This week in therapeutics

Indication	Target/marker/ pathway	Summary	Licensing status	Publication and contact information
Cancer				
Liver cancer	Notch 1 (NOTCH1)	<p>Mouse studies suggest suppressing NOTCH1 signaling could help treat intrahepatic cholangiocarcinomas (ICCs). In mice with labeled hepatocytes and chondrocytes, chemically induced ICC was traced to biliary lineage cells that were derived from hepatocytes rather than from chondrocytes. In mice, expression of a constitutively active Notch1 fragment in hepatocytes increased hepatocyte conversion to biliary lineage cells and malignant progression of ICC compared with no expression of the Notch1 fragment. In a separate study, overexpression of the NOTCH1 receptor intracellular domain in the livers of wild-type mice and delivery of a protein kinase B (PKB; PKBA; AKT; AKT1)-expressing vector resulted in tumors with ICC features. Fluorescence labeling showed that hepatocytes formed biliary lineage cells and ultimately differentiated into the tumors. Next steps include determining whether NOTCH inhibitors could suppress conversion of hepatocytes to biliary lineage cells. Aileron Therapeutics Inc. has a stapled peptide NOTCH1 inhibitor in preclinical testing to treat acute lymphoblastic leukemia (ALL).</p> <p>Aveo Pharmaceuticals Inc.'s AV-232, a mAb targeting NOTCH1, is in preclinical testing to treat cancer.</p> <p>OncoMed Pharmaceuticals Inc.'s OMP-52M51, an anti-NOTCH1 antibody, is in preclinical testing to treat solid tumors.</p> <p>SciBX 5(41); doi:10.1038/scibx.2012.1079 Published online Oct. 18, 2012</p>	<p>Findings in first study unpatented; unavailable for licensing</p> <p>Patent and licensing status unavailable for findings in second study</p>	<p>Sekiya, S. & Suzuki, A. <i>J. Clin. Invest.</i>; published online Oct. 1, 2012; doi:10.1172/JCI63065 Contact: Atsushi Suzuki, Kyushu University, Fukuoka, Japan e-mail: suzukicks@bioreg.kyushu-u.ac.jp</p> <p>Fan, B. <i>et al. J. Clin. Invest.</i>; published online July 17, 2012; doi:10.1172/JCI63212 Contact: Holger Willenbring, University of California, San Francisco, Calif. e-mail: willenbringh@stemcell.ucsf.edu</p>