This week in therapeutics

Indication	Target/marker/ pathway	Summary	Licensing status	Publication and contact information
Hepatic disease				
Cholestatic liver disease	Tumor necrosis factor receptor superfamily, member 10b (TNFRSF10B; DR5; TRAIL-R2); tumor necrosis factor (ligand) superfamily, member 10 (TNFSF10; TRAIL; APO2L)	Studies in cell culture, mice and human tissue samples suggest that antagonizing proapoptotic DR5 signaling in the liver could help treat primary biliary cirrhosis (PBC) and primary sclerosing cholangitis (PSC). In C57BL/6 mice treated with agonist anti-DR5 antibodies, DR5 knockout led to less cholestatic liver injury than that seen in wild-type mice. The antibodies increased fibrosis and inflammatory cell infiltration around bile ducts compared with what was seen using a control antibody. Finally, in cholangiocytes isolated from PSC and PBC patients, expression of the DR5 ligand TRAIL was significantly higher than that seen in samples from normal subjects ($p<0.05$). Next steps include further investigation of the mechanism of TRAIL and DR5 signaling in cholestatic liver disease. Lexatumumab, a mAb against TRAIL-R2 from Human Genome Sciences Inc., is in Phase I testing to treat cancer. AMG 655, a human mAb from Amgen Inc. that binds to the extracellular domain of human TRAIL-R2, is in Phase II testing to treat solid tumors and in preclinical testing for pancreatic cancer. Apomab, a human mAb agonist of the proapoptotic DR5 receptor is in Phase II testing by Genentech Inc. for various cancer indications.	Patent and licensing status undisclosed	Takeda, K. *et al. Proc. Natl. Acad. Sci. USA*; published online July 21, 2008; doi:10.1073/pnas.0802702105 **Contact:** Kazuyoshi Takeda, Juntendo University School of Medicine, Tokyo, Japan e-mail: ktakeda@med.juntendo.ac.jp