This week in therapeutics

Indication	Target/marker/ pathway	Summary	Licensing status	Publication and contact information
Cancer				
Breast cancer	Notch homolog 1 translocation-associated (Drosophila) (NOTCH1); protein (peptidylprolyl cis/trans isomerase) NIMA-interacting 1 (PIN1)	<p>Studies in mice and in cell culture suggest that inhibiting PIN1 may help increase the efficacy of γ-secretase inhibitors against breast cancer. In a mouse model of human breast cancer, inhibition of the Notch1 activator Pin1 significantly decreased tumor growth compared with that seen in controls ($p < 0.03$). Knockdown or pharmacological inhibition of PIN1 in combination with pharmacological inhibition of γ-secretase led to less proliferation of a human breast cancer cell line compared with the effects of inhibiting either target alone. Next steps include determining PIN1 and NOTCH1 levels in a variety of human tumor samples to assess the prognostic value of the findings.</p> <p>MK-0752, a small molecule γ-secretase inhibitor from Merck & Co. Inc., is in Phase I testing to treat breast cancer.</p> <p>OMP-21M18, a mAb targeting NOTCH receptor ligand DLL4 from OncoMed Pharmaceuticals Inc., is in Phase I testing to treat solid tumors.</p> <p>SL-301 and SL-302, small molecule γ-secretase inhibitors from Stemline Therapeutics Inc., are in preclinical testing to treat brain and other cancers.</p> <p>At least five companies have γ-secretase inhibitors in clinical development to treat Alzheimer's disease.</p> <p><i>SciBX</i> 2(5); doi:10.1038/scibx.2009.177 Published online Feb. 5, 2009</p>	Findings unpatented	<p>Rustighi, A. <i>et al. Nat. Cell Biol.</i>; published online Jan. 18, 2009; doi:10.1038/ncb1822</p> <p>Contact: Giannino Del Sal, National Laboratory CIB (LNCIB), Trieste, Italy e-mail: delsal@lncib.it</p>