This week in therapeutics

Indication	Target/marker/ pathway	Summary	Licensing status	Publication and contact information
Cancer				
Tuberous sclerosis complex (TSC)	Mammalian target of rapamycin complex 1 (mTORC1); tuberous sclerosis complex tumor suppressors 1 and 2 (TSC1 and TSC2); unfolded protein response (UPR)	A study in multiple TSC models suggests that mTORC1 and the UPR could be targeted to treat some types of benign tumors. TSC is a hereditary disorder caused by loss of tumor suppressors TSC1 or TSC2 and is characterized by multiple benign tumors. In murine embryonic fibroblasts, knockout of TSC1 or TSC2 increased mTORC1 activity, UPR and insulin resistance compared with those in wild-type cells. Kidney tumors in TSC2 heterozygous mice displayed higher mTORC1 activity and UPR than in healthy tissue from the same kidney, differences that were eliminated by treatment with the mTORC1 inhibitor rapamycin. In both models, thapsigargin, a compound that blocks the downstream effect of UPR activation, promoted apoptosis compared with that seen in untreated controls. Next steps include testing whether antagonists of mTORC1 or the UPR can reduce TSC or other benign tumors *in vivo*. Multiple companies, including Wyeth and Novartis AG, are developing or marketing rapamycin derivatives as immunosuppressants for use in organ transplants.	Patent application filed; licensed to Syndexa Pharmaceuticals Corp.	Ozcan, U. *et al. Mol. Cell*; published online March 12, 2008; doi:10.1016/j.molcel.2007.12.023 **Contact:** Gökhan S. Hotamisligil, Harvard University, Boston, Mass. e-mail: ghotamis@hsph.harvard.edu