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THE DISTILLERY

This week in therapeutics

Indication	Target/marker/pathway	Summary	Licensing status	Publication and contact information
Cancer				
Cancer	Smoothened (SMO)	Structural and cell culture studies suggest oxysterol-based inhibitors could help treat cancers driven by hedgehog signaling. SMO is associated with patched 1 (PTCH1) at the plasma membrane and activated by the PTCH1 ligand sonic hedgehog homolog (SHH) or oncogenic mutations in *SMO* itself. In cells expressing wild-type or an oncogenic mutant version of SMO, oxysterol-based compounds prevented SHH-dependent transcriptional activation. Structural studies showed that oxysterol ligands bound to the protein's extracellular, cysteine-rich domain, suggesting a mode of inhibition distinct from other known inhibitors. Next steps include investigating SARs of the oxysterol-binding site and developing the compounds into more potent inhibitors. Roche's Genentech Inc. unit markets the SMO inhibitor Erivedge vismodegib to treat basal cell carcinoma. At least four other companies have SMO inhibitors in Phase III or earlier testing to treat different cancers. *SciBX* 6(48); doi:10.1038/scibx.2013.1382 Published online Dec. 19, 2013	Unpatented; licensing status not applicable	Nachtergaele, S. *et al. eLife*; published online Oct. 29, 2013; doi:10.7554/eLife.01340 **Contact:** Christian Siebold, University of Oxford, Oxford, U.K. e-mail: christian@strubi.ox.ac.uk **Contact:** Rajat Rohatgi, Stanford University School of Medicine, Stanford, Calif. e-mail: rrohatgi@stanford.edu