This week in therapeutics

Indication	Target/marker/ pathway	Summary	Licensing status	Publication and contact information
Cancer				
Cancer	Hedgehog (Hh); Smoothened (Smo); MDM2; p53; cyclin D1 (CCND1); cyclin E1 (CCNE1); glioma-associated oncogene homolog 1 (Gli1); glioma-associated oncogene homolog 2 (Gli2)	A study in various cell types suggests that antagonizing signaling through Hh could increase downstream levels of the tumor suppressor p53 and thus help treat cancer. A mutant form of the Hh signal transducer Smo activated a PI3K/Akt/Gli pathway that led, stepwise, to increased phosphorylation of MDM2, increased MDM2-mediated degradation of p53 and reduced p53-induced apoptosis. In mouse embryonic fibroblasts, mutant Smo also enhanced the expression of CCND1 and CCNE1 to promote cell proliferation. Further work is needed to determine the cancers in which Hh signaling plays a tumorigenic role and to identify which MDM2-phosphorylating kinases are upregulated by Gli1 and Gli2. Partners Curis Inc. and Genentech Inc. have an Hh pathway antagonist in Phase II testing to treat solid tumors and in preclinical development to treat other cancers. Infinity Pharmaceuticals Inc.'s IPI-609 small molecule targeting the Hh pathway is in preclinical development for pancreatic cancer. At least seven other companies have inhibitors of MDM2-p53 or CCND1 in preclinical and clinical development to treat various cancers.	Not patented; unavailable for licensing	Abe, Y. *et al. Proc. Natl. Acad. Sci. USA*; published online March 10, 2008; doi:10.1073/pnas.0712216105 **Contact:** Nobuyuki Tanaka, Nippon Medical School, Kawasaki, Kanagawa, Japan e-mail: nobuta@nms.ac.jp