

This week in therapeutics

Indication	Target/marker/pathway	Summary	Licensing status	Publication and contact information
Cancer				
Cancer	Mammalian target of rapamycin (mTOR; FRAP; RAFT1); eukaryotic translation initiation factor 4E (EIF4EBP1; 4EBP1)	<p><i>In vitro</i> and mouse studies suggest that two new pyrazolopyrimidine mTOR inhibitors (PP242 and PP30) could potentially be used to treat rapamycin-resistant cancer. <i>In vitro</i> and in mice, the compounds inhibited both mTOR signaling complexes—mTORC1 and mTORC2. The compounds also blocked insulin-stimulated Akt phosphorylation, which can promote cell survival. In wild-type and mTORC2-deficient primary mouse embryonic fibroblasts, PP242 showed more effective inhibition of cellular proliferation than rapamycin, possibly as a result of the PP242 phosphorylation inhibition of the mTORC1 substrate 4EBP1, which was lacking with rapamycin. Next steps could include determining the mechanism by which 4EBP1 phosphorylation is resistant to rapamycin.</p> <p>At least eight companies have compounds targeting mTOR in development stages ranging from preclinical to marketed to treat cancer.</p> <p>SciBX 2(8); doi:10.1038/scibx.2009.311 Published online Feb. 26, 2009</p>	Patent applications covering PP242 filed by University of California, San Francisco; inhibitor licensed to Intellikine Inc.	<p>Feldman, M. <i>et al. PLoS Biol.</i>; published online Feb. 10, 2009; doi:10.1371/journal.pbio.1000038</p> <p>Contact: Kevan M. Shokat, University of California, San Francisco, Calif. e-mail: hokat@cmp.ucsf.edu</p>