This week in therapeutics

Indication	Target/marker/ pathway	Summary	Licensing status	Publication and contact information
Cancer				
Cancer	Repressor element-1–silencing transcription factor (REST); Skp1-Cul1-F-box protein complex containing the F-box protein β-TRCP ($SCF^{β\text{-}TRCP}$)	Two separate studies in cell culture suggest that targeting the $SCF^{β\text{-}TRCP}$ E3 ubiquitin ligase could modulate levels of REST and help treat some forms of cancer. Depending on cell type, REST is a transcriptional repressor, an oncogene or a tumor suppressor. The Harvard group showed that in human mammary epithelial cells, $SCF^{β\text{-}TRCP}$ overexpression resulted in lower REST levels and oncogenic transformation. The NYU group showed that in HCT116 cell lines, abnormally high REST levels caused by a degradation-resistant REST mutant resulted in multiple mitotic defects and subsequent chromosomal instability. The Harvard group is collaborating with Millennium Pharmaceuticals Inc. to research protein homeostasis and ubiquitin-like post-translational modification pathways that potentially affect multiple cancers. Next steps for the NYU group include identifying the protein kinase that phosphorylates REST and performing a mutagenesis analysis of REST in human brain tumors.	Patent and licensing status undisclosed	Guardavaccaro, D. *et al. Nature*; published online March 20, 2008; doi:10.1038/nature06641 **Contact:** Michele Pagano, New York University School of Medicine, New York, N.Y. e-mail: michele.pagano@nyumc.org Westbrook, T. *et al. Nature*; published online March 20, 2008; doi:10.1038/nature06780 **Contact:** Wade Harper, Harvard Medical School, Boston, Mass. e-mail: wade_harper@hms.harvard.edu