This week in therapeutics

Indication	Target/marker/pathway	Summary	Licensing status	Publication and contact information
Cancer				
Acute lymphoblastic leukemia (ALL)	Notch homolog 1 translocation-associated (Drosophila) (NOTCH1); mammalian target of rapamycin (mTOR; FRAP; RAFT1); γ -secretase	<p>Studies <i>in vitro</i> and in mice suggest that inhibiting both NOTCH1 and the mTOR pathway could help treat T cell ALL. In mouse T cell ALL (T-ALL) cells and <i>ex vivo</i> tumors, the notch pathway inhibitor MRK-003 increased apoptosis compared with that seen in controls. In leukemic mice, MRK-003 increased tumor cell apoptosis and survival while repressing NOTCH1 activity. In human and mouse T-ALL cell lines as well as in mice with subcutaneous human T-ALL tumors, a combination of MRK-003 and rapamycin inhibited tumor progression and increased survival compared with what was seen using either compound alone. Next steps include exploring the potential for this therapeutic strategy in mouse xenograft models of additional T-ALL cell lines.</p> <p>At least eight companies have compounds targeting mTOR in clinical and preclinical testing to treat cancer.</p> <p>At least five companies have compounds in development targeting the Notch signaling pathway, including γ-secretase inhibitors.</p> <p>SciBX 2(10); doi:10.1038/scibx.2009.393 Published online March 12, 2009</p>	Combination therapy unpatented; licensing status not applicable	<p>Cullion, K. <i>et al. Blood</i>; published online Feb. 26, 2009; doi:10.1182/blood-2008-02-136762</p> <p>Contact: Michelle A. Kelliher, University of Massachusetts Medical School, Worcester, Mass. e-mail: michelle.kelliher@umassmed.edu</p>