencemag.org>]